CHAPTER 2

REVIEW OF LITERATURE

2.1  GENERAL

This chapter presents the Literature reviewed on Blood Pressure estimation, cardiac risk prediction and ECG signal analysis. The analytical, experimental work, findings and the conclusions given by various authors are given in this chapter. The conclusions were analysed and the discrepancies in the conclusion were studied. These are summarized and the need for this research is given in the end of the chapter. For this research more than 50 papers have been reviewed. However details of about only 15 papers are presented in this, which are directly related to the proposed research.

2.2  LITERATURE REVIEWED

2.2.1  Augmentation Index Using Peripheral Arterial Tonometry

Eshan Patvardhan et al (2011) in their research on Augmentation Index have conducted a study to evaluate the association of peripheral AIx and cardiovascular risk factors. Similar to what has been found with AIx derived from applanation tonometry, PAT-derived AIx correlates with age, weight, BMI, heart rate, diastolic blood pressure, pulse pressure, and mean arterial pressure. PAT-AIx was also significantly related to age. Previous studies have noted that the increase in AIx with age is not linear. AIx values increased with age up to 65–70 years of age. Beyond that, the AIx values tended to plateau and then decrease shortly after that. It has been observed
that AIx measured by conventional applanation tonometry begins to plateau at the age of 60 years. Patients with >5 CRFs had a significantly higher PAT-AIx as compared with those having only a few CRFs.

It suggests that finger-derived AIx may be comparable to applanation tonometry for measurement of augmentation index and evaluation of cardiovascular risk. Only patients with >5 CRFs (cardiac risk factors) had a significantly higher PAT-AIx as compared with those having only a few CRFs. The usual charge for this testing itself is about $250 per test. Figure 2.1 is the correlation graph they have studied and plotted by analysing cardiac risk factors with AI.

![Correlation between AIx and cardiac risk factors](image)

**Figure 2.1 Comparison of Cardiac risk factors Vs AI**

### 2.2.2 Cardiovascular Risk Assessment

Ali R Khoshdel et al (2010) have conducted a study to evaluate arterial Stiffness and Pulse Wave Reflection for diabetic and non-diabetic kidney transplant recipients. Evidence demonstrates that cardiovascular risk reduces after kidney transplantation, but is still a major cause of death. With increasing inclusion of diabetic patients for kidney transplantation, the evaluation of cardiovascular disease in this population becomes more
important. The authors compared arterial stiffness and pulse wave reflection as well as other cardiovascular risk factors in kidney transplant patients with and without diabetes mellitus.

Augmentation index was measured using SphygmoCor, version 7.1, AtCor Medical. One hundred kidney transplant recipients, including 33 diabetic patients, were evaluated for their renalcardiovascular risk factors, including blood pressure, lipids, glucose control, homocysteine, and arterial stiffness indexes. The tests were repeated after 1 year in 47 individuals there was no significant difference in pulse wave velocity (PWV) between the diabetic and non-diabetic groups, despite a greater augmentation index (AI) in the diabetic group.

The novel finding of this study was the higher adjusted augmentation index in diabetic compared to non-diabetic kidney transplant patients. Kidney transplant patients with DM had comparable PWVs, but significantly greater AIs than their non-DM counterparts. Figure 2.2 is the output they have obtained using Sphygmocor and the Table 2.1 is the data given by the authors which compares the values of AI and PWV.

Figure 2.2 Output obtained from SphygmoCor
Table 2.1 Comparison of the values of AI and PWV

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DM (n = 33)</th>
<th>Non-DM (n = 67)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55.1 ± 2.2</td>
<td>48.8 ± 1.6</td>
<td>.03</td>
</tr>
<tr>
<td>Post transplant time, mo</td>
<td>56.7 ± 12.6</td>
<td>79.9 ± 9.0</td>
<td>.13</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>137.0 ± 3.0</td>
<td>134.4 ± 2.4</td>
<td>.51</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>75.0 ± 1.9</td>
<td>78.8 ± 1.8</td>
<td>.08</td>
</tr>
<tr>
<td>Heart Rate, beats/min</td>
<td>62.9 ± 2.3</td>
<td>68.0 ± 1.7</td>
<td>.47</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.6 ± 0.2</td>
<td>4.9 ± 0.2</td>
<td>.10</td>
</tr>
<tr>
<td>Homocysteine, umol/L</td>
<td>14.9 ± 1.0</td>
<td>16.6 ± 0.8</td>
<td>.20</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>6.2 ± 0.1</td>
<td>5.5 ± 0.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>GFR, ml/min</td>
<td>59.2 ± 3.6</td>
<td>54.0 ± 2.5</td>
<td>.29</td>
</tr>
<tr>
<td>CFPWV, m/sec</td>
<td>10.8 ± 0.6</td>
<td>10.0 ± 0.3</td>
<td>.19†</td>
</tr>
<tr>
<td>CRPWV, m/sec</td>
<td>10.4 ± 0.4</td>
<td>9.6 ± 0.2</td>
<td>.09†</td>
</tr>
<tr>
<td>Adjusted AI</td>
<td>20.5 ± 3.4</td>
<td>15.1 ± 2.2</td>
<td>.03</td>
</tr>
</tbody>
</table>

*DM indicates diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; GFR, glomerular filtration rate; CFPWV, carotid-femoral pulse wave velocity; CRPWV, carotid-radial pulse wave velocity; and AI, augmentation index.
†P values of nonparametric tests for CFPWV and homocysteine were .33 and .19, respectively.

Change in AI is greater than change in PWV

2.2.3 Arterial Blood Pressure Measurement and Pulse Wave Analysis

Alberto P Avolio et al (2010) in their research have conducted topical reviews which assess the techniques of pressure measurement that relate to the use of the cuff sphygmomanometer and to the non-invasive analysis of the peripheral and central arterial pressure waveform. They claim that improved assessment of cardiovascular function in relation to treatment and management of high blood pressure results from future developments in the indirect measurement of arterial blood pressure that involve the conventional cuff sphygmomanometer with the addition of information derived from the peripheral arterial pulse. The CVProfilor device was used to analyze the pulse wave. The authors used the following formula to find out the Augmentation Index (AI) which is used in the proposed work.

\[
AI_x = \frac{(Ps - Pi)}{(Ps - Pd)}
\]

Ps- systolic pressure point
Pi-point of inflection

Pd-diastolic pressure point.

Figure 2.3 shows two different types of pulse waves with points of interest which is used in AI calculation.

![Figure 2.3 Pulse wave with points of interest](image)

The authors have concluded that combination of sphygmomanometer and pulse waveform analysis characterises the cardiovascular function and stratification of cardiovascular risk.

### 2.2.4 Methods of Measurement of Arterial Stiffness

Satoru Sakuragi et al (2009) have conducted research and outlined the methods for the measurement of arterial stiffness, describe the physiological mechanisms that utilises arterial stiffness as an integrative marker of cardiovascular disease and detail the evidence examining the value of arterial stiffness for prediction of adverse cardiovascular events and mortality. The authors presented the following conclusions.
Arterial stiffness can be assessed noninvasively using the following methods:

i. relating change in vessel size (diameter or area) to distending pressure

ii. estimation of pulse wave velocity

iii. Pulse waveform analysis.

The first method uses echo tracking techniques and MRI to measure the vascular distensibility and compliance etc. But it can be done only on superficial arteries. In the second method PWV is calculated using Moens Korteweg Equation given in equation 2.2.

\[(PWV)^2 = \frac{(E*h)}{(2\pi)} \quad (2.2)\]

- \(E\) → slope of stress strain relationship of a given vessel
- \(\rho\) → density of fluid
- \(h/2r\) → wall thickness /diameter

In the third method PWA is performed using applanation tonometry and the formula used is given in equation 2.3.

\[AI \% = \frac{AP}{PP} \quad (2.3)\]

- \(AP\) → Augmented pressure- difference between the first and the second systolic peak
- \(PP\) → normal pulse pressure (difference between the systolic blood pressure and diastolic blood pressure)
The following are the limitations the authors conclude in the study. Method (i) and (ii) have complications to perform and it is very costly to use MRI in the procedure. Thereby they conclude that method (iii) is comparatively better.

2.2.5 Arterial Stiffness and Cardiovascular Outcomes

Sophia Zoungas and Ronald Asmar (2007) conducted research to assess arterial stiffness. The authors used three factors to assess arterial stiffness: pulse wave velocity, augmentation index calculation and systemic arterial compliance.

i. Pulse Wave Velocity (PWV) = \( \frac{D}{\Delta t} \) (m/s) \hspace{1cm} (2.4)

\( D \rightarrow \) distance travelled in metres.

\( \Delta t \rightarrow \) time interval in seconds.

ii. Augmentation Index (AI)\( \% = \frac{\Delta P}{PP} \times 100 \) \hspace{1cm} (2.5)

\( \Delta P \rightarrow \) (difference between shoulder of the wave and peak systolic pressure)

\( PP \rightarrow \) Pulse Pressure.

iii. SAC(systemic arterial compliance) = \( \frac{Ad}{R(Ps - Pd)} \) \hspace{1cm} (2.7)

\( Ad \rightarrow \) area under the diastolic portion of the pulse pressure contour.

\( R \rightarrow \) total peripheral resistance calculated as mean arterial blood pressure/mean blood flow

\( Ps/Pd \rightarrow \) end-systolic /diastolic aortic blood pressure
The authors have concluded that Augmentation index predict all-cause mortality and cardiovascular events in coronary and end stage renal disease patients. And their research conclude that in Corotid artery AIx increases with increase in cardiovascular risk. In Radial artery AIx increases with increase in coronary artery diseases. The authors also stated in their research that Systemic arterial compliance may be useful for studies of patients with known coronary disease.

2.2.6 Cardiovascular Risk Prediction using Photoplethysmography

Dirk Sommermeyer et al. 2002 conducted a research to study the arterial stiffness by using Photoplethysmography and Tensiomed Arteriograph. The objective of their research is to analyse and compare the relationship between the augmentation index derived from peripheral pulse wave measured by Photoplethysmography (PPG) and the two indices measured from an established device from Tensiomed Arteriograph.

Following are the formulae that the authors used in their work. Figure 2.4 presents the methodology used for the risk prediction using peripheral pulse wave.

\[ \text{AIx_amp\%} = \frac{P2 \times 100}{P1} \]  \hspace{2cm} (2.8)

\[ \text{AIx_time\%} = \frac{T1 \times 100}{T1} \]  \hspace{2cm} (2.9)

\[ \text{AIx_height\%} = \frac{\text{body-height} \times 100}{T1} \]  \hspace{2cm} (2.10)
The authors concluded that PPG appears to provide an accurate method to determine the arterial stiffness, which is an important marker for arthrosclerosis and prediction of cardiovascular risk since it is very simple, low cost and can be used for long term monitoring.

2.2.7 Heart Rate Extraction from Photoplethysmogram

Tsu-Hsun et al (2008) have conducted a research to extract heart rate using PPG signal using wavelet analysis. The authors instead of using heart rate variability from ECG signal which is commonly used in clinic in representing physiologic condition, used PPG which is commonly used in home care or sports medicine for monitoring HR. Since it is difficult to get the accurate heat rate when the amplitude of PPG is too low or in the presence of baseline fluctuation due to body movement, the authors used moving average filter and wavelet filter to enhance the PPG waveform for extracting the HR. Figure 2.5 shows the results that the authors have obtained by using moving average filter and wavelet filter.
Figure 2.5 Extraction of HR from PPG, (a) original waveform, (b) by wavelet filter,(c) by moving average filter

The authors have concluded that MRA wavelet transformation and thresholding approach have effectively improved the accuracy of using PPG waveform for HR detection.

2.2.8 Leg Crossing Posture On Pulse Transit Time and Heart rate Variability

Kang-Ming Chang and Keng-Ming Chang (2008) have conducted a research on posture variation based pulse transit time and heart rate variability. The PTT mentioned by the authors is measured from the ECG R-wave to characteristic point on the peripheral pulse by photoplethysmography. It has been reported that PTT has high correlation with heart rate and blood pressure. The purpose of their study was to distinguish between performance of HRV and PTT in detecting cardiovascular changes depending on leg posture. Similar feature extraction definitions of HRV parameters were used for PTT sequence analysis. Their discrimination performances of different postures were compared. The methodology used in their research to detect R peak and pulse peak is given below.
ECG R-WAVE PEAK DETECTION:- The R peak detection is based on Tompkins’s algorithm, with the following modifications. First a Butterworth band pass filter with order 3 and band width 0.1Hz to 50 Hz was applied to the raw ECG signals. Signal was then passed through a derivative filter and a square processor. After then a ten point moving average filter was applied. The threshold estimating the maximum peak in each period was chosen. By adjusting the drift between the position of maximum peak and the corresponding real R wave peak, final R-peak position has been obtained.

DETECTION OF PULSE PEAK AND ESTIMATION OF PTT:- For estimation of pulse peak averaging filter was used in which first a preset window of 0.8 seconds was defined and the location of maximum pulse peak in the window has been found then. Followed by this, a 0.7 second duration window was shifted and the process was repeated.

The entire pulse peak position is denoted as P[n]. The PTT sequence is given as:

$$PTT[n] = P[n] - R[n]$$  

(2.9)

Five min RR interval derived from R[n]-R [n-1] was used to estimate HRV parameter. HRV parameters, such as time, frequency, and the nonlinear Pointcare plot & wavelet packet powers are adopted & were compared to corresponding PTT parameters. The authors have concluded that PTT is the best method for evaluating cardiovascular function than traditional HRV approach.

2.2.9 Continuous Non-invasive BP measurement Using PTT

Parry Fung et al (2004) in their research study on continuous BP measurement using PTT have defined PTT as the time between the ECG R
peak and the corresponding maximum inclination in PPG. In their work ECG signal was decomposed into 512 sample segments and a 5 level stationary wavelet transform was performed. The highest frequency decomposition captured noise, and the lowest frequency bands contain most of the energy of the QRS waveform and a recursive rule based pattern recognition algorithm used in the work identifies the locations of R peak patterns. Upsampling was used to improve the accuracy of the peak location measurement. Detection of maximum slope of the PPG signal was accomplished using wavelet decomposition. 2 levels SWT with db3 wavelet was used to smoothen out and filter out noise in differentiated PPG. The rule based system processes the low frequency wavelet components and detects all maximum slopes of PPG. After R peaks of ECG and maximum slope of PPG were detected, the corresponding pairs are mapped together to compute PTT. In the proposed research work a similar algorithm is used to detect PTT for BP estimation.

### 2.2.10 QRS Detection Using Continuous Wavelet Transform

Ghaffari et al (2007) presented a new viewpoint in ECG detection using continuous wavelet transform (CWT). In order to magnify QRS complex and reduce the effects of other peaks, the concept of dominant rescaled wavelet coefficients (DRWC) was defined. Using this concept, the relations between the time duration of components of a QRS complex and their wavelet transforms were derived analytically. The proposed relations were used to define local search interval at the vicinity of each QRS complex components. Using DRWC concept, the proposed detection algorithm enabled to detect the R peaks even in the presence of long P and T peaks. Then the detected complex was classified based on its morphology. The classification was carried out regarding possible QRS patterns and their wavelet transform. The performance was assessed using standard manually annotated ECG databases. In their work some common problems such as misdetection of long
P and T peaks were solved using local interval definition. The authors have concluded that dominant rescaled wavelet coefficients decrease the noise content of the ECG to a greater extent, pertaining specifically to noisy subjects.

### 2.2.11 Automatic Detection of QRS boundaries

Daskalov and Christov (1999) in their research work have proposed a preprocessing method guaranteeing accurate preservation of the QRS boundaries, even in the existence of strong power-line or electromyogram noise. In this work QRS boundary detection was performed in two stages:

1. Delimitation of the time interval where the search is to be done
2. Boundary detection.

This application of well-established method for 50 Hz elimination in combination with the approximation filter entirely preserved the signal wave shape in the QRS boundary regions and proved very efficient in obtaining high noise immunity. A pre-processing method combining 50 Hz interference subtraction and approximation filtering was proposed, which virtually preserves the QRS boundaries even in the presence of 50 Hz and EMG noise of considerable amplitude. The application of a procedure computing at each sample the angle between adjacent segments of 10 millisecond duration and taking the minimum as the detected point, proved efficient especially in cases of smooth signal transitions on both sides of the QRS complex.

### 2.2.12 ECG Signal Denoising Using Wavelet Subbands

Sharma et al (2010) have proposed a novel denoising method based on evaluation of higher-order statistics at different wavelet bands for an
electrocardiogram (ECG) signal. Higher-order statistics at different wavelet bands provides significant information about the statistical nature of the data in time and frequency. The fourth order cumulant, Kurtosis, and the Energy Contribution Efficiency (ECE) of signal in a Wavelet subband are combined to assess the noise content in the signal. Four denoising factors are proposed in this work. Performance of the denoising factors was evaluated and compared with the soft thresholding method. The filtered signal quality was assessed using Percentage Root Mean Square Difference (PRD), Wavelet Weighted Percentage Root Mean Square Difference (WWPRD) and Wavelet Energy-based Diagnostic Distortion (WEDD) measures. It is observed that the proposed denoising scheme not only filters the signal effectively but also helps retain the diagnostic information.

In this work, four denoising factors are introduced for filtering of ECG signal. Best performance is observed with DFj which is based on HOS and ECE of Wavelet sub band signal. Kurtosis employed in this work, discriminate signal and noise. It is observed that the spikes or sudden change in signal frequency along with noise gives a higher value of Kurtosis. Taking advantage of this property of Kurtosis, DFj is scaled by ECE of MECG signal. The ECE value in higher level Wavelet band coefficients is more than lower ones, most of the energy of ECG signal remains in higher sub bands, hence lower sub bands, cD1, cD2 and cD3, are chosen for thresholding. It is observed that the proposed denoising factor or the threshold not only filters the signal effectively but also help retain the diagnostic information in the signal.

2.2.13 ST-Segment Analysis Using Hidden Markov Model

RV Andreao et al (2004) in their research work have proposed an original markovian approach for online beat detection and segmentation, providing a precise localization of all beat waves, particularly the PQ and ST
segment in Hidden Markov models (HMM) replace the heuristic rules commonly used for detecting the QRS complex and the beat waveforms multi-channel beat detection and segmentation, waveform models and unsupervised patient adaptation. Furthermore, this approach takes advantage of the Mexican Hat wavelet transform during a parameter extraction stage. Since wavelets are well localized both in time and frequency domain they are suitable for transient analysis and its sub band decomposition emphasizes the waves to the detriment of the noise. Finally, ischemia detection is carried out by a rule based system for two-channel ST-segment analysis which handles the information given by the markovian approach. The steps used by the authors is shown in Figure 2.6.

![Figure 2.6 Ischemic detection using Markovian Approach](image)

2.2.14 Morphological Classification of ST segment

Gu-Young Jeong and Kee-Ho Yu (2007) have conducted a research to classify ST segments using reference ST segment sets. Morphological change of ECG is the important diagnostic parameter to find the malfunction of a heart. An abnormal ST segment change especially is very important for finding myocardial ischemia. Long-term ECG recording is needed because an ST change is transient. Accordingly, physicians try to find the transient change of the ST segment. The aim of this study was to classify ST according to its shape using a polynomial approximation method and the reference STs
set. The developed algorithm consists of feature point detection, ST level detection and ST shape classification.

The first step of feature point detection was the detection of QRS complex, and this is accomplished using the morphological characteristics of QRS complex such as the steep slope and high amplitude. The other feature points are also detected using their morphological characteristics. An algorithm detects the ST level change, and then classifies the ST shape using the polynomial approximation. The algorithm finds the least squares curve for the data between S wave and T wave in ECG. This curve is used for the classification of the ST shapes. ST type is classified by comparing the slopes between the reference ST type and the least square curve. An algorithm was then applied to a standard database to evaluate the performance such as ST level change and shape.

2.2.15 ST Segment Change Detection using wavelets

Nebojsa Milosavljevic and Aleksandar Petrovic (2006) have conducted a research to detect various abnormal ST segments. This research aims to contribute to the automatic interpretation of long sequences of electrocardiograms (ECG) typical for Holter monitoring. They developed a method that uses wavelets for extracting ECG patterns that are characteristic for myocardial ischemia. The intention to detect the beats in the simplest possible manner and generate a quantitative estimate of myocardial ischemia likelihood which would suit needs of cardiologists. Bi orthogonal wavelets were applied in order to define ST segment properties at different scales. The new method was tested using the data from the European ST-T change database. Results show that this method is effective for distinguishing normal from ischemic ECG. The element that makes the distinction is the correlation of number of ST deviations with the time of consecutive appearances.
2.3 SUMMARY OF LITERATURE REVIEW

Eshan Patvardhan et al (2011) had used Peripheral Arterial Tonometry (PAT-AIx) to measure the augmentation index. The usual charge for this testing itself is about $250 per test. Ali Khoshdel et al (2010) used SphygmoCor, version 7.1, for the measurement of augmentation index. Satoru Sakuragi et al (2007) have stated that AI measurement is comparatively simple than any other method for risk prediction. Sophia zoungas et al (2007) has stated the reason for using PPG to determine AI. Alberto P Avolio et al (2010) had used the formula $\text{AIx} = \frac{(P_s - P_i)}{(P_s - P_d)}$ for finding augmentation index, which has been used in the proposed algorithm. Since it is economical to calculate AI using PPG itself which is effective too, the proposed work uses this AI based on PPG technique.

Tsu-Hsun Fu Shing et al (2008) used moving average filter and wavelet filter to enhance the PPG waveform for extracting the heart rate. In the proposed research work both moving average and wavelet filters are used for ECG and PPG preprocessing. Kang-Ming Chang et al (2008) measured PTT from the ECG R-wave to characteristic point on the peripheral pulse by photoplethysmography. It has been reported that PTT has high correlation with heart rate and blood pressure. In the proposed work this method has been adopted since the aim of this work is to extract as many cardiac parameters as possible using ECG and PPG signals.

Ghaffari et al (2007) used continuous wavelet transform (CWT) in ECG detection. L.N. Sharma et al(2010) propose a novel denoising method based on wavelet bands for an ECG signal. Andreao et al (2004) propose an original markovian approach for online beat detection and segmentation, providing a precise localization of all beat waves and particularly of the PQ and ST segment. In the literature it was found that wavelet based ECG
analysis is effective in extraction of individual segments of ECG. Hence for this proposed work wavelet technique is chosen.

The proposed research work aims to use the information from the recorded PPG and ECG signals to calculate Blood pressure, to monitor cardiac risk if any, and analyse the obtained signals using various algorithms and thereby improve the health care in hospitals. In the literature survey it was found that

1. Many methods are available to estimate blood pressure using PTT. It has been decided to adopt the PTT based on R peak of ECG and pulse peak of PPG technique.

2. The aortic augmentation index (AI) and aortic pulse wave velocity (PWV) are known to be the indicators of arterial stiffness. However from literature it is found that AI is significantly related to age, systolic aortic pressure, heart rate, left ventricular ejection time and height whereas aortic PWV is having association only with age and systolic aortic pressure. And because of another constraint that this research work aims at estimation of parameters with the use of single ECG and PPG sensor, AI is chosen to predict arterial stiffness, since measurement of pulse wave velocity requires two pressure sensors for simultaneous data acquisition.

3. In the morphological study of ECG and PPG signals, the use of DWT had proved to be good by giving promising results. Moreover baseline drift removal and denoising in real time signals are also found to be better performed by wavelets. Hence the wavelet technique has been adopted in the thesis.