Chapter 2

Literature Survey

2.1 Historical review.

Billman in 2011 has accounted historical overview of HRV. A ‘Physician’s Pulse watch’ was developed in 1707 by Greek physicians and scientists. This pulse watch accurately assessed changes in the pulse rate. [81] and [82] Rev. Stephen Hales was the first to note that pulse varied with respiration in 1733. He also stated that beat to beat variation related to variation of physical activity. Carl Ludwig was the first to record Respiratory Sinus Arrhythmia in 1847. Einthoven performed measurement of the ECG in 1895. After the advancement of digital signal processing techniques in the 1960s, investigation of HRV and its relationship to health and disease has witnessed explosion. Association of reduced HRV with a poorer prognosis for a wide range of clinical conditions and conversely, robust periodic changes in R–R interval are often a hallmark of health was stated by Thayler et al., 2010.[82] Time domain analysis was performed in 1960 followed by frequency domain analysis in 1970. Nonlinear HRV dynamics was noted in 1990. Ambulatory ECG with Holter monitoring and analysis was first performed in 1965. [55] Ambulatory ECG is a significant step in quick diagnosis. Holter monitoring is useful in statistical analysis of long term ECG but it is used in diagnosis only after an cardiac episode has occurred.

2.2 Literature survey leading to the problem definition.

Kalpa Sharma has stated about the high prevalence of cardiac diseases in the Indian subcontinent. [1] R. Srinivasan states that diagnostic modalities and medical expertise in India is highly competitive and the success rate of cardiac surgeries is about 98% and the morbidity and mortality rate due to surgery is equal to that of developed countries of Europe and America. [2] Due to very large population suffering from cardiac disease, access to medical advice is difficult. Prevalence of abysmally low ratio of population to cardiologist the need for a guideline is significantly justified. [77]

Martino Alessandrin et. al. in 2008 states the noisy nature of the echocardiographic image is responsible for intra operator variation in interpretation thereby justifying the need for the guideline for echocardiogram. [32]

K. D. Desai in 1996 in his doctoral thesis stated the significance of HRV study. The reason of high number of cardiac deaths is due to lack of routine diagnostic checks that
reveal the cardiac health status by a very cost effective noninvasive tool i.e. the HRV analysis. Study of HRV analysis, strength and significance of the same is studied. [3] Instantaneous HR against time axis has become a popular noninvasive tool for assessing activities of the autonomic nervous system. Hales (1733) demonstrated existence of correlation in arterial blood pressure, respiratory cycle and inter beat time interval. HRV analysis reliably reflects many physiological factors modulating the normal rhythm of the heart. It is a significant tool in observing the interplay between the sympathetic and parasympathetic nervous systems. Computer based analytical tools for in depth study of data over long intervals (as long as 24 hrs.) can be very useful in diagnostics. Therefore, the HRV signal parameters, extracted and analyzed using computers, are highly useful in diagnostics.

Joshi et al. in 2011 accounted for the problem definition from the study of different diagnostic modalities of cardiac diseases. [4] Need of safe and noninvasive diagnostic tool is emphasized. It can be concluded that all the modalities give the status of functioning of heart at the instance of examination. The slow deterioration of cardiac performance is not diagnosed in any of the diagnostic modules. Acharya et al. in 1996 stated the superiority of HRV analysis is the strength of early diagnosis at a preclinical stage. [3], [5] [6] and [9]

Acharya et al. in 1996 discusses the various applications of HRV and different linear, frequency domain, wavelet domain, nonlinear techniques used for the analysis of the HRV. Also the paper shows that the structure generating the signal is not only simply linear, but also involves nonlinear contributions. Heart rate (HR) is a nonstationary signal. Study conducted on response of autonomous nervous system by HRV analysis for subjects at before and in different levels of sedation during cardiac surgery and after cardiac surgery. European guideline and physical interpretation of HRV analysis indices and validates them. It also states the clinical use of the HRV indices. Linear and Non Linear methods of HRV analysis are compared. [6] [7] and [10] Voss et.al. in 2007 states dilated cardiomyopathy, the enlarged left ventricle is a cardiac complication with grim prognosis. The risk stratification of the same by different HRV analysis tools is used and detrended fluctuation analysis is concluded to be more specific. [56]

Hameed et al. in 2005 discuss the risk stratification of Left Ventricular hypertrophy (LVH) by Romhilt’s test. [33] Bauml in 2010 states LVH as a significant but overlooked risk factor in cardiovascular deaths. [61] Joshi et al. in 2015 evaluates the early diagnosis of LVH. [77]

Smith et al. in 1985 makes a comparative analysis between the electrocardiography and echocardiography to detect intra-operative myocardial ischemia and states that wall
motion abnormalities are clearly detected by echocardiography and ST segment change is not a reliable source. [36]

2.3 Versatility and applications of HRV

Nagpal et al. in 2013 has stated that HRV in post-traumatic stress disorder has marked change in the indices like shift in neuro humoral balance and increased sympathetic power. [13] Kumar et.al. in 2013 states that HRV is reduced in alcoholics than non-alcoholics of the same age and ethnicity.[16] Monzur et al. in 2013 states that HRV of age and ethnicity matched female population with sedentary class as control group and class of females performing deep relaxation techniques is much less. [17] HRV indices are also improved in case of subjects who perform meditation by visual concentration [15], vinyasa yoga [20], meditation with breath suspension [21] Tiina et.al. in 2014 states that HRV indices of subjects with stress at workplace and obese subjects have poorer HRV than their counterpart.[24] Pantelić et al. in 2013 states that the subjects with myocardial infarction who perform light exercise have lower HR, better oxygen uptake and lower systolic pressure.[18] Jagadamba et.al, in 2014 evaluates the .concludes that HRV is an effective non-invasive tool in assessing the interplay between sympathetic and vagal hormones in autonomous nervous system during perioperative period.[19] Huang et al. in 2014 states that HRV is observed for subjects who were extubated from an artificial ventilator after recovery from severe cardio-respiratory failure. He states that subjects that showed increased power in VLF band and total power showed better recovery [14]

2.4 Sympathetic and parasympathetic activity of Autonomous Nervous System (ANS)

Chiu and Kao in 2001 discuss the different factors that activate SA node are mathematically stated. The complex interplay between sympathetic parasympathetic hormonal effects on the SA node activation is described. The power density of the two frequency bands and their effects on SA node activity are described. [70] Desai et.al. in 2011 states that power spectrum in sympathetic and parasympathetic power is an indicator of health.[11] Acharya et al. in 2004 states that HRV is a sensitive tool to understand the dynamics of sympathetic and vagal interplay and has observed that HRV decreases with age. [12] Tulppo et al. in 1998e states that the Poincare plot index SD1n shows variation in distribution after exercise in young subjects. Whereas, not much variation is observed in aged subjects. He further states that impaired vagal modulation is an indicator of poor health.[80]

Kana in 2010 proposes a mathematical model control of autonomous nervous system on cardiovascular performance. [67] Vinogradova et al. in 2001discusses effect of β adrenergis stimulation on pacemaker activity. [66]
Borne et al. in 1997 and Rizas et.al. in 2014 state the effect of sympathetic activity on repolarization dynamics. Increase in repolarization rate associated with increase in sympathetic activity is a single predictor of death due to myocardial infarction. [58] and [47] Borne discusses absence of variability in sympathetic frequency band during sever heart failure. Rudchenko e. al. in 2014 observes that synaptic conduction of parasympathetic and sympathetic neural signals differ in diabetic condition. [43]

Michaels et al. in 1984 and Antelmi et.al. in 2010 demonstrated the effect of acetylcholine on pacemaker activity, the blood flow velocity in left ventricle and hence performance of heart.[65] and [42] Vinogradova et al. in 2001 and Bers et al. in 2000 discuss the effect of calcium on ventricular contraction [66] and [68]. Dell'Orto et.al. in 1986 discusses relationship between power spectral density of heart rate and arterial blood pressure as marker sympato vagal interaction is described in normal human and dog. [8]

2.5 Anatomy and physiology of human heart.

The basics of human anatomy and physiology of heart and different body functions are studied. Chapter -10 from the ‘Text book of Medical Physiology’ by Arthur C. Guyton. [37] The cellular activities resulting different body functions and the difference between the normal and diabetic cellular functions, anatomy, physiology of heart and SA node functioning is studied from the same book.

2.6 Complications due to diabetes and hypertension.

The diabetic metabolism, insulin resistance and it’s effects also are studied from Chapter -12 from ‘Text book of Medical Physiology’ by Arthur C. Guyton. [38] Dokken et al. in 2008 discusses pathophysiology of cardiovascular diseases in diabetic and hypertensive pathology.[40] Lindmark et.al. in 2005 discusses the link between shift in neuro-humoral axis and insulin resistance and visceral adiposity. [15] Boulton et al. in 2005, Dweck et al. in 2009 and K.D.Desai in 1996 discuss the complications of diabetes leading to diabetic autonomous neuropathy. [51], [44] and [3]. Dweck et al. in 2009 stated an algorithm for diagnosis based on the symptoms is stated for the detection of silent myocardial ischemia [44]

Limitation of measurement and quantification of cardiovascular autonomic neuropathy (CAN) in the current diagnostic practice and the complications of CAN resulting into morbidity and mortality. Tang et al. in 2014 states the higher resting HR value in diabetic subjects is correlated with probability of cardiovascular autonomic neuropathy. [53] Also there are several papers that describe the complications of diabetes that begin
with diabetic autonomous neuropathy (DAN) and gradually precipitate to silent myocardial ischemia and infarction and death due to cardiac failure. Since episode of myocardial ischemia is associated with chest pain and diabetic subject cannot perceive the pain because of diabetic autonomous neuropathy, the episode is called silent myocardial ischemia. [48]

Infusino et al. in 2010 discusses the association of low glucose level with the low HRV in Diabetes mellitus is demonstrated in paper from European department of cardiology and pharmacology. [45] Seyd et al. in 2008 discusses the variations in time and frequency domain indices of HRV analysis in diabetic, diabetic condition. [7] Joshi et al. in 2015 discusses correlation between HRV and cardiac performance [77]. Vinick et al. in 2013 discusses development of DAN and cardiovascular diseases and myocardial ischemia after prolonged diabetes. [52] and [54] Stoikov et al. in 2000 and Whackers et al. in 2005 discuss Heart rate variability and left ventricular function in diabetics after myocardial infarction is discussed. [46] and [48] Bigger et al. in 1993 states that power spectral analysis of short term R-R interval sample can predict mortality with equal accuracy in comparison with long term R-R intervals.[49]

Emily b. Schroeder in 2005 discussed the increased rate of atherosclerosis and lipid cells in diabetic patients and suggested risk stratification in hypertensives. [25] and [39]

2.7 Preventive measures for Cardiac complications in diabetic prevalence.

Rock et al. in 2013 discusses the preventive techniques in the diabetic condition. He states that with glycemic control and regular exercise controls the LDL and glycemic control.[50] Similar observations are recorded by different researchers.[84], [85] ,[86] and [87]. Bacon et al. in 2004 states that in prevailing hypertension, exercise and diet control reduce the systolic and diastolic pressures and reduce the arterial stiffness and left ventricular mass and wall thickness. Improvement in the peripheral vascular health is also observed. [51] Boulton et al. in 2004 states that weight control program in diabetics is observed to reduce the glucose level in the blood and the LDL levels. Improvement in prognosis by reducing the hyperglycaemia and atherosclerotic risk. [50] and [52].

2.8 Cardiac performance study.

Tumesnil et al. in 1979 discusses the effects of changes in the heart wall thickness and wall motion abnormalities on the performance of heart assessed by echocardiogram. [73] The mathematical model of left ventricular contraction and relaxation and the wall motion velocities are established and checked by observing the echocardiogram images and computing the change in systole and diastole thickness of wall and measuring the
time taken to relax and contract. Schweizer et.al. in 1984 discusses effect of heart rate changes on left ventricular blood volume and ejection fraction by echocardiography. [35] Paralikar proposes mathematical model of left ventricle helps in understanding the functioning of the left ventricle. He states the mathematical relationship between left ventricular blood volume and left ventricular elastance. [65] The left ventricular functioning is described in the form of a state diagram that clarifies the functioning details.

Armstrong in 2000 discusses the causes and prognosis of left ventricular diastolic dysfunction (LVDD). [70] and [34] Piskorski and Guzic in 2007 describe the physiological changes that are manifested as asymmetry in Poincare plot. [71] Brennan et al. in 2002 states the mathematical model that simulates the Poincare plot artificially. Theoretical link between frequency domain spectral analysis techniques and time domain Poincare plot analysis is discussed. [64] Joshi et.al in 2014 proposes technique to distinguish sympathetic and power spectral densities from RR interval plot and diagnose LVDD from of parasympathetic power. [63]

Ribeiro et al. in 2010 discusses effect on orthostatic stress and respiratory sinus arrhythmia in patients with Chagas' disease with preserved left ventricular global systolic function. [58].

2.9 Extraction of HRV from ECG.

Clifford et.al. in 2006 discusses tools and methods in ECG analysis.[27] Automatic QRS detection, denoising the signal from muscle artefacts, supply frequency interference, integrating the moving window techniques etc are described. Pavlatos et al. in 2005 describes the algorithm and procedure of extraction of RR interval samples from the ECG signals acquired making the system deployable. [26] LABVIEW software interface of data acquisition is studied from reference papers of National instruments tutorial. [29]

Open source simulator known as ‘Kubios HRV simulator’ developed by Physionet is studied and results are simulated from the same.[28]

Niskanen et al. in 2002 describes the HRV analysis methods used software interface with ECG data acquisition protocol is studied. [30]

2.10 Statistical analysis.

Miller and Freund explain the statistical techniques and applications of statistics in the research studies. Lane discusses Significance of Pearson’s coefficient of correlation and critical values. [75], [76]

Kleinbaum in 2013 explains about regression analysis techniques. [79] Research
methodology is studied from []

2.11 Concluding remarks from the literature survey.

Early diagnosis of cardiac performance in diabetes is very essential. Validation of HRV indices is required for the same. Validation of HRV indices is possible by establishing correlation between HRV analysis indices and performance indicator i.e. the LVEF. In diabetic conditions, the slow deterioration of central and peripheral nervous system is observable only by HRV analysis. This analysis can further be useful to assess the risk stratification due to prevailing diabetic condition at preclinical stage and can control the morbidity and mortality rate.