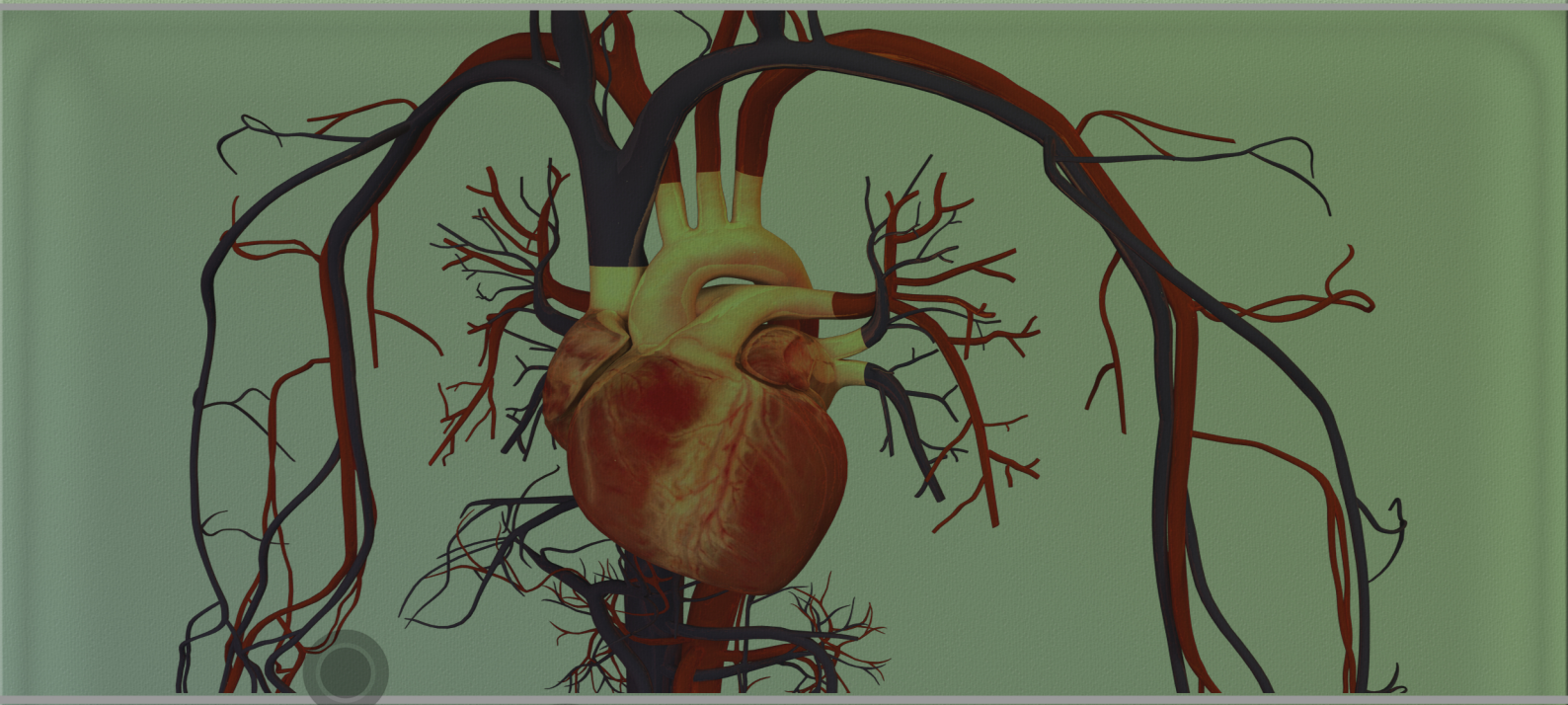
April, 2015 • Volume 2, Issue 1

Openventio PUBLISHERS

ISSN 2377-164X

HEART RESEARCH

Open Journal



www.openventio.org

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X

Open Journal

TABLE OF CONTENTS

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

Research

*Corresponding author:
Goutam Saha, PhD
Professor
Department of Electronics and Electrical Communication, Engineering, Indian Institute of Technology, Kharagpur 721302, India
E-mail: gsaha@ece.iitkgp.ernet.in

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2105

Article History:
Received: February 27th, 2015
Accepted: March 9th, 2015
Published: March 10th, 2015

Citation:
Kumar AK, Saha G. Interpretation of heart sound signal through automated artifact-free segmentation. *Heart Res Open J*. 2015; 2(1): 25-34.

Interpretation of Heart Sound Signal through Automated Artifact-Free Segmentation

A. Kishore Kumar and Goutam Saha*

Department of Electronics and Electrical Communication Engineering, Indian Institute of Technology, Kharagpur 721302, India

ABSTRACT

Purpose: Digital recording of heart sounds commonly known as Phonocardiogram (PCG) signal, is a convenient primary diagnostic tool for analyzing condition of heart. Phonocardiogram aids physicians to visualize the acoustic energies that results from mechanical aspect of cardiac activity. PCG signal cycle segmentation is an essential processing step towards heart sound signal analysis. Sound artifacts due to inappropriate placement of stethoscope, body movement, cough etc. makes segmentation difficult. Artifact-free segmented heart sound cycles are convenient for physicians to interpret and it is also useful for computerized automated classification of abnormality.
Methods: We have developed a framework which selects good quality heart sound subsequences which are artifact-free and reused the features involved in this processing in segmentation. In this work, we have used information contained in frequency subbands by decomposing the signal using Discrete Wavelet Packet Transform (DWPT). The algorithm identifies the parts of the signal where artifacts are prominent and it also detects major events in heart sound cycles.
Results: The algorithm shows good results when tested on normal and five commonly occurring pathological heart sound signals. An average accuracy of 93.71% is registered for artifact-free subsequence selection process. The cycle segmentation algorithm gives an accuracy of 98.36%, 98.18% and 93.97% respectively for three databases used in the experiment.
Conclusions: The work provides a solution for artifact-free segmentation of heart sound cycles to assist interpretation of heart sound by physicians in objective analysis through recording in a computer. It is also useful for development of an automated decision support system on heart sound abnormality.

MAIN KEY FINDINGS

• Artifact free subsequence detection is preferable over attempt to reduce the effect of artifacts due to overlap of information content.
• DWPT is useful for detection of artifact contaminated subsequences due to its ability to provide for more detailed information of higher frequency components.
• DWPT features of subsequence detection can be reused for automatic segmentation of heart sound.
• The artifact-free segmented heart sound cycle detection system can work in real-time.

KEYWORDS: Heart Sounds; PCG Signal; Discrete Wavelet Packet Transform; Segmentation; Artifact removal; Artifact-free subsequence.

ABBREVIATIONS: PCG: Phoncardiogram; HS: Heart Sound; DWT: Discrete Wavelet Transform; DWPT: Discrete Wavelet Packet Transform; ASS: Artifact-free Subsequence Selection;

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

LPF: Lowpass filter, DB: Database; FAR: False Acceptance Ratio; FRR: False Rejection Ratio.

INTRODUCTION

Stethoscope sound is used as primary tool for detecting murmurs in heart signals. This is an audio clue and somewhat subjective, as interpretation depends on the training and skills of the physician. There is a possibility of mishearing important indications, while listening to the heart sounds by using a stethoscope.[1] It has been reported that there is a constant decline in competency on cardiac auscultation and this lack of ability to either hear or interpret an abnormality, starts in medical school.[2] Phonocardiogram based approach can be useful here in providing a visual clue in addition to audio clue. Here an electronic stethoscope is used to pick up heart sounds and with proper signal conditioning, the digitized version of heart sound is collected in the computer. The difficulty with this machine based approach is the presence of artifact in the data collection process when a stethoscope is placed on the chest. A human listener has the capacity of appreciating heart sound part by separating it from the artifact and then focusing on a heart sound cycle to interpret the murmurs based on its location, say systole, diastole or type say crescendo, decrescendo etc. But for a computer based visual representation, there is a need to develop efficient algorithm to separate artifact-free subsequences of heart sound and also extract respective segmented heart sound cycles for further analysis and interpretation. There is an additional requirement to perform algorithmic processing in real-time, so that it is useful as a primary diagnostic tool.

Artifacts can be defined as any undesired signal variation due to any source other than the desired signal source. These artifacts include instrument noise, noise from body sounds, noise due to subject motion and movement of stethoscope diaphragms. Artifacts occur randomly in time and usually have high amplitude and last for a small duration of time.[3] For real-time point of care diagnosis, it is often found that some parts of PCG signal are contaminated by different kinds of artifacts, that occur during signal acquisition.[4,5] In some part, artifact effect is severe while in others it affects mildly. Artifact corrupted PCG signal gives erroneous results in different applications. There are two approaches to deal with this problem. One is to remove artifacts while keeping the signal as a whole and the other is to discard the segment affected by the artifacts. Adaptive filtering, Independent Component Analysis (ICA), Canonical Correlation Analysis (CCA), Morphological Component Analysis (MCA) and Wavelet ICA are some of the techniques reported,[6] in the context of removal of artifacts from physiological signals. These techniques suffer from requirement of additional sensors and reference signal, adaptability and usability for on-line operation. Also, in this approach, removal of artifacts also results in loss of information because of frequency overlap between PCG signal and artifact as shown in Figure 1, and that leads to improper diagnosis.

Since PCG signal recording is usually for larger duration than 4-5 cycles required for its interpretation,[7] an alternate framework can be proposed. In this, a signal quality index can be found out to obtain a subsequence with better signal quality with respect to the rest of the cycles. In this regard, the work of Li T, et al.[8] has proposed an optimum heart sound selection scheme based on cycle frequency spectral density. In this approach, the quality of the heart sound signal depends on the periodicity of heart signal. In the PCG signal quality is analysed for automatic biometric application.[5] They have proposed a quality index measure based on cepstral distance between homogeneous cardiac sound (S1 and S2 sounds). However, this scheme requires a pre-processing step, i.e. segmentation of the heart sound signals, which is often inaccurate in presence of artifacts.

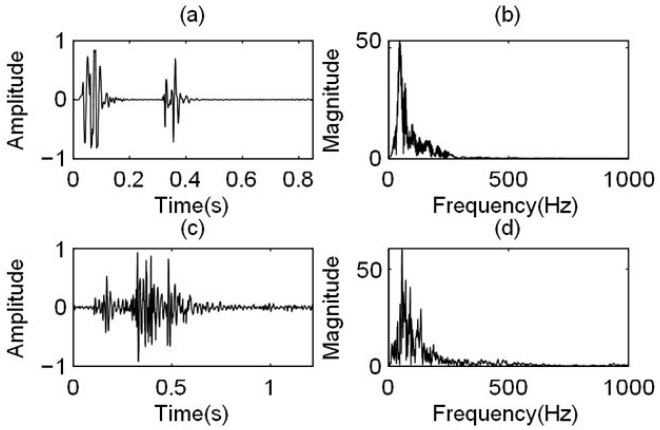


Figure 1: Normal heart sound cycle in time domain (a) and its frequency spectrum (b), Artifact in time domain (c) and its frequency spectrum (d)

In this paper, we investigate the use of time-frequency information along with quasi-periodic property of hearts sound signal to discard artifact-affected subsequences. In biomedical signal processing, wavelet transform has been found to be one of the preferred transforms for analyzing transient and non-stationary signals, such as PCG signal as wavelets provide a reasonable resolution in both the time and frequency domain.[9] To get time-frequency information we used Discrete Wavelet Packet Transform (DWPT) in this work instead of Discrete Wavelet Transform (DWT) as it is better for appreciating information contained in high-frequency subbands in different time windows which helps in artifact detection.

Quasi-periodicity of the heart sound signal can be used as a quality measure for selecting a subsequence from a continuous heart sound signal.[10] When a person is at rest, heart rate does not vary much and it lies in the range of 40 to 150 beats/min. This gives a heart cycle duration in the range of 0.4 seconds to 1.5 seconds.[11] Autocorrelation of the envelope of the heart sound energy signal can give an idea of cycle duration of PCG signal. The index of the maximum value of autocorrelation corresponds to the cycle duration. To illustrate this, we

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

have recorded PCG signal of a subject that has clean and artifact contaminated segments. Figure 2 illustrates the autocorrelation function of envelope of energy signal of clean and artifact contaminated PCG signal. The vertical dotted lines represent the periodicity of the heart sound signal. In case of artifact, the periodicity is not visible as in the previous case, though the signal has been taken from the same subject. We use this quasi periodicity property together with DWPT for automatic subsequence detection which is explained later.

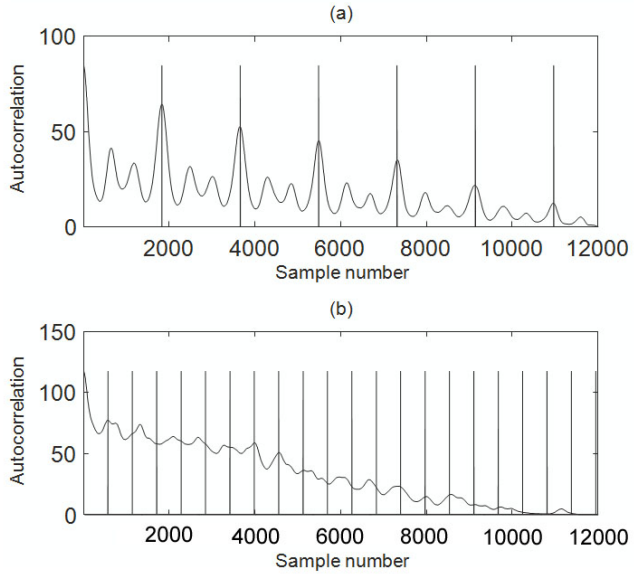


Figure 2: Autocorrelation function of signal energy envelope of (a) Clean PCG signal, (b) Artifact added PCG signal.

The artifact-free subsequences can further be segmented to cycles for understanding the morphological features of heart by listening to and visualizing the PCG cycles individually. Alternatively, it can be fed into automated system, which can classify the signal between normal and diseased cases. PCG signal segmentation is considered as a very essential operation for detection and partitioning individual components of a the cardiac cycle.

A normal PCG signal consists of S1 sound followed by systole period and S2 sound followed by diastole period to complete a full cycle of PCG signal. Some time, murmurs may appear at different instances of systolic or diastolic period at every cycle. Murmurs are extra sounds, primarily due to valvular disorders related to stenosis and insufficiency. Over the years, a number of heart sound segmentation algorithms have been proposed. Wavelet transform has been used to determine the peak positions related to primary heart sounds using approximation and detailed coefficients of decomposed signal.[12] To distinguish murmurs from normal heart sounds, work by Hedayioglu F, et al.[13] has used matching pursuit decomposition analysis based on wavelet transform. Ari S, et al.[14] authors have used a simple and robust energy based feature to locate S1 and S2 peaks due to primary heart sounds. All of these methods do not consider presence of artifacts in PCG. The presence of artifact, even in a single cycle, may reduce the performance of the automatic diagnostic system because; the machine may interpret this extra sound as characteristic murmur of heart.

This work presents a method of selecting artifact-free subsequence of heart sound and reuses features of this subsequence detection to perform segmentation that can aid real time analysis. The segmented visual of heart sound cycle can be analysed by physician manually against such cycles of normal or diseased cases to reach a conclusion. Alternatively, these can be subjected to a machine learning paradigm to arrive at computer based automated interpretation. Such segmented heart sounds can also be played through a speaker and stored for future reference or comparison. The said scheme has been depicted in Figure 3.

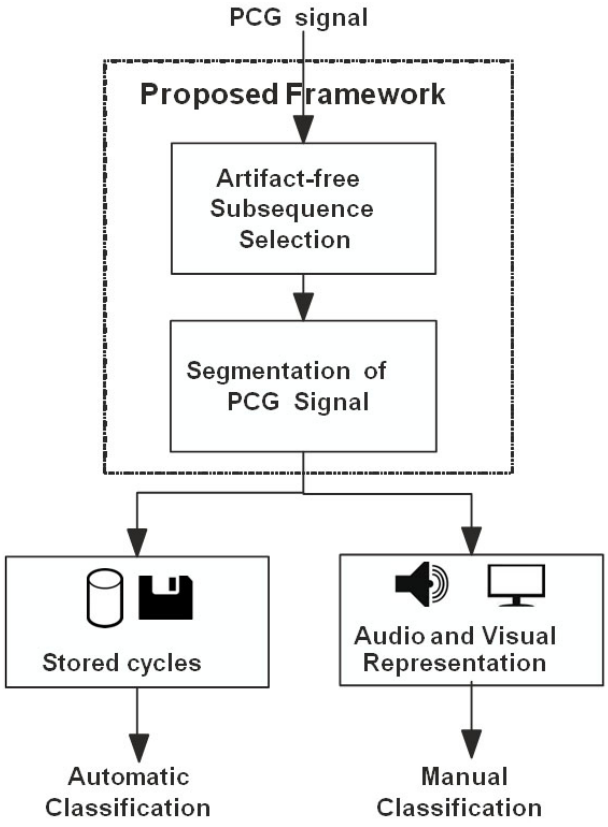


Figure 3: Block diagram of system flow for PCG signal analysis.

MATERIALS AND METHODS

Discrete Wavelet Packet Transform

Multi-resolution analysis can be performed by wavelet transform, which is narrow in window size for high frequencies and wide for low frequencies. It provides useful time-frequency information for its adaptive time and frequency resolution.[15]

DWPT is preferable over DWT as it further decomposes high-frequency subbands[16] for which we get detailed information about the artifact, both in time and frequency.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

DWPT is an extension of DWT whereby all nodes (subbands) in the tree structure are allowed to split further at each level of decomposition. In DWT, only approximation coefficients are decomposed at each level of decomposition, however, in DWPT both the approximation and detail coefficients are decomposed into approximation and detailed components. The DWPT of signal x(t) is defined as follows:[15]

$$x_p^{n,s} = \int_R x(t)\psi_n(2^{-s}t - p)dt, \qquad 0 \le n \le 2^L\text{-}1 \qquad (1)$$

where n is subband number,s is the number of decomposition level, or scale parameter, p is the translation parameter, $\psi_n(t)$ is the mother wavelet, and L is the maximum decomposition level. After the decomposition of signal x(t) by DWPT, 2^L subbands are produced at L^{th} level. The wavelet packet coefficients at different scales and positions of a signal are calculated efficiently as follows:

$$WP_{f,p}^{s} = \sum_k h(p-2k)WP_{2f,p}^{s-1} + \sum_k g(p-2k)WP_{2f+1,p}^{s-1} \qquad (2)$$

h(n) and g(n) are low-pass and high-pass filters respectively, such that $g(k) = (-1)^k h(1-k)$. Two levels of the wavelet packet decomposition with the high-pass and low-pass filters were illustrated in Figure 4. This structure can be repeated further to obtain subsequent approximation and detail coefficients till a proper level is reached which is suitable for characterizing PCG signal and artifacts separately.

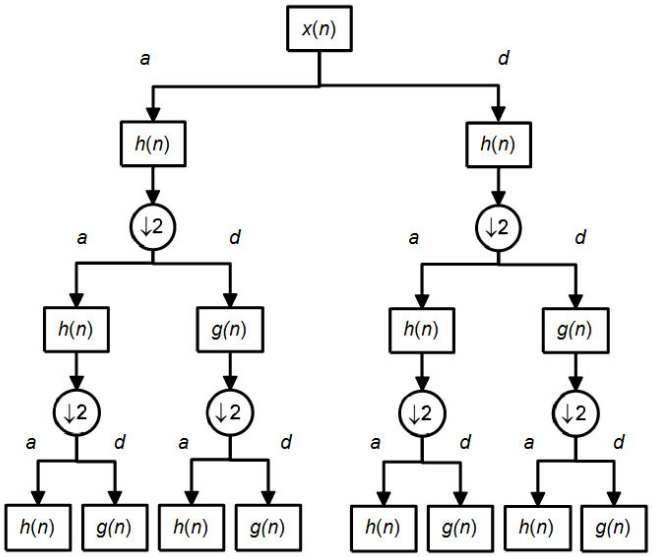


Figure 4: Two level of the discrete wavelet packet decomposition.

Database Preparation

We conducted experiments on three types of databases. For simulation experiments, artifacts are added manually on heart sound signals at random places. These artifacts are recorded separately and are due to body movement, stethoscope movement and due to physiological signals like coughing, deep and heavy breathing etc and are randomly distributed in time. Next, we describe the databases.

1. Database I - Clean heart sound signals taken from five healthy male subjects in two sessions: morning and evening. The age group is 25-33 years. Total 10 signals are recorded, two from each subject. Artifacts which were recorded separately are manually added to this database. Three types of artifacts are added to prepare the database that has total 30 contaminated signals.

2. Database II - Clean but pathological heart sound signals are taken from different medical centres, mostly from Maulana Azad Medical Institute, Delhi, India. These are commonly occurring pathological heart sound signals like ejection click, early systolic murmur, late systolic murmur, opening snap and pan systolic murmur. This database is made from 10 signals, two signals taken from each type of pathological signal. Here too, three types of artifacts are added separately to prepare the database.

3. Database III - The difference in this database and database I is that, in this database artifact are not added manually, instead they are recorded along with the PCG signal by asking the subject to move, cough, deep breathe or by moving stethoscope diaphragm. In this case too, we have taken 10 recordings, two from each subject which are artifact-infected.

Overall, we have 30 signals in each database I and II, and 10 signals in database III. One typical signal from each database is shown in figure 5. Artifacts parts are highlighted by circles. All signals were saved separately in *.wav file in 16 bit, PCM, Mono audio format at sampling frequency of 8 kHz.

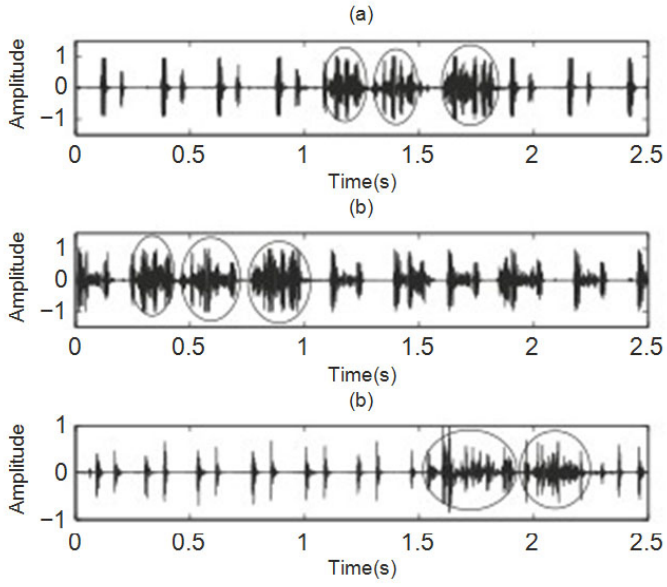


Figure 5: (a) and (b) are normal and diseased PCG signals from database I and II, (c) is the normal signal with artifacts from database III.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

Development Framework

The objective of this study is to select artifact-free subsequence from the original PCG signal and then perform segmentation. PCG signal consists of S1 sound followed by systole period and S2 sound followed by diastole period, and that complete one entire cycle. We are using this property to evaluate PCG segment quality. The proposed algorithm is based on discrete wavelet packet transform. The algorithm is described in block diagram shown in figure 6 and details of each block are presented next.

Preprocessing

Preprocessing includes low-pass filtering, resampling, amplitude normalization. The frequency band of primary heart sounds, including different types of murmurs is below 1000 Hz, hence, 10th order low-pass Butterworth filter of cut-off frequency of 1000 Hz[16] is applied to heart sound signal. After filtering, the signal is down sampled from 8 kHz to 2 kHz. Amplitude normalization is done with the signal to minimize the variation in the amplitude due to variation in gain factor due to recording instrument or body composition of the subject.

Wavelet packet coefficient

The PCG signals are decomposed using DWPT up to 5th level. The mother wavelet used here is Daubechies db10.[16,17]

At 5th level, we get 32 subbands, each subband frequency resolution is 31.25 Hz, i.e., $0.5f_s/2^L$, where f_s is the sampling frequency (2kHz) and L is the maximum number of levels for which DWPT decomposition was done. The subbands are arranged in order of frequency in table 1.

Node	Freq. Range (Hz)	Node	Freq. Range (Hz)
(5,0)	0-31.25	(5,24)	500-531.25
(5,1)	31.25-62.5	(5,25)	531.25-562.5
(5,3)	62.5-93.75	(5,27)	562.5-593.75
(5,2)	93.75-125	(5,26)	593.75-625
(5,6)	125-156.25	(5,30)	625-656.25
(5,7)	156.25-187.5	(5,31)	656.25-687.5
(5,5)	187.5-218.75	(5,29)	687.5-718.75
(5,4)	218.75-250	(5,28)	718.75-750
(5,12)	250-281.25	(5,20)	750-781.25
(5,13)	281.25-312.5	(5,21)	782.25-812.5
(5,15)	312.5-343.75	(5,23)	812.5-834.75
(5,14)	343.75-375	(5,22)	834.75-875
(5,10)	375-406.25	(5,18)	875-906.25
(5,11)	406.25-437.5	(5,19)	906.25-937.5
(5,9)	437.5-468.75	(5,17)	937.5-968.75
(5,8)	468.75-500	(5,16)	968.75-1000

Table 1: Subband frequency range at 5th Level of DWPT.

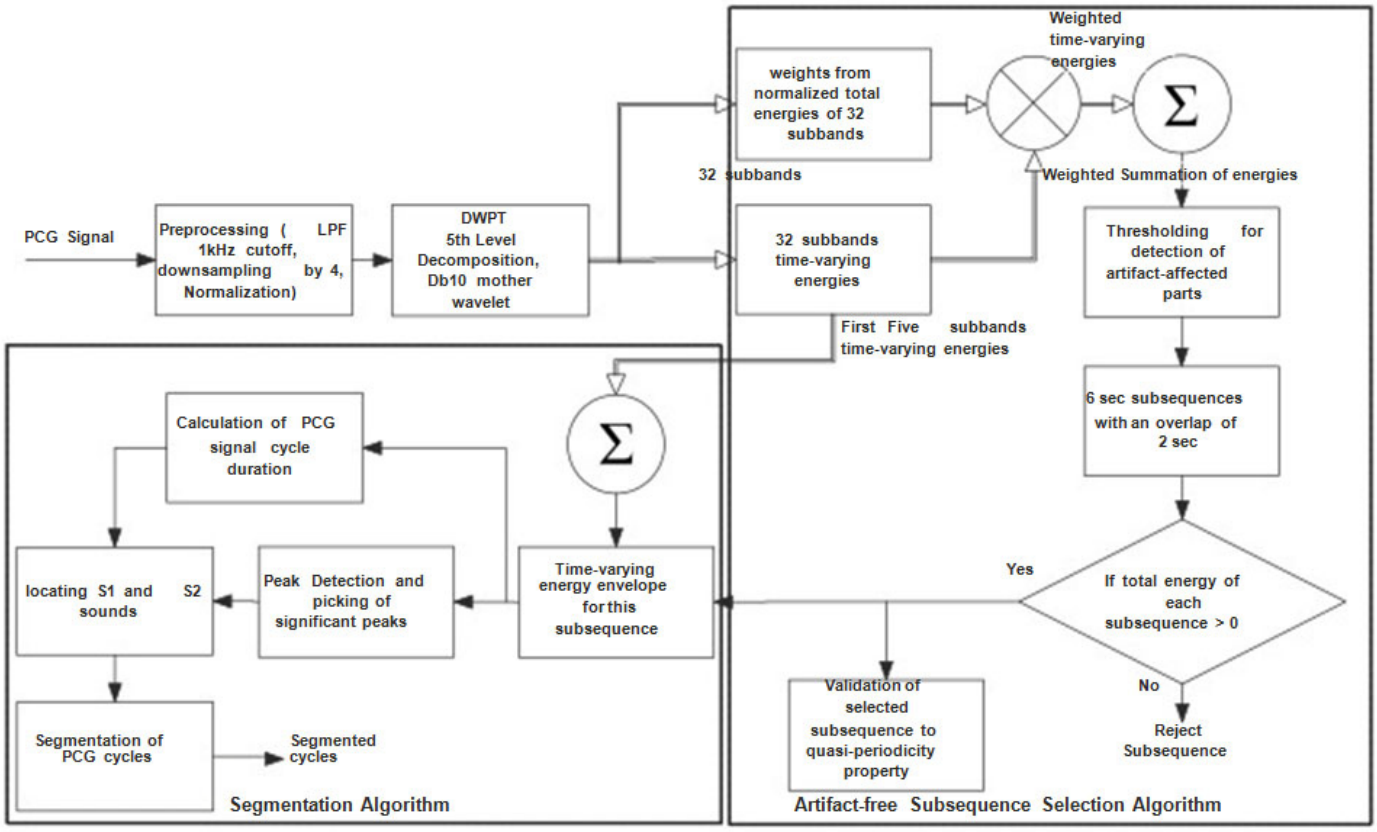


Figure 6: Block diagram of proposed algorithm.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

Artifact-free Subsequence Selection (ASS) algorithm

We compute two different energy parameters on each subband at fifth level of decomposition, one is time-varying wavelet packet energy given by equation 3 and the other is the total energy of each subband represented by equation 4.

$$E_p(n) = \sum_{k=0}^{N-1} \left| W(n-k) \right|^2 \quad (3)$$

$$E_{total,p} = \sum_n \left| W_p \right|^2 \quad (4)$$

Here $E_p(n)$ is energy signal of pth subband, n is the sample number, W (n) is the subband signal after reconstruction, N is the window length, which in this case is 150 samples, $E_{total,p}$ is total energy of p^{th} subband. This quantity provides useful information about the time location of the artifacts in the signal. Total energy is used along with time-varying energy to detect the noisy part of the PCG signal. The steps are as follows:

1. Computation of total energy of each subband $E_{total,p}$.

2. Normalization of the total energy which is shown in figure 7 and given as:

$$E_{norm,p} = E_{total,p} / MAX(E_{total,p}) \quad (5)$$

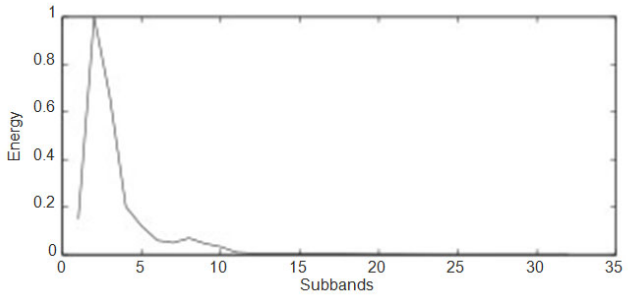


Figure 7: Normalized total energy of wavelet packet subbands.

Lower subbands have large $E_{norm,p}$ mostly due to heart sounds and higher subbands have small $E_{nomr,p}$ because of artifacts. figure 8 shows reconstructed subband signals on left plane and corresponding time-varying energy signal on the right.

3. Weighted summation of time-varying energy is given in the following equation:

$$E_{w,p}(n) = \sum_{p=0}^{P-1} W_p E_p(n) \quad (6)$$

W_p is weighting factor for pth subband and P is total number of subbands. This weighting factor suppresses the subbands with large $E_{norm,p}$ while retaining the subbands with smaller values. Therefore, weighted time-varying energy signal has more artifacts energy which provides artifact's location in the original signal.

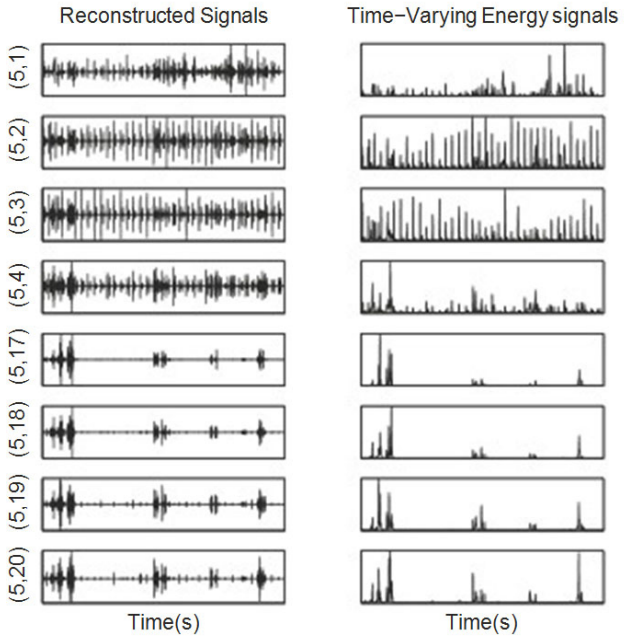


Figure 8: Reconstructed subband signal (decomposition level, subband number) and its time-varying energy signal.

4. Thresholding to 20% of the maximum of $E_{w,p}(n)$ to discard the lower energies due to primary heart sounds. figure 9 shows the weighted time-varying energy signal before and after thresholding.

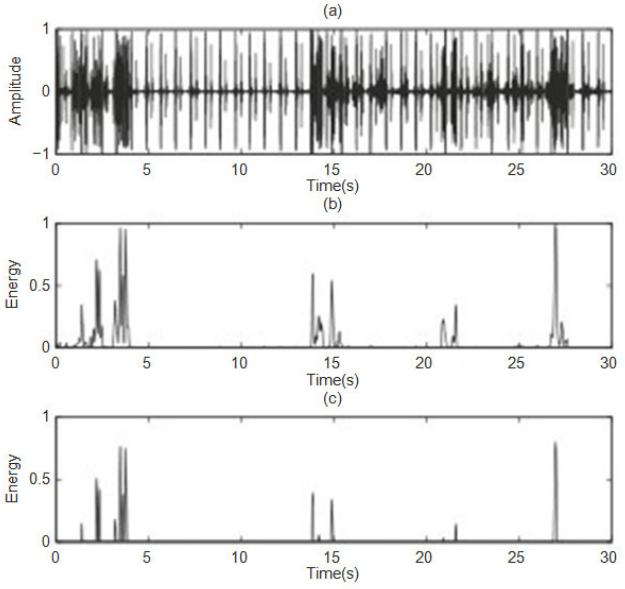


Figure 9: (a) Heart Sound Signal, (b) and (c) weighted time-varying energy signal before and after thresholding.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

5. Next, the energy signal of figure 9(c) is segmented into subsequences of length six seconds with an overlap of two seconds so that we have total seven segments from each 30 seconds heart sound signal. The total energy of each subsequence is computed; if its value is greater than zero, the subsequence will be discarded. Corresponding subsequences from the original PCG signal are rejected.

6. The clean subsequences are tested for quasi-periodicity property of PCG signals using the autocorrelation function of envelope of energy signal which has been explained in section I. Cycle duration is considered in the range of 0.4 seconds to 1.5 seconds. Moreover, quasi-periodicity property of PCG signal helps to improve false rejection or false acceptance parameter by providing additional parametric support

Segmentation of PCG Cycles

Segmentation of PCG signal cycle is a necessary operation for extracting major cardiac events which occur at regular intervals of time. The first step towards segmentation of PCG cycles is calculation of the value of cycle duration. Artifacts in PCG signal will give rise to incorrect estimation of cycle duration; as a consequence segmented cycles may not contain desirable events of heart sound. For example, the cycle duration that was evolved in case of signal shown in figure 2(b) is smaller than figure 2(a). In fact, both the signals are acquired from the same subject, so cycles extracted from the previous signal may miss one of the S1 or S2 sounds, or some part of murmur. Only primary heart sound energy information is sufficient for PCG signal segmentation. The maximum energy of S1 and S2 sounds lies below 150 Hz.[14] As such, frequency resolution of each subband is 31.25 Hz, for this, first starting five subbands of time-varying energy signals are enough to get the S1 and S2 energies for peak detection. The energy is computed by using Equation 7. We summed up them to have an single energy signal. After that, steps given below are followed:

$$E_{env,p}(n) = \sum_{p=0}^{4} E_p(n) \quad (7)$$

• Envelope of energy signal is computed using Hilbert transform.[18,19]
• From the energy envelope, a simple peak detection algorithm has been applied to get the time locations of energy peaks due to S1 and S2 sounds. A window size of 0.05 seconds is used to search the significant peaks, and reject undesirable peaks due to murmur, if exist.[14] Since, some of the information of the murmurs still exists even after taking the energies below 150 Hz. In figure 10(c), the blue colored vertical lines are significant peaks and red colored lines are unwanted peaks which were rejected.
• Consecutively, cycle duration has been computed using the autocorrelation function of envelope signal. This has been explained in Section I.
• The detection of S1 and S2 peaks from the time-domain peaks are based on the following biomedical features:
  o Duration of diastolic period is greater than the systolic period
  o The systolic period generally remains constant
  o The duration of systolic period is 30% of the complete cycle duration
• The S1 and S2 sounds are located by implementing a method, which is described in.[14] Figure 10(d) depicts the located S1 and S2 sounds.
• After locating S1 and S2 sounds, the cycles are extracted from the signal by following the fundamental pattern of events in a heart sound cycle, i.e. S1 sound with systole period followed by S2 sound with diastole period.

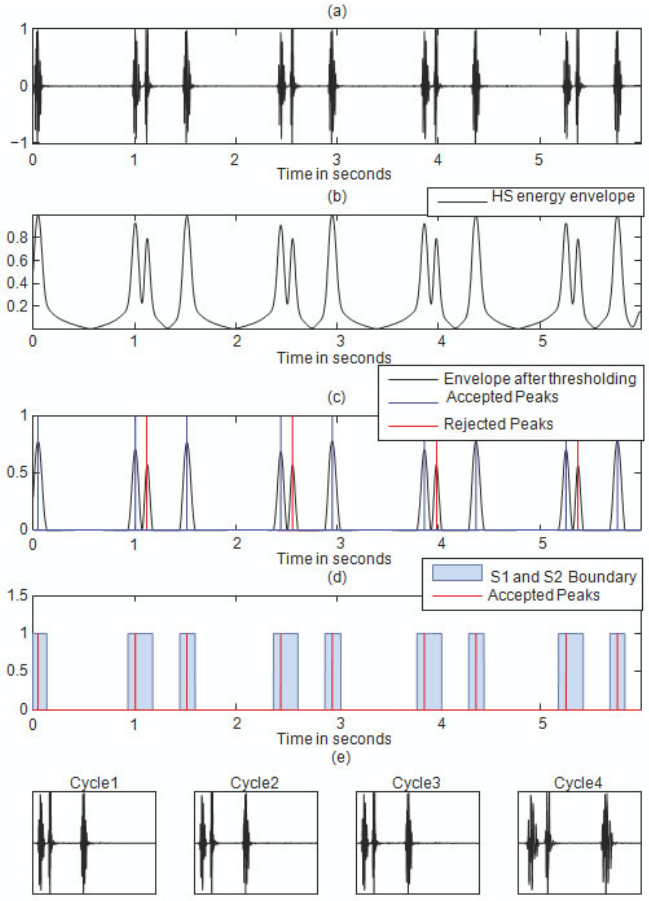


Figure 10: (a) An Ejection Click murmur PCG signal subsequence without artifacts, (b) Subbands energy envelope from artifact-free subsequence operation, (c) Peak detection and picking of significant peaks from the envelope, (d) Locating S1 and S2 sounds and (e) extracted cycles of PCG signal.

• Figure 10(e) shows the extracted cycles.

RESULTS AND DISCUSSIONS

The performance of the proposed algorithm is evaluated on all the three databases described in section III.

Performance of ASS algorithm

We have calculated the percentage of accuracy of the

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

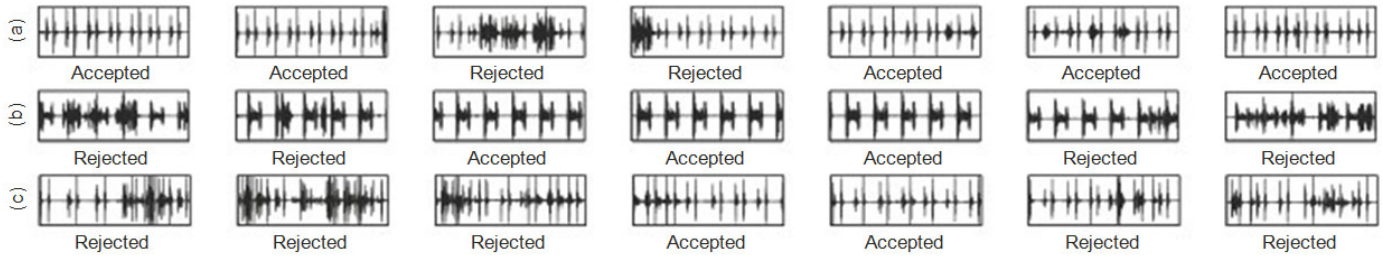


Figure 11: (a) and (b) are subsequences of normal and diseased PCG signal in which artifacts are added manually. (c) Subsequences of normal PCG signal with artifacts recorded in real time

subsequence selection algorithm separately for all the databases. False Acceptance Ratio (FAR) is the measure of the likelihood that the system has incorrectly accepted the segments which are artifacts infected. Whereas False Rejection Ratio (FRR) is the measure of the chances that the system has incorrectly rejects the segments which are actually free of artifacts. First results are shown for only DWPT based approach without using quasi-periodicity property in table 2. Some of the signals of which are segmented by this are shown in figure 11. Validation of selected artifact-free subsequences to quasi-periodicity property of PCG signal.

	No .of segments tested for ASS	FAR	FRR	Accuracy(%)
DB I	210	0.20	0.05	79.78
DB II	210	0.06	0.12	94.12
DB III	70	0.31	0.23	69.23

Table 2: Results of proposed ASS algorithm.

Next, the subsequences which are selected as artifact-free segments from the proposed method undergo the quasi-periodicity check and are considered, if passed. The results are shown in table 3. Number of subsequences selected from ASS algorithm are 89, 85 and 13 for database I, II and III respectively. FAR is registered after quasi-periodicity validation, because some of the segments considered as artifact-free by ASS algorithm actually consist of artifacts. These artifacts are significant enough to vary estimate of the cyclic period of the PCG signal. Due to this, some of the subsequences are rejected in this validation. It is observed that FAR is reduced to 0.01, 0.02 and 0.15 respectively. FRR is zero for all cases, because rejected segments are not validated, since our main concern is to obtain artifact-free subsequences.

	No. of segments obtained from ASS algorithm	FAR	Accuracy(%)
DB I	89	0.01	98.88
DB II	85	0.02	97.65
DB III	13	0.15	84.62

Table 3: Results of quasi-periodicity validation of selected.

Segmentation algorithm results

Accepted subsequences which are artifact-free are passed through the segmentation operation, the results are tabulated in table 4. A lesser accuracy has been registered for database III because the false acceptance ratio is higher in this case in artifact-free subsequence selection process. Figure 10, shows an accepted artifact-free subsequence from ASS algorithm, which has been segmented to corresponding cycles. On the other hand, in figure 12, artifacts are severely corrupted the signal, these are high amplitude and overlapped with the primary heart sounds. The cycles obtained from segmentation are more than what it actually has, in this case the actual number of cycles the subsequence has is four, because estimated cycle duration (0.39 Sec) is less than the actual duration (1.42 Sec). From extracted cycles, some of them containing either S1 sound or S2 sound or a combination of S1 and S2 sounds and artifact peaks. Such cycles increase the false alarm rate of the system, to which these cycles are fed to. We have checked that the algorithm is suitable for real-time operation as it takes 0.4 second of processing time for every second of acquired signal length.

	Segmented Subsequences	Cycles actually present	Cycles incorrectly Segmented	Accuracy(%)
DB I	89	552	9	98.36
DB II	85	440	8	98.18
DB III	13	83	5	93.97

Table 4: Results for segmentation algorithm.

CONCLUSION

This work presents a novel integrated framework is to obtain artifact-free subsequences of PCG signal which is followed by automated heart sound cycle segmentation. The utilization of common features for both artifact-free subsequence selection and cycle segmentation makes the system simpler. Such preprocessing is suitable for real-time implementation of heart sound analyzer. The method is found to be effective for both normal and pathological heart sounds. An accuracy of above 90% is registered for all three databases used in the experiment. Such algorithms will be useful in practical environments which often cannot ensure artifact free data collection

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

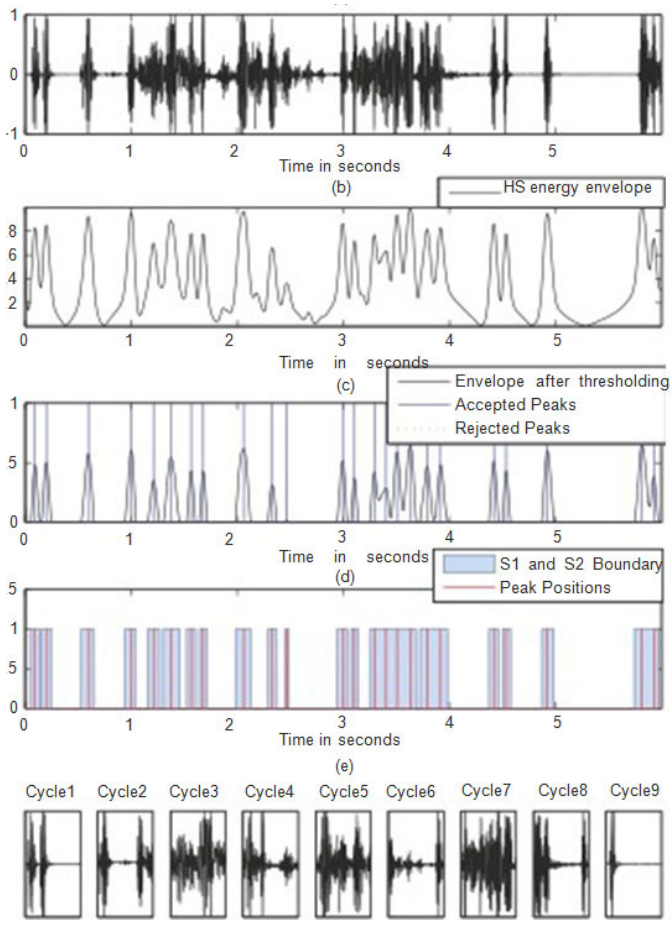


Figure 12: (a) Heavily artifact corrupted Ejection Click murmur PCG signal subsequence, (b) Envelope of energy signal, (c) Peak detection and picking of significant peaks from the envelope, (d) Locating S1 and S2 sounds and (e) extracted cycles of PCG signal.

DISCLOSURE OF INTEREST

The authors declare no conflict of interest concerning this article.

ACKNOWLEDGMENT

The authors would like to thank Dr. Samit Ari, Mr. Kriti Sen Sharma, Mr. Koushik Hembram and Mr. Prasanta Pattadar upon whose initial research, this specific work is done, and also Mr. Syed Naser Daimi for the technical input provided.

REFERENCES

1. Alam U, Asghar O, Khan SQ, Hayat S, Malik RA. Cardiac auscultation: an essential clinical skill in decline. *Br J Cardiol.* 2010; 17(1): 8-10.

2. Mangione S, Nieman LZ. Cardiac auscultatory skills of internal medicine and family practice trainees: a comparison of diagnostic proficiency. *JAMA*. 1997; 278(9): 717-722. doi: 10.1001/jama.1997.03550090041030

3. Tang H, Li T, Park Y, Qiu T. Separation of heart sound signal from noise in joint cycle frequency-time-frequency domains based on fuzzy detection. *Biomedical Engineering, IEEE Transactions on.* 2010; 57(10): 2438-2447. doi: 10.1109/TBME.2010.2051225

4. Sweeney KT, Leamy DJ, Ward TE, McLoone S. Intelligent artifact classification for ambulatory physiological signals. *Engineering in Medicine and Biology Society (EMBC), 2010 Annual International Conference of the IEEE*. 2010; 6349-6352.

5. Beritelli F, Spadaccini A. Heart sounds quality analysis for automatic cardiac biometry applications, in Information Forensics and Security, 2009. WIFS 2009. *First IEEE International Workshop on IEEE*. 2009; 61-65.

6. Sweeney KT, Ward TE, McLoone SF. Artifact removal in physiological signals-practices and possibilities. *Information Technology in Biomedicine, IEEE Transactions on*. 2012; 16(3): 488-500. doi: 10.1109/TITB.2012.2188536

7. Ari S. Analysis and characterization of phonocardiogram signal for diagnosing valvular heart disease, Ph.D. dissertation, IIT Kharagpur, India, August 2009.

8. Li T, Qiu T, Tang H. Optimum heart sound signal selection based on the cyclostationary property. *Computers in biology and medicine*. 2013; 43(6): 607-612.

9. Choi S, Shin Y, Park H-K. Selection of wavelet packet measures for insufficiency murmur identification, Expert Systems with Applications. 2011; 38(4): 4264-4271.

10. Kumar D, Carvalho P, Antunes M, Paiva R, Henriques J. Noise detection during heart sound recording using periodicity signatures, Physiological measurement. 2011; 32(5): 599.

11. Friedman HH. Diagnostic electrocardiography and vectorcardiography. McGraw-Hill Inc., New York, 1977.

12. Kumar D, Carvalho Pd, Antunes M, et al. Wavelet transform and simplicity based heart murmur segmentation, in Computers in Cardiology, 2006. *IEEE*. 2006: 173-176. doi: 10.1016/j.compbiomed.2013.03.002

13. Hedayioglu F, Jafari M, Mattos S, Plumbley M, Coimbra M. Denoising and segmentation of the second heart sound using matching pursuit, in Engineering in International Conference of Medicine and Biology Society, San Diego, CA, USA. 2012: 3440-3443.

14. Ari S, Kumar P, Saha G. A robust heart sound segmentation algorithm for commonly occurring heart valve diseases. *Journal of Medical Engineering & Technology*. 2008; 32(6): 456-465. doi: 10.1080/03091900601015162

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-105

15. Safara F, Doraisamy S, Azman A, Jantan A, Ranga S. Wavelet packet entropy for heart murmurs classification. *Advances in bioinformatics*. 2012; 2012. doi: 10.1155/2012/327269

16. Choi S. Detection of valvular heart disorders using wavelet packet decomposition and support vector machine. *Expert Systems with Applications*. 2008; 35(4): 1679-1687. doi: 10.1016/j.eswa.2007.08.078

17. Choi S, Shin Y, Park H-K. Selection of wavelet packet measures for insufficiency murmur identification. *Expert Systems with Applications*. 2011; 38(4): 4264-4271. doi: 10.1016/j.eswa.2010.09.094

18. Feldman M. Nonparametric identification of asymmetric nonlinear vibration systems with the hilbert transform. *Journal of Sound and Vibration*. 2012; 331(14): 3386-3396. doi: 10.1016/j.jsv.2012.02.025

19. Mondal A, Kumar AK, Bhattacharya P, Saha G. Boundary estimation of cardiac events s1 and s2 based on hilbert transform and adaptive thresholding approach. *Medical Informatics and Telemedicine (ICMIT)*, 2013 *Indian Conference on. IEEE*. 2013: 43-47. doi: 10.1109/IndianCMIT.2013.6529406

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

Case Report

*Corresponding author:
Danish Mahmood, M. Pharm, PhD
Lecturer
Department of Pharmacology and Toxicology, Unaizah College of Pharmacy, Qassim University
Unaizah, Saudi Arabia
Tel. +966-594016751
E-mail: ma.alam@qu.edu.sa

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2106

Article History:
Received: December 18th, 2014
Accepted: March 17th, 2015
Published: March 18th, 2015

Citation:
Mahmood D, Siddique A. A case report of the management of residual cardiovascular risk in a dyslipidaemic patient with metabolic syndrome. *Heart Res Open J*. 2015; 2(1): 35-38.

A Case Report of the Management of Residual Cardiovascular Risk in a Dyslipidaemic Patient with Metabolic Syndrome

Danish Mahmood[1*] and Abubakar Siddique[2]

[1]Department of Pharmacology & Toxicology, Unaizah College of Pharmacy, Qassim University, Unaizah, Saudi Arabia

[2]Department of Pharmacy Practice, Unaizah College of Pharmacy, Qassim University, Unaizah, Saudi Arabia

ABSTRACT

Metabolic Syndrome (MS) is a clustering of metabolic and underlying risk factors which doubles the risk of atherosclerotic cardiovascular disease. It is more prevalent in some ethnic groups, especially in the Asian world. Global urbanization and sedentary life habits have increased the underlying risk factors characterised by physical inactivity, atherogenic diet and obesity. Therefore, its detection, prevention, and treatment serve as an important approach for the reduction of cardiovascular risk in the general population and strictly emphasized on strict therapeutic lifestyle changes. In our case report, we present effective management of a dyslipidaemic patient with MS by medication. However, her underlying risk factors were not controlled due to her inability to strictly adopt therapeutic lifestyle changes.

INTRODUCTION

The new worldwide International Diabetes Federation (IDF) defines, Metabolic Syndrome (MS) as having central obesity (defined as waist circumference ≥94 cm for Europid men and ≥80cm for Europid women, with ethnicity specific values for other groups) and any two of the following four factors which include first, raised TG level: ≥150 mg/dL (1.7 mmol/L), Second, reduced High Density Lipoprotein Cholesterol (HDL-C): <40 mg/dL (1.03 mmol/L) in males and <50 mg/dL (1.29 mmol/L) in females, third, the raised blood pressure: systolic BP ≥130 or diastolic BP ≥85 mm Hg, fourth, raised Fasting Plasma Glucose (FPG) ≥100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. Central obesity and insulin resistance have been regarded as important causative factor, however, the pathogenesis of MS and its components have remained poorly understood (www.idf.org).[1] We present a case report of management of residual CVD risk in a female dyslipidaemic patient with MS.

CASE REPORT

A 62-year old Mexican American woman went to a routine clinical visit. Her Body Mass Index (BMI), waist circumference, FPG, and BP were 31.2 kg/m^2, 36 inches (91.44 cm), 115 mg/dL and 136/77 mm Hg, respectively. She was already on Angiotensin Converting Enzyme (ACE) inhibitor, the antihypertensive medication, which helped to reduce her BP. Her lipid profile revealed borderline elevation of various lipid parameters, including total cholesterol (227 mg/dL), LDL-C (130 mg/dL), HDL-C (40 mg/dL), TG (285 mg/dL), and non-HDL-C (187 mg/dL). Her clinician diagnosed her with impaired fasting glucose and MS and reported her Framingham risk score of 12%. Her 10-year risk of Atherosclerotic cardiovascular disease (ASCVD) was 15.7% as calculated using pooled cohort risk assessment equations. He prescribed atorvastatin (10 mg/day) and suggested to adopt therapeutic lifestyle changes (diet,

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

exercise) and stop smoking.

During her follow up visit after 3 months (Visit 1), she reported that her smoking habits were reduced from 1 pack to half pack a day. However, there was no change in her BMI (31.8 kg/m^2) and waist circumference (36.5 inches). Her BP was slightly raised (from 136/77 mm Hg to 138/80 mm Hg). To normalize her BP, the clinician prescribed amlodipine, a calcium channel blocker, in addition to existing ACE inhibitor. After the use of atorvastatin a change in her lipid profile was observed. Her total cholesterol, LDL-C, non-HDL-C, and TG were reduced from 227 to 181 mg/dL; 130 to 89 mg/dL; 187 to 139 mg/dL, and 285 mg/dL to 248 mg/dL, respectively and HDL-C levels were increased from 40 to 42 mg/dL. She reached her target goal of LDL-C (<100 mg/dL) but did not reach target goal of non-HDL-C (<130 mg/dL) as per ATP III guidelines (Table 1). Though there was an overall improvement in the metabolic parameters, her FPG was elevated (132 mg/dL) and was diagnosed with type 2 diabetes. The clinician prescribed metformin (500 mg, twice a day) to reduce her FPG levels and added fenofibrate (145 mg/day) to existing atorvastatin therapy to further elevate HDL-C and lower TG levels. He explained the importance of lifestyle changes and again stressed her to strictly adopt lifestyle changes.

Three months after Visit-1, no change in BMI and waist circumference was observed in spite of her reduced smoking habit. The combination of amlodipine plus ACE inhibitor normalised her BP (from 138/80 mm Hg to 122/74 mm Hg) and metformin reduced her FPG (from 132 mg/dL to 114 mg/dL). After treatment with fenofibrate and atorvastatin her lipid profile was further improved. Her total cholesterol, LDL-C, non-HDL-C, and TG reduced to 158 mg/dL, 80 mg/dL, 110 mg/dL, and 148 mg/dL, respectively, and her HDL-C increased to 48 mg/dL. Since she did not experience any adverse muscle, liver, or kidney events, the treatment was continued. The medications helped her lower presence of most of her metabolic and major risk factors. However, no changes in underlying risk factors were observed owing to her inability to adopt to a strict lifestyle changes.

DISCUSSION

The two most widely accepted criteria for the diagnosis of MS in the United States have been proposed by the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI). International Diabetes Federation (IDF) was similar to NCEP ATP III and AHA/NHLBI criteria except that it included central obesity plus two or more than two criteria (Table 2).[1] Enlarged waist plus elevated triglycerides serves as a stronger predictor of cardiovascular mortality and all-cause mortality after adjustment of age, smoking status, and LDL-C levels.[1,2] In our report, the patient was a 62-year old female of Mexican American descent with enlarged waist (91.44 cm) and borderline elevation of lipid parameters with elevated TG levels (285 mg/dL), and was diagnosed with MS.

Central (abdominal) obesity can be easily assessed using waist circumference which is independently associated with all components of MS including insulin resistance, and is a prerequisite risk factor for the diagnosis of the syndrome in the new definition of IDF. Table 2 present the IDF recommended cut-points for waist circumference for diagnosis of MS in different ethnic group. In reference to the IDF cut-point on waist circumference as presented in here in table 2, the cut point defining abdominal obesity and those of Central American ancestry is 80 cm and the so patient in the present case study has a waist circumference far above that, and hence she meets the criteria

NCEP III	NHLBI/AHA Criteria	IDF Criteria
	Any 3 or more criteria	Central obesity + any 2 or more criteria
Waist circumference: men ≥102 cm (40 in); women ≥35 in (88 cm)	Waist circumference: men ≥102 cm (≥40 inches); women ≥88 cm (≥35 inches); lower cut-points for insulin-resistant individuals	Waist circumference ethnicity specific
TG ≥150 mg/dL (1.7 mmol/L)	TG >150 mg/dL (1.7 mmol/L) or on specific treatment	TG >150 mg/dL (1.7 mmol/L) or on specific treatment
HDL-C: men <40 mg/dL (1.03 mmol/L) Women <50 mg/dL (1.3mmol/L)	HDL-C: men <40 mg/dL (1.03 mmol/L); women <50 mg/dL (1.29 mmol/L)	HDL-C: men <40 mg/dL (1.03 mmol/L); women <50 mg/dL (1.29 mmol/L) or on specific treatment
SBP ≥130 mm Hg or DBP ≥85 mm Hg	SBP ≥130 mm Hg or DBP ≥85 mm Hg or antihypertensive medication	SBP ≥130 mm Hg or DBP ≥85 mm Hg or antihypertensive medication
FBG ≥110 mg/dL	FBG ≥100 mg/dL (5.6 mmol/L) or on drug treatment for elevated glucose	FBG ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 DM

DBP = Diastolic Blood Pressure; FBG = Fasting Blood Glucose; HDL-C = High-Density Lipoprotein Cholesterol; IDF: International Diabetes Federation; NHLBI/AHA: National Heart Lung Blood Institute/American Heart Association; SBP = Systolic Blood Pressure; TG = Triglyceride

Table 1: NHLBI/AHA and IDF Diagnostic Criteria for Metabolic Syndrome.[1,2]

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

for the diagnosis of MS as per new IDF definition. Although, there are inadequate data in other racial groups, such as Hispanics, Asians, and American-Indian populations. It has been reported that in comparison to non-Hispanic white or Caucasians, the risk of ASCVD is generally found to be lower among Hispanic-American and Asian-American populations, and generally higher among American-Indian populations.[3] Our results corroborated with earlier reports where females aged >60 years, enlarged waist, elevated TG and the Mexican American descent have higher predisposition to MS.

Non-HDL-C reported as a stronger predictor of CVD risk than LDL-C[4,5] and was considered as a secondary target after attainment of LDL-C goal with TGs ≥200 mg/dL (5.17 mmol/L).[6,7] During her follow up visit her LDL-C, total cholesterol, TG got reduced by 31.5%, 20.2%, and 13%, respectively, and HDL-C goal was elevated by 5% after the use of atorvastatin (10 mg/day). Our results were in agreement with the previous study where standard doses of statins (simvastatin 10-40 mg/day, pravastatin 40 mg/day and lovastatin 20-40 mg/day) reduced total cholesterol by 18-26%, LDL-C by 25-30% and TG by 11-17%, and increased HDL-C by 5-7%.[6] However, other studies reported statins to be inadequate in the residual CVD risk associated with lipid abnormalities, especially above TG >220 mg/dL.[7-9]

As per NCEP ATP III guidelines, statins or TG lowering drugs, such as fibrates or niacin served a vital role in achieving non HDL-C and LDL-C goals where the non-HDL-C goal was always 30 mg/dL higher than the LDL-C goal.[10] In our report too, we observed that the patient after treatment with fenofibrate and atorvastatin achieved the largest goal of LDL-C and non-HDL-C. In the present case, the patient calculated ASCVD risk was 27.8% indicating that this patient was at elevated 10-year risk (≥7.5%) for ASCVD. In diabetics (40-75 years, LDL 70-189 mg/dL), a high-intensity statin should be considered with a 10-year ASCVD risk ≥7.5%. The 2013 ACC/AHA guidelines recommend either a high-intensity or moderate-intensity statin regimen in patients who have an elevated ASCVD risk (≥7.5%) for primary prevention of cardiovascular disease. The recommended doses of moderate intensity atorvastatin dose ranges between 10-20 mg. Hence, this patient was prescribed atorvastatin dose of 10 mg, and advised to adopt therapeutic lifestyle changes as the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline have emphasized that lifestyle modification (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) constitutes an important element in the health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol lowering drug therapies.[11,12] The new ACC/AHA guideline emphasizes matching the intensity of statin treatment to the level of ASCVD risk and replaces the old paradigm of pursuing LDL-C targets (Table 3).

During her follow up visit after 3 months that there was no change in her BMI (31.8 kg/m^2) and waist circumfer-

Gender	Waist Circumference (cm)					
	Europids	South Asian	Chinese	Japanese	Ethnic South and Central Americans	Eastern Mediterranean & Middle East (Arab)
Male	≥94	≥90	≥90	≥90	≥90	≥94
Female	≥80	≥80	≥80	≥80	≥80	≥80

Table 2: Waist circumference cut-point for diagnosis of metabolic syndrome in different ethnic group[1]

Clinical risk categories	Treatment
Those with clinical ASCVD	High-intensity statin therapy. If 50% reduction is not reached drug combination may be considered
Diabetes mellitus (Type I or Type II) without ASCVD but with LDL-C between 1.8 and 4.9 mmol/L	Diabetes with high risk: High-intensity statin therapy. Diabetes with low risk: Moderate-intensity statin therapy
Those with primary elevation of LDL-C >4.9 mmol/L	High-intensity statin therapy, aimed at achieving at least 50% reduction of LDL-C
If none of the above but with estimated 10-year ASCVD risk of 7.5% or more using a pooled populations risk calculator If risk-based assessment treatment decision uncertain assessment of 1 or more of family history, hs-C-reactive protein, CAC Score or ABPI may be considered, contribution of Apo B, CKD, microalbuminuria or cardio-respiratory fitness is uncertain and CIMT is not recommended for routine assessment of individual patients	Moderate-to-high-intensity statin therapy if ASCVD risk >7.5%. If risk 5-7.5% risk of CVD event: Reasonable to consider moderate-intensity statin therapy

ABPI: Ankle Brachial Pressure Index; ASCVD: Atherosclerotic cardiovascular disease; Apo B: Apoprotein B; CAC: Coronary Artery Calcification; CKD: Chronic Kidney Disease; CIMT: Coronary Intima Media Thickness; LDL-C: Low Density Lipoprotein Cholesterol

Table 3: 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce ASCVD risk in adults[12]

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

ence (36.5 inches) despite reducing her smoking from 1 pack to half pack a day. The current cut-points for overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) compared with normal weight (BMI 18.5 to <25 kg/m^2) has been associated with elevated risk of combined fatal and nonfatal coronary heart disease. The new ACC/AHA guideline on obesity recommends healthcare providers to develop individualized weight loss plans that should include three key components - a moderately reduced calorie diet, a program of increased physical activity and the use of behavioral strategies to help patients achieve and maintain a healthy body weight. In order to better manage weight reduction and obesity, physician should advice patients to undertake multiple sessions with dietician. No change in BMI as reported by the patients after 3 months underscores inadequate instruction on weight reduction plan was provided by the healthcare provider.

The NCEP ATP III and the AHA/NHLBI recognized HDL-C as a tertiary target but did not set an HDL-C goal level. These two organisations including ADA advocated the use of fibrates to reduce TG and elevate HDL-C in patients with the MS or diabetes and suggested that fenofibrate combination with statin may be an effective and safer alternative than statin alone. We also observed that the patient did not experience any side-effects with the combination therapy of atorvastatin and fenofibrate and hence prescribed to continue her treatment.

In conclusion, the metabolic risk factors for MS in dyslipidaemics can be well managed by appropriate treatment but the underlying risk factors could only be managed by adopting strict therapeutic life style changes.

REFERNCES

1. International Diabetes Foundation. The IDF consensus worldwide definition of the metabolic syndrome. http://www.idf.org/webdata/docs/MetS_def_update2006.pdf. 2007; Accessed 2007.

2. Tankó LB, Bagger YZ, Qin G, Alexandersen P, Larsen PJ, Christiansen C. Enlarged waist combined with elevated triglycerides is a strong predictor of accelerated atherogenesis and related cardiovascular mortality in postmenopausal women. *Circulation*. 2005; 111: 1883-1890. doi: 10.1161/01.CIR.0000161801.65408.8D

3. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics-2013 update: a report from the American Heart Association. *Circulation*. 2013; 127(1): e6-e245. doi: 10.1161/CIR.0b013e31828124ad

4. Cui Y, Blumenthal RS, Flaws JA, et al. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. *Arch Intern Med*. 2001; 161: 1413-1419. doi: 10.1001/archinte.161.11.1413

5. Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *JAMA*. 2005; 294: 326-333. doi: 10.1001/jama.294.3.326

6. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med*. 2005; 352: 1425-1435. doi: 10.1056/NEJMoa050461

7. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006; 3: 2011-2030. doi: 10.1371/journal.pmed.0030442

8. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002; 360: 7-22. doi: 10.1016/S0140-6736(02)09327-3

9. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106: 3143-3421.

10. Grundy SM, Cleeman JI, Merz BN, et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation*. 2004; 110: 227-239. doi: 10.1161/01.CIR.0000133317.49796.0E

11. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014; 129(25 Suppl 2): S1-S45. doi: 10.1161/01.cir.0000437738.63853.7a

12. Ray KK, Kastelein JP, Boekholdt SM, et al. The ACC/AHA 2013 guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: the good the bad and the uncertain: a comparison with ESC/EAS guidelines for the management of dyslipidaemias 2011. *Eur Heart J*. 2014; 35: 960-968.

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

Review

*Corresponding author:
Emmanuel Andrès, MD
Professor
Department of Internal Medicine
Diabetes and Metabolic Diseases Clinic B
University Hospital of Strasbourg
1 Place de l'Hôpital, 67000 Strasbourg
France
Centre for Educational Research of the Strasbourg, Faculty of Medicine
University of Strasbourg (UdS)
4 Rue Blaise Pascal, 67081 Strasbourg
France
Tel. +33 (0)388115066
Fax: +33 (0)388116262
E-mail: emmanuel.andres@chru-strasbourg.fr

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2107

Article History:
Received: February 25th, 2015
Accepted: March 27th, 2015
Published: March 30th, 2015

Citation:
Andrès E, Talha S, Hajjam M, Hajjam J, Ervé S, Hajjam A. E-care project: a promising e-platform for optimizing management of chronic heart failure and other chronic diseases. *Heart Res Open J*. 2015; 2(1): 39-45.

E-Care Project: A Promising E-Platform for Optimizing Management of Chronic Heart Failure and Other Chronic Diseases

Emmanuel Andrès[1*], Samy Talha[2], Mohamed Hajjam[3], Jawad Hajjam[4], Sylvie Ervé[4] and Amir Hajjam[5]

[1]Department of Internal Medicine, Diabetes and Metabolic Diseases Clinic B, University Hospital of Strasbourg, Strasbourg; Centre for Educational Research of the Strasbourg, Faculty of Medicine, University of Strasbourg (UdS), 4 Rue Blaise Pascal, 67081 Strasbourg, France

[2]Service Physiology and Functional Explorations, and Strasbourg University Hospital Faculty of Medicine, University of Strasbourg (UdS), Strasbourg, France

[3]Newel, 36 Rue Paul Cézanne, 68200 Mulhouse, France

[4]ICT Centre of Expertise for Autonomy (CenTich) and French Mutuality Anjou-Mayenne (MFAM), Angers, France

[5]Laboratory IRTES-SeT, University of Technology of Belfort-Montbéliard (UTBM), Belfort-Montbéliard, Rue de Leupe, 90400 Sevenans, France

ABSTRACT

Monitoring patients with heart failure by using telemedicine systems is a potential means for optimizing the management of these patients. The E-care project is developing an "intelligent" communicative platform enabling the home monitoring of patients with New York Heart Association (NYHA) Stage III heart failure using non-invasive sensors. As a result, this platform will assist health care professionals by providing an automated processing of these sensors' transmitted data in order to detect and report signs of cardiac decompensation early.

KEYWORDS: Heart failure; Telemedicine; Home support; Detecting signs of cardiac decompensation.

INTRODUCTION

Heart Failure (HF) is a serious chronic disease that, in addition to its significant morbidity and 50% mortality rate at 5 years for New York Heart Association (NYHA) Stages III – IV, involves frequent re-hospitalizations that impede patient quality of life, some of which could be prevented through early action.[1]

In France, nearly 1 million people suffer from HF, and over 120,000 new cases are diagnosed every year, thus presenting a major public health issue. Managing HF is a complex, lengthy, often difficult task, with great cost to our society, both in terms of healthcare and treatment time as well as from a financial standpoint.

Yet while HF treatment is currently well-standardized, according to evidence-based medicine, and has enabled undeniable progress, particularly with regard to mortality rates, there are still potential advances to be made in terms of life expectancy and the quality of life of these patients, notably by centering long-term management in the home.[1] Monitoring HF patients by using telemedicine systems is a potential means for optimizing the patient management process.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

In this paper, we discuss the role to be played by telemedicine in HF management and present a new e-platform that promises to optimize the management and monitoring of this chronic disorder.

The Role of Telemedicine in the Management of Chronic Diseases like Heart Failure

The monitoring of chronic disease patients using telemedicine systems is theoretically a promising means for optimizing patient management in these cases, as already demonstrated in certain diseases, such as diabetes or chronic HF.[2-6] Advances in telecommunication technologies have created new opportunities to provide telemedical care as complementary treatment to the medical management of HF patients. Meta-analyses have suggested that telemedicine can reduce morbidity and mortality in patients with these types of disorder.

Nevertheless, the results of telemonitoring studies and meta-analyses have been controversial. In reviews assessing these methods, telemedicine approaches range from computer-based support systems to ones founded on structured telephone support, or even to programs led by nurses and physicians.[2,6] It is thus difficult to have a definitive opinion based on what we know now on whether or not telemedicine has a significant role to play in HF management.

In the thorough 2011 meta-analysis from Anker et al., published in The Lancet, the results with respect to mortality and HF-related hospitalization decreases, in addition to improved quality of life, were well-documented.[4] In this meta-analysis, 11 studies were analyzed in the setting of a comparison between the effects of telemonitoring versus usual care (noninvasive telemedicine). Telemonitoring was found to reduce the following rates: all-cause mortality, achieving 147 events/1,410 patients (10.4%) vs. 200/1,300 (15.4%) ($p < 0.0001$); all-cause hospital admission, with 582 events/1,232 patients (47.2%) *vs.* 579/1,111 (52.1%) ($p=0.02$); hospital admission related to chronic HF, with 189 events/844 patients (22.4%) *vs.* 207/726 (28.5%) ($p=0.008$).

Similar results were reported in a more dated meta-analysis from the Cochrane group.[5] Of the 25 full peer-reviewed studies meta-analyzed, 16 evaluated structured telephone support (n=5,613 participants), 11 telemonitoring (n=2,710 participants), and two both interventions (included in counts). Telemonitoring was demonstrated able to reduce all-cause mortality (Hazard Ratio [HR]: 0.66; 95% CI: 0.54-0.81, $p < 0.0001$), with structured telephone support demonstrating a non-significant positive effect (HR: 0.88; 95% CI: 0.76-1.01, $p=0.08$). Both structured telephone support (HR: 0.77; 95% CI: 0.68-0.87, $p < 0.0001$) and telemonitoring (HR: 0.79; 95% CI: 0.67-0.94, $p=0.008$) reduced chronic HF-related hospitalizations. For both interventions, several studies reported improved quality of life, reduced healthcare costs, and high patient acceptance.

As described below, meta-analyses have indicated that telemedicine could reduce morbidity and mortality in these patients. Still, two prospective clinical trials have produced results that do not support these findings.[7,8] The Tele-HF trial randomly assigned patients hospitalized for HF to either telemonitoring (n=826) or standard care (n=827).[7] The noninvasive telemonitoring system was an asynchronous, telephone-based interactive voice-response system that obtained daily information on the patient's symptoms and bodyweight. In this trial, no significant difference was noted between the telemonitoring and control groups in terms of rate of any readmission or death from any cause within 180 days of inclusion, which concerned 432 patients (52%) in the telemonitoring group and 426 (51%) in the usual-care group (HR: 1.04; 95% CI: 0.91-1.19).

The TIM-HF trial in Germany randomly assigned stable chronic HF patients to either telemonitoring (n=354) or usual care (n=356).[8] The noninvasive, synchronous telemonitoring system was based on a wireless Bluetooth device together with a personal digital assistant as the main structural element, all data being transferred to the telemedical center by cell phone. The integrated sensor network consisted of a 3-lead Electrocardiogram (EKG), blood pressure device, and weighing scales. The patient conducted his or her own daily self-assessment using these devices, with the data transferred to the telemedical center, which provided continuous physician-led medical support for the total study period. The telemedical center physician contacted the patients in accordance with the standard operating procedures or on patient request. The center contacted the patient's local physician at least every 3 months. In this trial, the total mortality rate for the primary outcome of death for any cause was 8.4 per 100 patient-years of follow-up in the telemedical group, compared to 8.7 per 100 patient-years of follow-up in the usual-care group (HR: 0.97; 95% CI: 0.67-1.41; $p=0.87$).[8]

The Role of Telemedicine in the Management of Heart Failure in France

In recent years, there has appeared to be renewed interest in France in the field of telemedicine and its applications for HF, with the development of several projects, such as SCAD (Suivi Cardiologique A Distance, remote cardiological monitoring); PIMP's (Plateforme Interactive Médecins Patients santé, doctor-patient interactive healthcare platform); OSICAT (Optimisation de la Surveillance Ambulatoire des Insuffisants CArdiaques par Télécardiologie, optimization of ambulatory heart failure monitoring with telecardiology), and MEDICA (Monitorage Electronique à Domicile de l'Insuffisance CArdiaque chronique, home electronic monitoring of chronic heart failure).[9-12] At the time of writing, no published results were available from these projects.

All these projects are non-invasive and designed to enable patient management at home or in nursing homes. They are mostly based on standard tools for monitoring HF, namely blood

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

pressure monitors, weighing scales, and so on, at times integrating tools enabling the feedback and transmission of collected information (Bluetooth, 3G, 4G, etc.) as well as patient-healthcare professional interaction (call center, digital tablet, website, etc.).[13] Certain projects have also integrated motivational and educational tools. The PIMP's project also includes biological telemonitoring, with Brain Natriuretic Peptide (BNP) telemonitoring.[10]

These are based on prospective or cohort studies of HF patients, with widely varying sample sizes of 100 to 1000 patients, and different follow-up periods ranging from 3 months to 2 years, for the most part stemming from evidence-based medicine.[4]

It is important to emphasize that the objectives or indicators of these various projects vary from modest to the more ambitious, defined as anything from improved morbidity and mortality to reduced readmissions, enhanced quality of life, and improved health economic costs.

E-care: An Innovative Platform for the Early Detection and Reporting of Risk Situations in Heart Failure Patients

The E-care project,[14] selected in 2011 as part of the call for projects in "Health and autonomy at home through digital technology", from Investissements d'Avenir, (a national group for funding innovative research projects in France), was designed with the principal objective of optimizing patient monitoring by detecting precursor signs of cardiac decompensation or acute HF *via* a telemedicine system, combined with motivational and educational tools. This project should theoretically enable i) the reduction of the number of readmissions; ii) the reduction of the total number of hospital days, a figure that progressively and systematically increases when the patient is hospitalized; and, ultimately iii) improvement of quality of life for these patients.

The E-care platform enables patients with NYHA Stage III HF to be monitored, notably at home, using non-invasive sensors.[14] It provides assistance to the medical staff by automating the processing of data sent from the sensors, automatically generating alerts in order to detect and report risk situations of HF early (Figure 1).[15,16] This platform also enables the sharing and management of heterogeneous data so as to integrate the necessary information required for monitoring any underlying pathology, such as diabetes mellitus, renal failure, respiratory insufficiency, and so on.

The early detection of cardiac decompensation involves processing data from multiple factors, namely the signal from the EKG, heart sounds (Phonocardiogram [PCG] signal), weight, Blood Pressure (BP), oxygen saturation, patient ergonomics, in

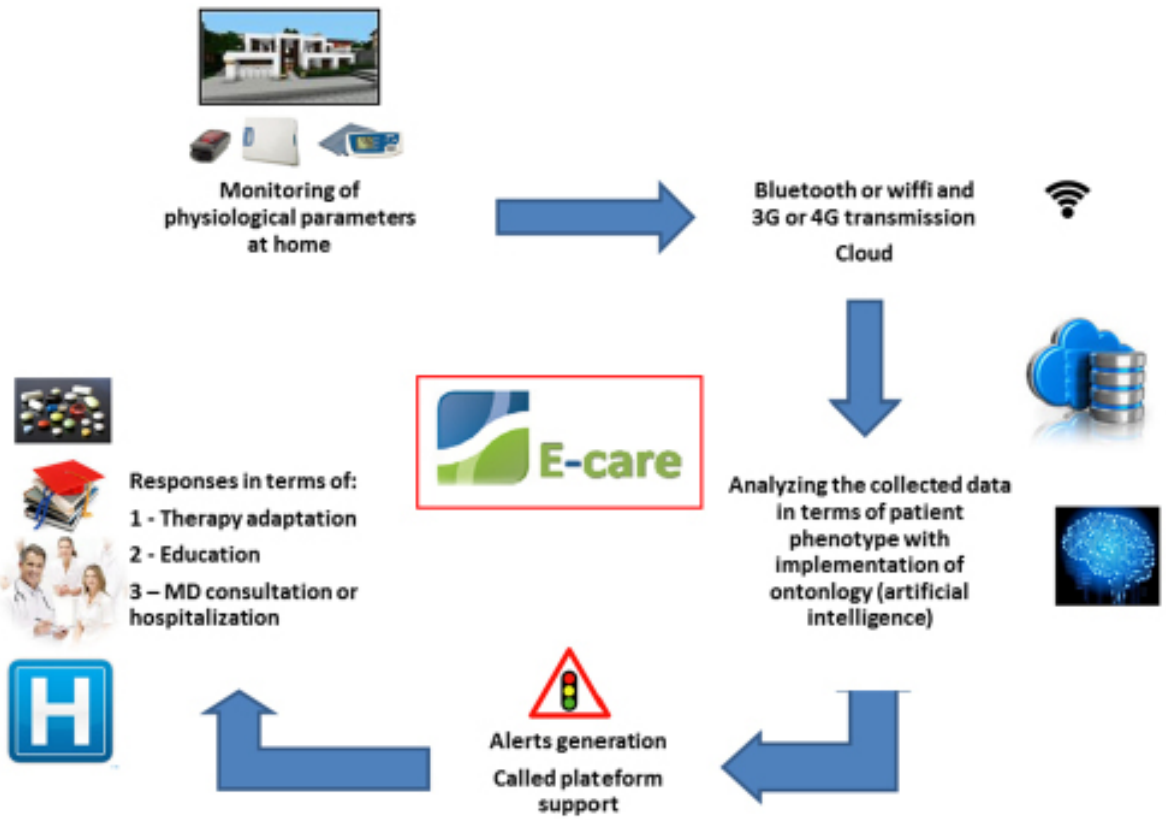


Figure 1: Overall architecture of the E-care platform for monitoring heart failure.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

addition to dietary monitoring, based on the phenotypic data of each patient (personalized medicine).[14-16] All of these consolidated elements, combined with each patient's individual profile, facilitate not only the detection of cardiac abnormalities, but also the prevention of cardiac decompensation risk factors.

The E-care platform uses an ontology designed to define a controlled vocabulary of diseases, medications, symptoms, and so on, as well as to model concepts related to HF monitoring. The effective use of ontology for the purposes of reasoning assumes the addition of operational semantics, which specifies the manner in which the model findings in the ontology will be used for reasoning and to produce new knowledge automatically.[15-17] The reasoning portion is based on an inference engine in which the rules are either introduced by medical experts or generated by a data search and subsequently validated by medical experts. The E-care system fully capitalizes on its ability to consolidate different data information concerning the patient. For each patient, E-care processes in real-time the personal data collected by the sensors, then analyzing it in conjunction with the domain ontologies describing their pathologies, medications, and symptoms. This first inference constitutes its first learning process by adding new information to the patient ontology. In the second stage, E-care consolidates all the information relative to all patients in order to enhance the system. New rules are then added by searching for similar patterns describing critical events. This second step is effective as soon as there is a lot of data to process.

Compared to other telemedicine projects, the E-Care project thus envisages an "intelligent" and communicative platform to carry out home monitoring, using non-invasive sensors, of patients with NYHA Stage III HF.[14] As such, this platform assists the medical team by automating the processing of information transmitted by these sensors in order to detect and report risk situations of cardiac decompensation early.

The platform is built around:

• A console installed in the patient's home, for collecting vital signs;
• Non-stationary signal description tools (emitted from the sensors) for the association and synchronization of measurements (EKG and PCG);
• A central application for the reasoning and processing of physiological and medical data based on semantic web technologies.

The console, installed in the patient's home, will enable the management, collection, collation, and integration of the data generated from the different non-invasive medical sensors .[14-17]

All of the above data sets will be input into a computer tablet in order to allow greater patient autonomy.

This console will be comprised of (Figure 2):

• Medical sensors: BP monitor, thermometer, weigh scale, and pulse oximeter;
• A tablet-type computer interface connected to all of these medical sensors enabling the data to be transferred and accessed.

E-care: A Prototype in Use at the Strasbourg University Hospital since October 2013

Our experimentation with the E-care system (Figure 3) began, in the first phase, at the University Hospital of Strasbourg (Strasbourg, France) in October 2013.[18] This enabled us to pro-

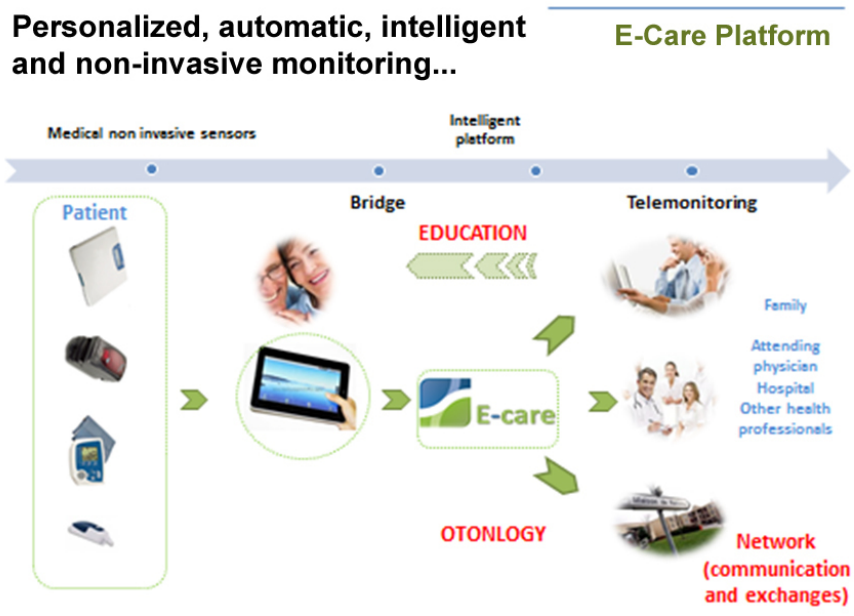


Figure 2: Version 1 of the E-care platform deployed in the Department of Internal Medicine, Diabetes and Metabolic Diseases of the University Hospital of Strasbourg.

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

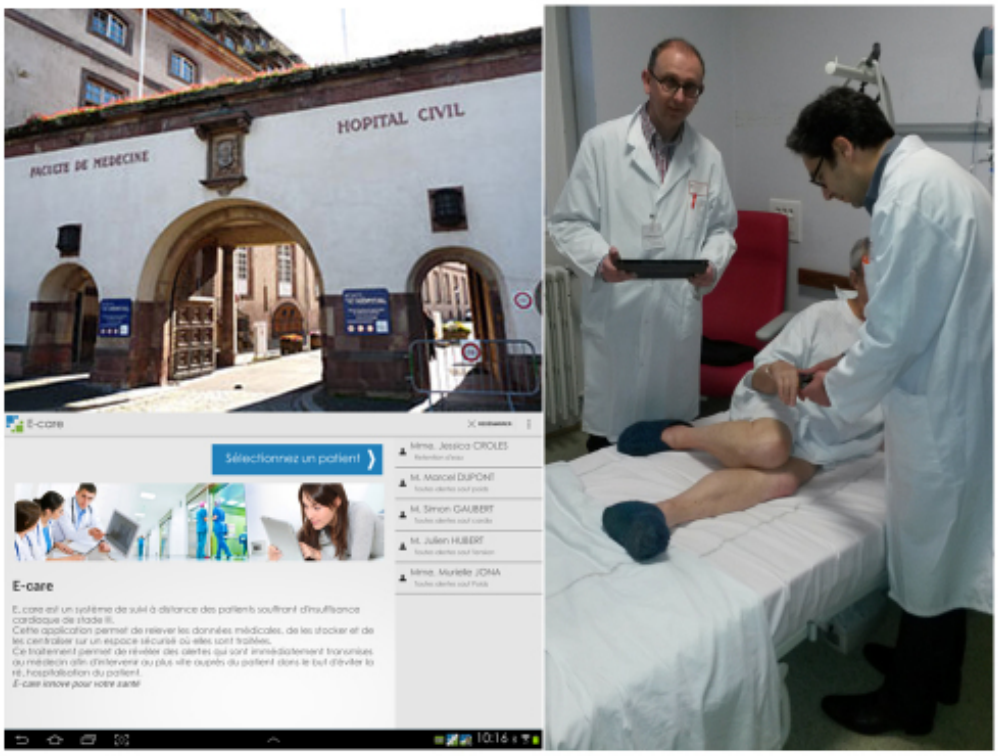


Figure 3: E-care system tested by Prof. E. Andrès and Dr. S. Talha at a patient's bedside at the Strasbourg University Hospital.

duce a preliminary report, test the various functions, improve the ergonomics, detect any vulnerabilities, and identify its strengths, with the primary objective of validating the technological and medical choices made.

The system has been deployed for 10 months, counting from the time of writing, in a 20-bed unit of the Department of Internal Medicine, Diabetes and Metabolic Diseases of the Medical Clinic B of the Strasbourg University Hospital (France). This unit is "open" to the emergency wards and constitutes part of the HF division implemented at the Strasbourg University Hospital. The patient profile included in this experiment is an elderly patient, as is the case in over 90% of cases (chronic HF >60%, anemia >40%, arrhythmia due to Atrial fibrillation (AAF) >30%, Type 2 diabetes >30%, Chronic Obstructive Pulmonary Disease (COPD) >30%, cancer 20%, renal failure >15%, higher function disorders 15%, and stroke 10%), taking more than 17 pills a day on average, with loss of autonomy observed in 25% of cases.[18]

In the first experimental phase, lasting 2 months, we validated the selected sensors deployed as part of the E-care platform using a protocol of comparative measurements from conventional hospital measuring devices (BP, heart rate, oxygen saturation, and weight) and those of the E-care system. Over 150 measurements were performed by 5th and 6th year medical students of the Faculty of Medicine of Strasbourg during their full-time immersion internship in the Department.

The retrospective analysis of these various measurements revealed a concordance between the different devices used on a daily basis in the hospital and those proposed by the E-care solution. The system operated perfectly and the experimental phase enabled us to validate the technological choices. A qualitative survey of the students helped to positively assess the system's ergonomics. A preliminary analysis of the relevance of alerts with our first inference engine design resulted in no malfunctions. In the second phase, we tested the system using (pre) determined indicators, verifying the relevance of triggered alerts, in order to assess improvements that could lead to improved patient management. The goal was to detect risk situations of cardiac decompensation early, before they degraded into acute HF. At the time of writing, the second test phase was underway in the Department, commenced in February 2014.[18] To date, over 130 patients have been enrolled and over 1,000 measurements performed. Nurses use the E-care measurement devices on a daily basis when carrying out their patient rounds. This phase relies notably on the establishment of a new human-machine interface and new inference engine. This phase includes a satisfaction and practical use survey of the system's ergonomics, filled out by caregivers and patients. The continuous gathering of data during this second phase enables us to obtain the critical mass of patients needed to conduct a more detailed analysis of the relevance of the alerts.

Once the system consolidates all the data, the third phase will consist in implementing E-care in patients' homes, first in the Strasbourg and Angers areas, as well as in mid-term hospital stays, post-care, long-term care, and in retirement homes (Figure

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-107

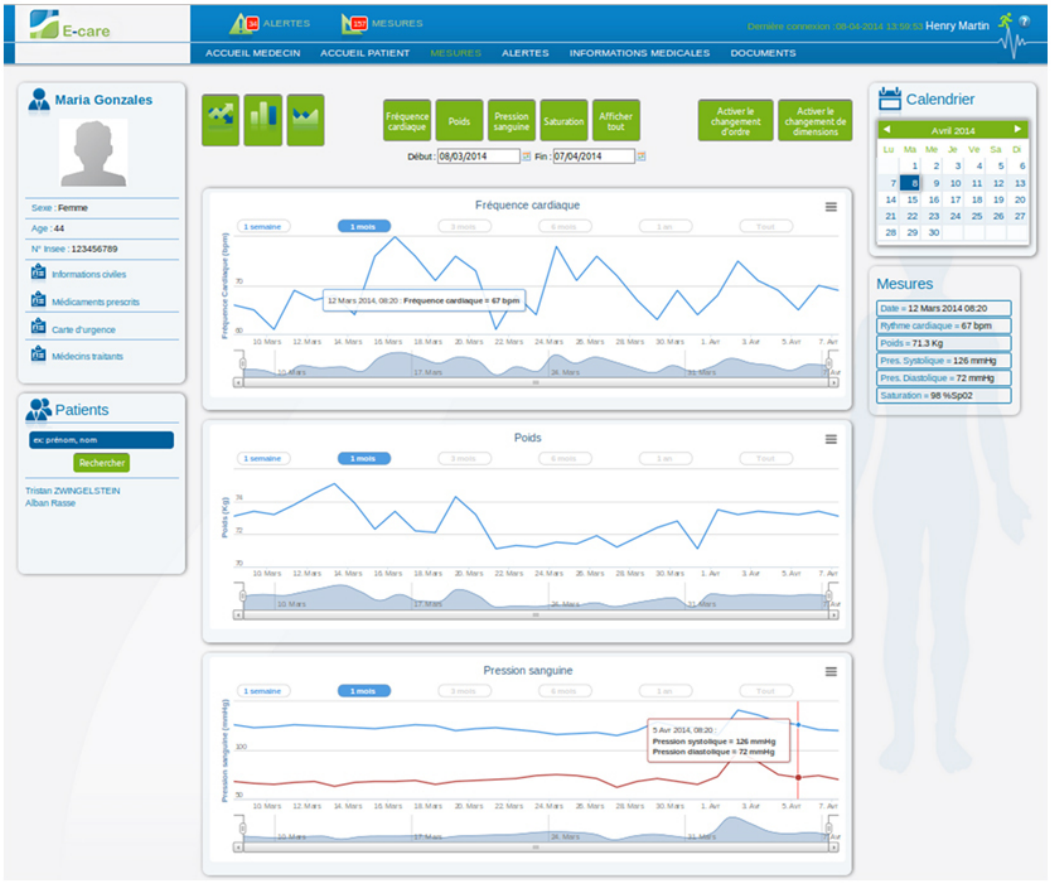


Figure 4: Version 2 of the E-care system deployed in mid-term hospital stays, post care, long-term care, and in retirement homes, as well as in patient homes.

4). This phase is expected to last 6-12 months before the solution can be marketed. The *Agence Regionale de Santé* (ARS – the French regional healthy authority) *d'Alsace* (Alsace branch) (France) (INCADO project) will provide funding for this phase as part of a national project for telemedicine HF management. This last phase will enable us to conduct a comprehensive study, notably in order to work on improving medical diagnosis by promoting the self-learning capacity of the system, therefore improving the detection of any anomaly at an even earlier stage.

The expected future development of this platform in providing a coherent solution in the field of medical monitoring will involve taking into account various diseases and equipment limitations. E-Care is an open and scalable platform enabling the sharing and management of heterogeneous data relating to different diseases.

In the future, the E-care platform should progressively be enriched with other communicating sensors, such as EKG, the electronic stethoscope, and so on, which will integrate signal processing tools enabling us to refine the detection of risk factors. Other communicating sensors could also be envisaged, such as an electronic spirometer, in order to further improve the E-care platform and extend its application to other chronic diseases, such as COPD, chronic renal failure, and other.[19,20]

CONCLUSIONS

The benefit of telemonitoring in HF remains controversial. However, this approach's various design possibilities (type of trial, number of patients, follow up, type of endpoint, etc.), technologies (structured phone support, computer support), and devices, in addition to the varying presence or absence of human intervention, have been so heterogeneous that no definitive conclusion could be made. In our opinion, recent well-designed home telemonitoring programs that used more advanced technology in HF patients have proven successful in reducing unnecessary hospitalizations.

Our telemonitoring E-Care platform uses advanced technology in order to ensure the home telemonitoring of vital signs. E-Care assists the medical staff by automating the processing of information transmitted by the sensors, automatically generating alerts in order to detect and report risk situations of HF early. The E-care platform uses an ontology designed to define a controlled vocabulary (diseases, medications, symptoms,

etc.) and to model concepts related to the monitoring of HF.

ACKNOWLEDGEMENT

All the authors collaborated on this work. E. Andrès and S. Talha designed the study, wrote the protocol, and wrote the first draft of the manuscript. E. Andrès, S. Talha, and A. Hajjam conducted the literature searches and the analysis of the results of the study. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST: None.

REFERENCES

1. Jessup M, Brozena S. Heart failure. *N Engl J Med*. 2003; 348: 2007-18. doi: 10.1056/NEJMra021498

2. Martínez-González NA, Berchtold P, Ullman K, Busato A, Egger M. Integrated care programmes for adults with chronic conditions: a meta-review. *Int J Qual Health Care*. 2014; 26(5): 561-570. doi: 10.1093/intqhc/mzu071

3. Willemse E, Adriaenssens J, Dilles T, Remmen R. Do telemonitoring projects of heart failure fit the Chronic Care Model? *Int J Integr Care*. 2014; 14: e023.

4. Anker SD, Koehler F, Abraham WT. Telemedicine and remote management of patients with heart failure. *Lancet*. 2011; 378: 731-739. doi: 10.1016/S0140-6736(11)61229-4

5. Inglis SC, Clark RA, McAlister FA, Ball J, Lewinter C, Cullington D, Stewart S, Cleland JGF. Structured telephone support or telemonitoring programmes. *Cochrane Database Syst Rev*. 2010; (8): CD007228. doi: 10.1002/14651858.CD007228.pub2

6. Feltner C, Jones CD, Cené CW, Zheng ZJ, Sueta CA, Coker-Schwimmer EJ, et al. Transitional care interventions to prevent readmissions for persons with heart failure: a systematic review and meta-analysis. *Ann Intern Med*. 2014; 160: 774-784. doi: 10.7326/M14-0083

7. Chaudhry SI, Mattera JA, Curtis JP, et al. Telemonitoring in patients with heart failure. *N Engl J Med.* 2010; 363: 2301-2309. doi: 10.1056/NEJMoa1010029

8. Koehler F, Winkler S, Schieber M, et al. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation.* 2011; 123: 1873-1880. doi: 10.1161/CIRCULATIONAHA.111.018473

9. Telesante bassenormanide. SCAD (Suivi Clinique A Domicile). Website: http://www.telesante-basse-normandie.fr/l-enrs-et-les-projets/scad,1642,1346.html. 2014; Accessed 2014.

10. Pimps. Implication, coordination, renforcement educative et biomarqueurs. Website: https://www.pimps.fr/. 2014; Accessed 2014.

11. Osicat. Optimization of Ambulatory Monitoring of heart failure patients by Telecardiology. Website: https://www.osicat.fr/. 2014; Accessed 2014.

12. Reunica. Les intérimaires et leur santé. Website: http://www.groupe.reunica.com/files/live/sites/reucorp/files/VousInformer/EspacePresse/Dossiers/PreventionSanteInterim131114.pdf. 2014; Accessed 2014.

13. Talha S. Andrès E. Place of telemedicine and e-Care project. Workshop e-Care "Knowledge engineering and signal processing for telemedicine", University of Haute Alsace, Mulhouse. 2014.

14. E-care. Project E-care. Website: http://www.projet-e-care.fr/. 2014; Accessed 2014.

15. Ahmed Benyahia A, Hajjam A, Talha S, Hajjam M, Andrès E, Hilaire V. E-care: Evolution ontologique et amélioration des connaissances pour le suivi des insuffisants cardiaques. *Médecine Thérapeutique*. 2014; 20: 79-86. doi: 10.1684/met.2014.0451

16. Ahmed Benyahia A, Moukadem A, Dieterlen A, Hajjam A, Talha S, Andrès E. Adding ontologies based on PCG analysis in E-care project. *International Journal of Engineering and Innovative Technology*. 2013; 5: 2277-3754.

17. Ahmed Benyahia A, Hajjam A, Andrès E, Hajjam M, Hilaire V. Including other system in E-Care telemonitoring platform. *Stud Health Technol Inform*. 2013; 190: 115-117. doi: 10.3233/978-1-61499-276-9-115

18. Andrès E, Talha S, Ahmed Benyahia A, et al. Project E-care: deployment of an automated system for detecting cardiac decompensation risk situations in an internal medicine unit. Congress of the French National Society of Internal Medicine of Paris, Paris, 10-12 December 2014. *Rev Med Interne*. 2014.

19. Elasri H, Sekkaki A, Hajjam A, Benmimoune L, Talha S, Andrès E. Ontologies et intégration des connaissances pour un suivi polypathologique. *Médecine Thérapeutique*. 2014; 20: 67-78. doi: 10.1684/met.2014.0449

20. Andrès E, Hajjam A, Brandt C. Advances and innovations in the field of auscultation with a special focus on the development of new intelligent communicating stethoscope systems. *Health Technol*. 2012; 2: 5-16. doi: 10.1007/s12553-012-0017-4

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

Research

*Corresponding author:
Yanmin Xu, MD, PhD
Institute of Cardiovascular Tianjin PR China, No 23 Ping Jiang Road HE XI District, Tianjin, China
Tel. 0086-13702029695
Fax: 0086-22-88328119
E-mail: xuyanminphd@aliyun.com

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2108

Article History:
Received: March 3rd, 2015
Accepted: April 10th, 2015
Published: April 13th, 2015

Citation:
Xu Y, Tian B, Sharma D, Guo X, Wang X, Fu H. The related factors and clinical predictive value of left atrial spontaneous echo contrast in patient with nonvalvular chronic atrial fibrillation. *Heart Res Open J*. 2015; 2(1): 46-50.

The Related Factors and Clinical Predictive Value of Left Atrial Spontaneous Echo Contrast in Patient with Nonvalvular Chronic Atrial Fibrillation

Yanmin Xu[2*], Bing Tian[2], Deepak Sharma[1], Xingmei Guo[2], Xindong Wang[2] and Huaying Fu[1]

[1]College of International Tianjin Medical University, Tianjin PR China, No.10 Qi Xiang Tai Road, HE PING District, Tianjin, China

[2]Institude of Cardiovascular Tianjin PR China, No 23 Ping Jiang Road, HE XI District, Tianjin, China

ABSTRACT

Background: To investigate left atrial or left atrial appendage spontaneous echo by transesophageal echocardiography for clinical risk assessment, providing an important basis for guiding treatment and so on.
Methods: Select 113 atrial fibrillation patients who did not have formal warfarin treatment in 2011-2014 and did transesophageal echocardiography, after excluding substandard patients, 92 patients were divided into LASEC positive group (n=63) and negative group (n=29). Analyses the clinical features and echocardiographic parameters. Evaluate the diagnostic value with results of multivariate analysis.
Results: The study found a significant difference ($P<0.05$) between the two groups in the type of AF (permanent AF), hypertension, left atrial diameter, left ventricular diastolic function, among these factors, persistent atrial fibrillation, left atrial diameter >40 mm and hypertension have a extremely significant difference ($P<0.01$). CHA_2DS_2-VASC score, D-dimer in plasma have a predictive value for LASEC patients with atrial fibrillation.
Conclusion: Patients with persistent AF have a higher LASEC incidence, LASEC has clinical predictive value, there are certain guiding significance in clinical practice.

KEYWORDS: Left atrial spontaneous echo contrast; Atrial fibrillation; Transesophageal Echocardiography.

ABBREVIATIONS: AF: Atrial Fibrillation; LASEC: Left Atrial Spontaneous Echo Contrast; LA: Left Atrium; LAD: Left Atrial Diameter; LVEF: Left Ventricular Ejection Fraction; LAA: Left Atrial Appendage; ANOVA: Analysis of variance; CK: Creatinekinase; PTS: Prethrombotic state; AF: Atrial Fibrillation.

INTRODUCTION

Atrial Fibrillation (AF) is one of the most common arrhythmia encountered in clinical practice that has been associated with an increased mortality and morbidity from thromboembolic complications. Transesophageal echocardiography is frequently used to identify the presence of atrial thrombogenesis, which is a useful diagnostic method to exclude atrial thrombus in patients with atrial fibrillation before undergoing radiofrequency ablation.

Left Atrial Spontaneous Echo Contrast (LASEC), which is observed as a dynamic

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

like-cloud echo signal by transthoracic and transesophageal echocardiography in the Left Atrium (LA) under the condition of non-radiography, has a varying density and morphological characters so it has no obvious contour.[1] Atrial fibrillation is the most common predisposing factor in the formation of LASEC, which is mainly related to a low left atrium blood flow velocity, blood stasis, the left atrium dysfunction and enlarged left atrium. In addition, it has been showed that AF has been associated with thromboembolic events. Some investigates showed that it was prone to LASEC when get atrial fibrillation means the change of hemodynamics and clotting mechanisms in the left atrium, which was considered prothrombotic state.[2] No doubt, the left atrial thrombus in AF patients by transesophageal echocardiography should be given anticoagulation therapy, however, some research showed that the cerebral embolism events likely up to 22% in AF patients with LASEC is an independent predictor of thromboembolic events,[3] but the formation mechanism of LASEC is not yet entirely clear, moreover, there is no an unified standard between the clinical laboratory indicators and anticoagulation therapy. This study was designed to investigate the relevance between the formation in AF patients with LASEC without formal anticoagulation therapy and multiple risk factors, and the clinical significance of the incidence of the left atrium or left atrial appendage thrombus in these patients, which could guide clinical anticoagulation therapy.

MATERIALS AND METHODS

General Information of Study Population

92 cases of patients with atrial fibrillation had no formal warfarin anticoagulation therapy, and they were all examined by transesophageal echocardiography. These selected patients were diagnosed atrial fibrillation by 24 hours dynamic electro-cardiogram, simultaneously; rheumatic valvular heart disease, congenital heart disease and prosthetic heart valve had been excluded. Among them, there are 50 males and 42 females, and mean age was 60.89±8.94 years old. According to whether LASEC existed or not, the two groups included positive and negative groups, and negative group patients had no thrombosis.

Study Protocol

Characteristics of patients were age, gender, type of atrial fibrillation, BMI, coronary heart disease, hypertension, diabetes, clinical laboratory indication and so on. CHA_2DS_2-VASC score was calculated based on risk factors. Philips iE color Doppler ultrasonography (Siemens Company, Bavaria, Germany) was used with multi-plane TEE probe, and the frequency was at 3.5~7.0 MHz. All patients signed informed consent, then TEE were performed after at least six hours of fasting, using oropharynx 2% lidocaine gel posterior pharyngeal anesthesia. In left lateral position, patients were checked by the probe to enter into a deep of 30~40 cm in esophagus, with a adjustable rear section in the left atrium to obtain the horizontal section images in pulmonary artery bifurcation levels of the Left Atrium (LA) and Left Atrial Appendage (LAA), including longitudinal section, aortic short axis section, atrial septal level and four-chamber section. The presence of SEC was diagnosed when dynamic and swirling intracavitary smoke-like echoes were detected, which were differentiated from white noise artifact by their characteristic swirling pattern and by careful attention to the gain settings.[4] At the same time 12-lead ECG was recording. All these patients underwent transthoracic echocardiography before TEE was performed.

Observed Indicators

Left Atrial Diameter (LAD), Left Ventricular Ejection Fraction (LVEF) blood velocity by mitral valve, mitral regurgitation, and diastolic function underwent transthoracic echocardiography before TEE was performed.

Statistical analysis

The statistical analyses were performed using SPSS 18.0. Metric variable were presented as mean±SD. Measurement data were analyzed by independent-samples T test. The comparisons of means between groups used Analysis of variance (ANOVA). Categorical data were analyzed using the chi-square (χ^2), and relation of data were evaluated using linear regression analysis. A p value <0.05 was considered statistically significant, and a p value <0.01 had extremely statistically significant.

RESULTS

Relation between CHA_2DS_2VASC score with risk of SEC

As summarized in Table 1, no statistically significant interaction by participant some variables, including age, BMI, abdominal girth, were detected. Also, some laboratory indicators were obtained with non significant, like Creatinekinase (CK), CK-MB, fibrinogen, blood lipid spectrum, etc, (Table 2). On the other hand, there were significant differences between the two groups in levels of D-dimer, LAD, CHA_2DS_2VASC, of which, the LAD had a extremely statistically significant ($P<0.01$), and a higher CHA_2DS_2VASC score was associated with higher risk of SEC (2.32±1,255 *vs.* 1.69±1.1, P=0.023).

The Possibility of the Presence of LA or LAA Thrombus in AF Patients

In the SEC group analysis, 44% patients had thrombogenesis (28/63) with a high morbidity that means the possibility of the presence of LA or LAA thrombus in AF patients was great. The association was stronger in patients with a decline of LV diastolic function than comparison group, which means that the decline of LV diastolic function might be one of risk factors. However, there was no statistically significant in some risk factors, like gender, CHD, DM and mitral regurgitation.

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

Presence of SEC had a Positive Correlation with Hypertension

As summarized in Table 3, there was an extremely significant difference of hypertension between two groups (P=0.007), moreover, atrial fibrillation with hypertension classification was associated with higher risk of SEC, compared with no SEC patients, the presence of SEC had a positive correlation to hypertension classification (P<0.005).

Parameter	Group with SEC(n=63)	Group without SEC(n=29)	t	P
Age	61.41±8.998	60.65±8.975	-0.379	0.706
BMI	26.43±3.78	24.92±3.29	-1.848	0.068
Abdominal Girth	84.52±10.4	84.31±7.865	-0.098	0.922
Serum creatinine	72.74±17.75	69.71±14.71	-0.802	0.425
CK	81±52.85	63.68±26.63	-1.667	0.099
CKMB	11.876±5.11	10.57±4.3	-1.19	0.237
D-dimer	0.43±0.47	0.22±0.157	-2.28	0.025▲
Fobrinogen	2.87±0.65	2.99±0.76	0.806	0.422
WBC	5.95±1.28	6.21±1.28	0.896	0.372
RBC	4.46±0.47	4.59±0.46	1.275	0.206
PLT	207.05±31.27	219.69±47.2	1.524	0.131
HCT	0.412±0.043	0.419±0.037	0.724	0.471
A/G	1.69±0.25	1.62±0.2	-1.376	0.172
TC	4.57±1.03	4.84±1.44	1.031	0.305
TG	1.7±0.848	1.72±1.22	0.07	0.945
LDL	2.87±0.817	2.98±0.911	0.568	0.571
HDL	1.05±0.28	1.13±0.28	1.166	0.247
LAD	43.73±6	37.7±5.38	-4.57	0.000▲
LVEF	59.24±6.27	59.99±5.93	0.543	0.589
MV-velocity	96.72±22.18	89.02±15.7	-1.68	0.096
CHA_2DS_2-VASC	2.32±1,255	1.69±1.1	-2.31	0.023▲

Table 1: General Characteristics of study population in two groups ($\bar{\chi}$±s, T test).

Parameter	0 class (n=27)	1 class (n=5)	2 class (n=29)	3 class (n=31)	P
Positive group (n=63)	13(48.15%)	1(20%)	26(89.6%)	23(74.19%)	P<0.005▲
Negative (n-29)	14(51.85%)	4(80%)	3(10.34%)	8 (25.8%)	

Table 2: Correlation analysis between severity of hypertension and SEC.

Parameter	Group with SEC (n=63)	Group without SEC (n=29)	chi-square value	P
Gender(femal)	26 (41.2%)	16 (55%)	1.547	0.214
CHD	29 (46%)	10 (34.4%)	1.085	0.298
Hypertension	50 (79.3%)	15 (51.7%)	7.317	0.007▲
Diabetes mellitus	14 (22.2%)	7 (24%)	0.041	0.839
LAD>40 mm	45 (73%)	7 (24%)	18.07	0.000▲
permanent AF	21 (33%)	1 (3.4 %)	9.748	0.002▲
mitral regurgitation	17 (26.9%)	7 (24.1%)	0.083	0.773
decline of LVDF	24 (38%)	18 (62%)	4.6	0.032▲

Table 3: The comparison of risk factors between two groups (χ^2 test).

DISCUSSION

In the present study, patients with SEC had thrombogenesis with a high morbidity in LA or LAA by TEE examination. There were statistical significance in presence of SEC with respect to permanent AF, hypertension, LAD >40 mm, decline of LV diastolic function. While CHA_2DS_2-VASC score and D-dimer had a predictive value to the formation of SEC.

Numerous clinical and animal experiments show that the formation of SEC was usual accompanied by thrombus and thrombogenesis almost corresponded with blood stasis. Previous studies showed that SEC could reflect hypercoagulability in LA blood,[5] which was called Prethrombotic state (PTS). PTS is a pathological process about blood coagulation fibrinolytic system involved in many factors and it is prone to cause hematological change to have a high risk for thromboembolism which increases blood coagulation, and tiny thrombosis that can increase the occurrence of thromboembolism has formed virtually with no positive presence by imageological examination. If intervention and identification are taken earlier, it may avoid thromboembolic events. However, currently, there is no uniform diagnostic criteria for PTS. D-dimer, as a maker of fibrin that has a procedure of product and degradation reflected PTS by someone, which has already reflected a slightly pathological change in blood coagulation fibrinolytic system, is quite sensitive and specificity.[6] The level of D-dimer changes has already signed thrombogenesis or thrombolysis.[7] In this study, D-dimer was found a certain predictive value to support above views, but there were no other PTS specific molecular markers, which cannot be assessed a higher predictive value of clinical laboratory indicators.

The study found that there was an extremely significant difference of hypertension between two groups (P=0.007), moreover, the presence of SEC had a positive correlation to hypertension classification. Hypertension was the most important risk factor in Nonvalvular atrial fibrillation patients,[8] and the chronic hypertension impairs myocardial contractility, then the increased left ventricular diastolic pressure overload leads to elevation of the left atrial pressure, which causes decompensated LA enlargement, thus bloodstream slows down to result in blood stasis, sequentially Red Blood Cell (RBC) makes conglutination and aggregation to form local hypercoagulable state. Blood stasis in LA or LAA is one of the important mechanisms of LASEC formation. Our study found that incidence rate of LASEC had a positive correlation to hypertension classification that means hypertension was same as the main risk factor in LASEC patients.

The CHA_2DS_2-VASc score was calculated from the sum of risk predictors of congestive heart failure; hypertension; age ≥75 years; type 2 diabetes; previous stroke, TIA, or thromboembolism ; vascular disease; and sex category. Score of ≥2 means high-risk, score of 1 means moderate risk, low risk score is 0. The $CHADS_2$ and CHA_2DS_2-VASc scores are originally formulated for risk assessment of stroke in patients with

non-valvular Atrial Fibrillation (AF). A recent study found that CHA_2DS_2-VASC had better discrimination than $CHADS_2$ for predicting risk for thromboembolism in atrial fibrillation,[9] and the CHA_2DS_2-VASc score is believed to have better prognostic predictive value for thrombotic events in low-risk patients. In this study, there was statistical significant difference of two groups assessed by CHA_2DS_2-VASc score, which means the higher risk of stroke in the group with LASEC, indicating CHA_2DS_2-VASc score that could apply to AF patients with LASEC, and it perhaps was regarded as a routine evalution system to predict stroke. CHA_2DS_2-VASC score is also a risk index for predicting stroke in patients with SEC, and not only it contributes to identify PTS timely, but also it guides valid anticoagulation therapy to prevent serious thromboembolism complication.

In this study, the indices to diagnose left ventricular diastolic function was spectral tissue doppler imaging of the lateral mitral annulus early diastolic velocity (e) / late diastolic velocity (a) [e/a], or pulsed-wave doppler recording of early diastolic mitral inflow velocity (E) / e [E/e], which was significantly different (P =0.032). Doukky R, et al.[10] found that the diastolic function indices E:e' and e' velocity were independently associated with LAAT in Nonvalvular AF patients and might help identify patients at risk for LAAT, which was coincided with this study that the diastolic function indicate also predicted SEC independently.

It has been reported that 85% patients with thromboembolism had LASEC or AF. The earliest study was Daniel, et al.[11] that they found LA thrombogenesis usually existed with LASEC, and a low thrombotic incidence in patients without SEC through the study of 52 patients with severe mitral stenosis, thus SEC was considered as a predictive index before MS or prosthetic heart valve surgery. Takayuki, et al.[12] divided 84 AF patients with SEC from anticoagulant group and non- anticoagulant group, after 8~14 weeks follow-up, there was a statistical significant difference that the former incidence of cerebral embolism was 0%, the latter was 11.9%, which suggested that LASEC patients were high risk group. In addition, fresh LA thrombus is easy to fall off or dissolve by fibrinolysin without visualized place or size by ultrasonic probe, therefore, LASEC could get a long-time existence to have a higher prediction of stroke, and it also prompts clinicists to take anticoagulation therapy to prevent thrombogenesis.

CONCLUSION

LASEC could get a long-time existence to have a higher prediction of stroke, and it also prompts clinicists to take anticoagulation therapy to prevent thrombogenesis.

ACKNOWLEDGEMENTS

Dr. Xu is the guarantor for this article, and takes responsibility for the integrity of the work as a whole.

FUNDING

Supported in part by grants from foundation and ministry of health of Tian Jin.

CONFLICTS OF INTEREST: None declared.

REFERENCES

1. Fatkin D, Kell RP, Feneley MP. Relation between left atrial appendage blood flow velocity aspontaneous echocardioghraphic contrast and thromboembolic risk *in vivo*. *J Am Coll Cardial.* 1994; 23(4): 961-969. doi: 10.1016/0735-1097(94)90644-0

2. Zhang Y, Zhang M, Ge ZM. International echocardiography. *Shandong*. 2000; 2000: 477.

3. Bernhardt P, Schmidt H. Patients with atrial fibrillation and dense spontaneous echo contrast at high risk. *JACC.* 2005; 45 (11): 1807-1812. doi: 10.1016/j.jacc.2004.11.071

4. Sahin T, Acar E, Celikyurt U, et al. Relation of hs-CRP and BNP levels with the atrial spontaneous echo contrast and thrombi in permanent atrial fibrillation patients with different etiologies. 2012; 18(2): CR78–CR87. doi: 10.12659/MSM.882461

5. Wan A, Harrison JK, Bashore TM, et al. Correlation between quantitative left atrial spontaneous echocardiography contrast and intact fibrinoen levels in mitral stenosis. *J Am Soc Echocardiography.* 2001; 14(4): 285-291. doi: 10.1067/mje.2001.111266

6. Mahe I, Drouet L, Simoneau G, et al. D-dimer can predict survival in patients with chronic atrial fibrillation. *J Blood Coagul Fibrinolysis*. 2004; 15(5): 413-417.

7. Lixin RAO, Muhuab Li. The effect of warfarin in treatment atrial fibrillation with cerebrella infarction and the change of D-Dimmer. *Chinese Clinic Neorology.* 2010; 13(20): 5-7.

8. Healey JS, Connolly SJ. Atrial fibrillation : hypertension as a causative agent risk factor for complications and potential therapeutic target. *Am J Cardiol.* 2003; 91(10A): 9G-14G. doi: 10.1161/CIRCULATIONAHA.107.760777

9. Cairns JA. CHA_2DS_2-VASC had better discrimination than CHADS2 for predicting risk for thromboembolism in atrial fibrillation. *Ann Intern Med.* 2011; 154(10): JC5-JC13.

10. Doukky R, Garcia-Sayan E. The value of diastolic function parameters in the prediction of left atrial appendage thrombus in patients with nonvalvular atrial fibrillation. *J Cardiovascular Ultrasound.* 2014; 12: 10. doi: 10.1186/1476-7120-12-10

11. Daniel WG, Nellessen V, Schroder E, et al. Left Atrial spontaneous echo contrast in mitral valve disease: An indicator for an increased thromboembolic risk. *J Am Coll Cardiol*. 1988; 11(6):

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

1204. doi: 10.1016/0735-1097(88)90283-5

12. Hirabaya S, Mochizuki N, Miymto N, et al. Spontaneous contrast echo raises and warfarin treatment reduces the risk of cerebral embolism in patient with nonvalvular chronic atrial fibrillation. *Circulation.* 1992; 86(4 suppl): I-398.

HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-109

Illustration

Corresponding author:
Vineet Bhatia, MBBS, MD, DM, DNB, MNAMS, FESC
Senior Consultant Cardiologist
Department of Cardiology
Fortis Hospital
Noida, India
E-mail: vinmonica@yahoo.co.in

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2109

Article History:
Received: April 8th, 2015
Accepted: April 14th, 2015
Published: April 16th, 2015

Citation:
Bhatia V, Arora P, Minocha A. Saddle thrombus seen on transthoracic echo: a rare feature in pulmonary embolism. *Heart Res Open J*. 2015; 2(1): 51-52.

Saddle Thrombus seen on Transthoracic Echo: A Rare Feature in Pulmonary Embolism

Vineet Bhatia*, Parneesh Arora and Anil Minocha

Department of Cardiology, Fortis Hospital, Noida, India

The Saddle thrombus is a rare condition characterized by presence of a large thrombus which straddles the main pulmonary arterial trunk and its bifurcation leading to acute massive Pulmonary Embolism (PE). Its incidence among patients diagnosed with PE is approximately 2.6%.[1] Saddle PE frequently results in significant hemodynamic instability and signals the potential for imminent hemodynamic collapse. This is rarely seen on Trans-thoracic echocardiography (TTE). We recently came across a patient who presented with breathlessness following transatlantic air travel. His TTE (routine and 3D) revealed a saddle thrombus in the main pulmonary arterial trunk extending into its two main branches (Figures 1 and 2). A CT pulmonary angiogram confirmed the same (Figure 3). He was subsequently successfully thrombolyzed and made an uneventful recovery.

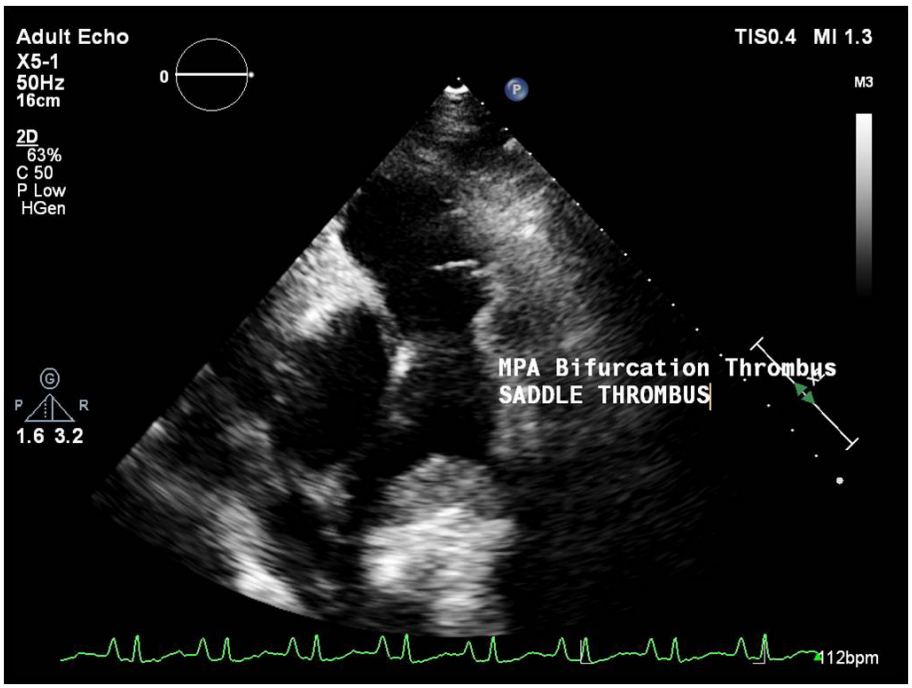


Figure 1: Echocardiographic Parasternal short axis view (PSAX) shows a saddle thrombus at the Main Pulmonary artery bifurcation extending into its two branches (marked by an arrow).

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-109

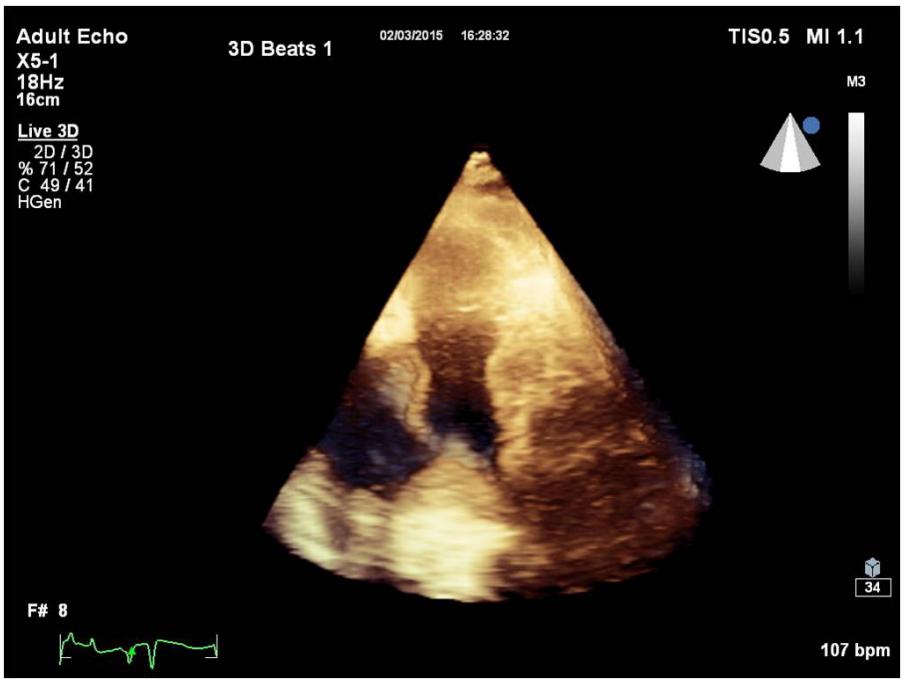


Figure 2: 3 dimensional Echocardiographic Parasternal short axis view (PSAX) shows a saddle thrombus at the Main Pulmonary artery bifurcation extending into its two branches.

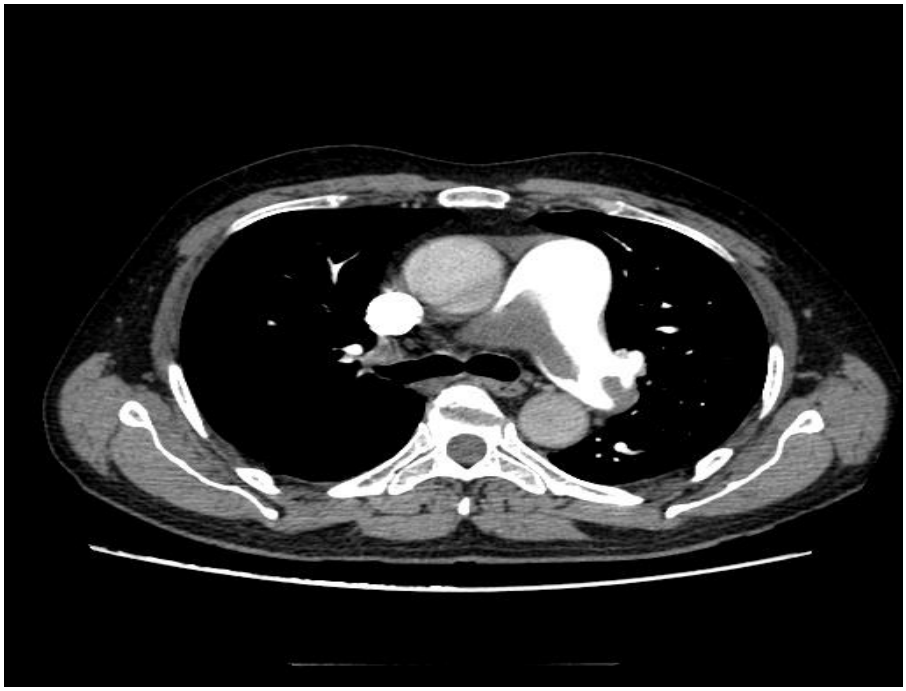


Figure 3: A CT pulmonary angiogram showing the saddle thrombus.

CONFLICTS OF INTEREST: None.

REFERENCES

1. Pruszczyk P, Pacho R, Ciurzynski M, et al. Short term clinical outcome of acute saddle pulmonary embolism. Heart. 2003; 89: 335-336. doi: 10.1136/heart.89.3.335