Modeling of the Effect of Dilated Cardiomyopathy on the Behavior of the Heart

Fatma H. Mohammed

Biomedical Engineering

Department

Helwan University

Helwan, Cairo, Egypt

eng.fatma.hanafy@gmail.com

Essam M. Shafei

Biomedical Engineering

Department

Helwan University

Helwan, Cairo, Egypt

shafei essam@hotmail.com

Ahmed M. El-Garhy

Communication Engineering

Department

Helwan University

Helwan, Cairo, Egypt
agarhy2003@yahoo.co.in

Mohammed A. El-Dosoky

Biomedical Engineering

Department

Helwan University

Helwan, Cairo, Egypt

hm1 eldosoky@hotmail.com

Abstract— In this study, a nonlinear time-varying lumped parameter mathematical model of left sided heart failure had been proposed. One of the causes of systolic heart failure is Dilated Cardiomyopathy, was studied. Many tries were done to know the appropriate parameters in the model to express Dilated Cardiomyopathy as a case of heart failure. Ventricular elastance was found to be the most suitable parameter to present Dilated Cardiomyopathy. Mathematical equations for the change of heart rate and left ventricular pressure with time with decreasing ventricular elastance were concluded. The effects of Dilated Cardiomyopathy on heart rate, left ventricular pressure-volume loop (P-V loop), left ventricular pressure, stroke volume and ejection fraction were modeled.

Keywords—Heart Failure, Dilated Cardiomyopathy, Cardiovascular System, Systolic Heart Failure, Modeling.

I. INTRODUCTION

More than 26 million people world-wide suffer from Heart Failure (HF) [1]. Approximately half of patients who suffer from HF die within 5 years of diagnosis [2, 3].

HF has three types: left-sided heart failure, right-sided heart failure and congestive heart failure [4].

The human cardiovascular system is one of the important systems in human body. It is not easy to be modelled, where it is a time-varying nonlinear system. Cardiovascular system lumped parameter models have been developed for many years for a variety of objectives [5-11]. Mathematical modelling facilitates studying of heart failure in the practical areas of clinical diagnosis and treatment.

Previous studies have been used to model Heart Failure (HF) without studying any of its causes [6, 8, 10, 11]. In these studies, one heart failure condition was studied. None of them had simulated the effect of any of causes of HF on the behavior of the heart. Thus the main purpose of this paper is to study one of causes of the Systolic Heart Failure (SHF) in details. These by studying the effect of the worsening SHF condition on the behavior of the heart.

The most common causes of SHF are summarized: Coronary artery disease, past heart attack (myocardial infarction), High blood pressure (hypertension or HBP), abnormal heart valves, Heart muscle disease (dilated cardiomyopathy, hypertrophic cardiomyopathy) or inflammation (myocarditis), Heart defects present at birth (congenital heart disease), severe lung disease, Diabetes, Obesity, and Sleep Apnea [12].

In this study, one of causes of SHF is dilated cardiomyopathy, was studied and modelled. Dilated Cardiomyopathy (DCM) is defined as an extension of the left ventricular (LV) cavity diameter without the existence of hypertension or valve disease. Consequently, dysfunction happens to left ventricular systolic. As a result of DCM a notable increment of chamber volumes and ventricular wall thickness are occur [13]. It often extends to the right ventricle and then to the atria. Thus, heart muscle cannot contract as normal. So, it cannot pump blood very well, and the heart becomes weaker [14].

In Heart Failure patients, Left Ventricular Ejection Fraction (LVEF) is about 40% or less, but in normal case LVEF is about 50% to 70% [15, 16].

In this paper, a lumped parameter model of the systemic and pulmonary circulations with baroreflex control was implemented using Matlab/Simulink program. Many tries were done to know the appropriate parameters in the model to express DCM as a case of HF. Ventricular elastance represents ventricular muscle ability to contract. Consequently, Ventricular elastance is the most suitable parameter to model DCM as a case of HF. As ventricular elastance decreases, the ability of ventricular muscle to contract decreases. Therefore, the output blood from heart decreases.

Simulations were performed for many cases. These include nominal steady state condition and different DCM as a case of HF conditions. Each case was studied separately. Results for heart rate (HR), left ventricular pressure-volume loop (P-V loop), left ventricular pressure (P_{lv}), stroke volume (SV) and ejection fraction (EF) were reviewed for each case. All results were compared with normal case. Relations between decreasing Ventricular elastance and HR, P_{lv} , SV, EF were estimated. Previous studies did not estimate this relations. Therefore, the most suitable design of ventricular assistant device (VAD) for each condition can be known.

It was found that as ventricular elastance decreases, HR and left ventricular diastolic pressure increases and SV, EF

and left ventricular systolic pressure decrease. This will be reviewed in detail in this paper.

Results of simulation display that this model is well-suited to mimic DCM as a case of HF.

II. PROPOSED WORK

Mathematical relations between decreasing Ventricular elastance and HR, P_{lv}, SV, EF were not previously concluded. Previous studies have been used to model and study one heart failure condition [6, 8, 10, 11]. So, in this paper a lumped parameter model of the systemic and pulmonary circulations was implemented using Matlab/Simulink program. This model is used to model DCM as a case of HF. Many tries were done to know the appropriate parameters in the model to express DCM as a case of HF. Ventricular elastance represents ventricular muscle ability to contract [17-20]. Consequently, Ventricular elastance is the most suitable parameter to model DCM as a case of HF. Thus, DCM is modelled by decreasing left ventricular elastance (E_{max,lv}). Then results for HR, P_{lv}, SV and EF were reviewed. Mathematical equations for the change of HR and P_{lv} with time with decreasing $E_{max,lv}$ were concluded.

III. MATERIAL AND METHOD

A. Cardiovascular Model

Ursino nonlinear time-varying lumped parameter model of the circulatory system [5] was modified to simulate DCM. The constituents of cardiovascular system were simulated using electrical analogs. [8, 9].

B. Case Study of Dilated Cardiomyopathy (DCM)

Simulations were performed for different cases. These include nominal steady state condition and different DCM conditions. Each case was studied separately. The Matlab/Simulink program was used to perform all simulations. The value of $E_{\text{max,lv}}$ was obtained as in [5]

value of
$$E_{\text{max,lv}}$$
 was obtained as in [5]
$$\sigma_{\text{Emax,lv}}(t) = \begin{cases} G_{\text{Emax,lv}} \cdot \ln \left[f_{\text{es}}(t - D_{\text{Emax,lv}}) - f_{\text{es,min}} + 1 \right] & \text{if } f_{\text{es}} \ge f_{\text{es,min}} \\ 0 & \text{if } f_{\text{es}} \le f_{\text{es,min}} \end{cases}$$

$$(d\Delta E_{\text{max,lv}}(t) / dt) = (1 / \mathbb{T}_{\text{Emax,lv}}) \cdot (-\Delta E_{\text{max,lv}}(t) + \sigma_{\text{Emax,lv}}(t)) \qquad (2)$$

$$E_{\text{max,lv}}(t) = \Delta E_{\text{max,lv}}(t) + E_{\text{maxlv},0}$$
 (3)

Where $\sigma_{E_{max,lv}}$ is the output of the static characteristic, $G_{E_{max,lv}}$ is elastance gain for left ventricle and equals 0.475 mmHg/mL/v, $D_{E_{max,lv}}$ is time delay for elastance of left ventricle and equals 2 sec, $f_{es,min}$ is the minimum sympathetic stimulation and equals 2.66 spikes/sec, f_{es} is the frequency of spikes in the efferent sympathetic nerves, $\tau_{E_{max}}$ iv is time constant for elastance of left ventricle and equals 8 sec, $\Delta E_{max,lv}$ is the change in elastance of left ventricle caused by sympathetic stimulation, $E_{max,lv,0}$ is basal level of maximum end-systolic elastance of left ventricle and equals 2.392 mmHg/ml.

Here, The value of $E_{max,lv}$ was simulated to represent the weak heart muscle as decrement by value (1/*i*) of its nominal value and *i* was expressed as alternative values between 1 and 7. Hence

$$E_{\text{max,lv, new}} = (1/i) * E_{\text{max,lv}}$$
 (4)

Then HR, P_{lv} and left ventricular pressure-volume (P-V) loops were affected and modelled for each case, and from (P-V) loops the following indices were estimated: left ventricular stroke volume (SV),

$$SV = EDV - ESV$$
 (5)

and left ventricular ejection fraction (LVEF),

$$LVEF = ((EDV - ESV)/EDV) \times 100\%$$
 (6)

The simulation results were compared with normal case. The relation between $E_{\text{max,lv}}$ and heart rate (HR), left ventricular pressure-volume loop (P-V loop), left ventricular pressure (P_{lv}), stroke volume and ejection fraction were reviewed. Then, by Using curve fitting tool in MATLAB, mathematical equations for the change of HR and P_{lv} with time with decreasing $E_{\text{max,lv}}$ were concluded.

IV. RESULTS AND DISCUSSION

 $E_{\text{max,lv}}$ has a major effect in heart performance. Fig. 1 shows the effect of decreasing $E_{\text{max,lv}}$ on P-V loop. It was noted that as $E_{\text{max,lv}}$ decreases it means heart muscle going to be weaker. Therefore, the dilated ventricle had a maximal point of preload reserve, beyond which incremental distention caused a decline in output. Consequently, P-V loops were shifted to right. Thus, left ventricular pressure (P_{lv}) decreases, end systolic and diastolic blood volumes in left ventricle increase and Stroke Volume and ejection fraction decreases, next a detailed study of each one of them.

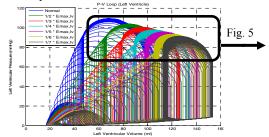


Fig. 1. Left Ventricular P-V Loops when decreasing Emax,lv

A. Heart Rate (HR)

When $E_{max,lv}$ decreases, the heart muscle is weakened, which affects its ability to pump properly. AS a result, the cardiac output decrease. Therefore, Heart tries to pump faster to increase the cardiac output, which means heart rate increases [21]. Thus, Heart rate changes as $E_{max,lv}$ changes in an inversely relation. Fig. 2 shows the simulated HR from the model.

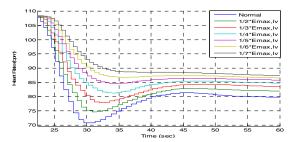


Fig. 2. Heart Rate when decreasing $E_{max,lv}$

Using curve fitting tool in MATLAB, Heart Rate was found to change similar to the behavior of the following equation:

$$HR(t) = a_1 * \sin(b_1 * t + c_1) + a_2 * \sin(b_2 * t + c_2) + a_3 * \sin(b_3 * t + c_3) + a_4 * \sin(b_4 * t + c_4)$$

$$Where 22 \le t \le 58$$
(7)

The coefficients a_1 , b_1 , c_1 ,, a_4 , b_4 , c_4 changes in each case in range from -3.5 to 155.6. Fig. 3 shows the simulated HR from (7). Equation (7) is valid in time range from t = 22 sec to t = 58 sec.

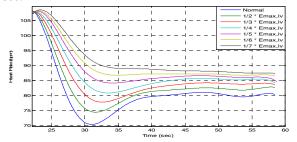


Fig. 3. Heart Rate waveforms when decreasing Emax,lv result from (7)

B. End Systolic pressure-Volume Relationship (ESPVR)

ESPVR changes according to [17]:

$$P_{lv}(t) = E(t)*(V_{lv}(t) - V_{u,lv})$$
 (8)

Where E, ventricle elastance at the instant of maximum contraction, changes in each case in range from 0.85 to 3.03. Fig. 4 shows the simulated ESPVR from the model at $t\approx45$ sec.

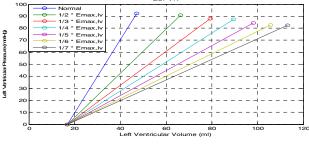


Fig. 4. ESPVR when decreasing $E_{\text{max,lv}}$

As Noted in Fig. 4 as $E_{max,lv}$ decreases ESPVR decrease. The change of E from normal case (ΔE) at t≈45 sec is in range between -2.1762 and -1.201. As $E_{max,lv}$ decreases ΔE decreases. Consequently, the end systolic volume increases, end systolic pressure decreases and E decreases.

C. Left Ventricular Pressure:

When heart can't pump properly this means Left Ventricular Systolic Pressure is less than its normal value so less blood out from left ventricle than normal. Also, more blood residual in LV, so LV diastolic pressure increases.

1) Left Ventricular Systolic Pressure

It decreases as $E_{max,lv}$ decreases. Fig. 5 shows the simulated maximum left ventricular systolic Pressure ($P_{lv,max,sys}$) from the model.

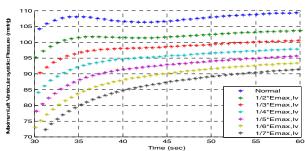


Fig. 5. Maximum left ventricular systolic Pressure when decreasing $$E_{\mbox{\scriptsize max,lv}}$$

Using curve fitting tool in MATLAB, P_{lv,max,sys} was found to change similar to the behavior of the following equation:

$$\begin{split} P_{lv,max,sys}(t) &= p_1*t^5 + p_2*t^4 + p_3*t^3 + p_4*t^2 + p_5*t + p_6 \\ &\text{The coefficients } p_1,....,p_6 \text{ changes in each case in range} \\ &\text{from -2567.4 to 296.87. Fig. 6 shows the simulated maximum} \end{split}$$

left ventricular systolic Pressure from (9)

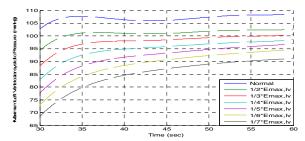


Fig. 6. Maximum left ventricular systolic Pressure when decreasing E_{max,Ix} result from (9)

At constant time: t≈45 sec, the change of maximum left ventricular systolic pressure from normal case ($\Delta P_{lv,max,sys}$) is in range between -19.265 and -5. As $E_{max,lv}$ decreases $\Delta P_{lv,max,sys}$ decreases by mean -2.853.

2) Left Ventricular Diastolic Pressure

It increases as $E_{\text{max,Iv}}$ decreases, and was found to change as shown in Fig. 7

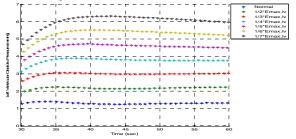


Fig. 7. Left Ventricular Diastolic Pressure when decreasing E_{max,lv}

At time: $t\approx 45$ sec, the change of initial left ventricular diastolic pressure from normal case ($\Delta P_{lv,dia}$) is in range between 0.891 and 5.041. As $E_{max,lv}$ decreases $\Delta P_{lv,dia}$ increases by mean 0.83.

D. Stroke Volume (SV)

It decreases as $E_{max,lv}$ decreases. At time: t \approx 45 sec, the value of SV in each case was shown in Fig. 8

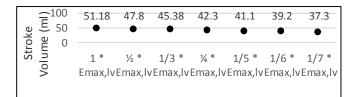


Fig. 8. Stroke Volume when decreasing $E_{max,lv}$ at $t\approx 45$ sec The change of stroke volume from normal case (ΔSV) at time $t{\approx}45$ sec is in range between -13.88 between -3.38, and as $E_{max,lv}$ decreases ΔSV decreases by mean -2.1.

E. Left Ventricular Ejection Fraction (LVEF)

In normal Heart, Left Ventricular Ejection Fraction (LVEF) is about 50% to 70% and in Heart Failure is about 40% or less [19, 20]. In this Model, at time $t\approx 45$ sec for normal heart LVEF is equal to 52.33% and for SHF, LVEF is about 36.538% when $E_{\text{max,lv}}$ is about 1/3 of its nominal value. The value of LVEF (%) with decreasing $E_{\text{max,lv}}$ at time: $t\approx 45$ sec is shown in Fig. 9.

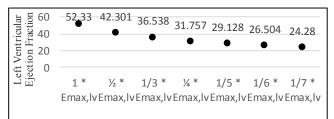


Fig. 9. Left Ventricular EF when decreasing E_{max,lv}

The change of left ventricular ejection fraction from normal case ($\Delta LVEF$) at time t \approx 45 sec is in range between -28.05 and -10.029, and as $E_{max,lv}$ decreases $\Delta LVEF$ decreases by mean -3.6.

V. CONCLUSION

A nonlinear time-varying lumped parameter model of the circulatory system had been proposed to simulate DCM disease by decreasing $E_{\text{max,lv}}$. Using Matlab/Simulink program simulations were done for nominal and different DCM cases. Mathematical equations for the change of HR and P_{lv} with time with decreasing $E_{\text{max,lv}}$ were concluded.

It was found that as $E_{max,lv}$ decreases contractility of heart muscle decreases so SV, EF and left ventricular systolic pressure decrease and HR and left ventricular diastolic pressure increases. Results of simulation display that this model is well-suited to mimic DCM as a case of HF.

REFERENCES

- Gianluigi Savarese and Lars H Lund. Global Public Health Burden of Heart Failure. © 2017, Radcliffe Cardiology. Cardiac Failure Review 2017;3(1):7–11.
- [2] Centers for Diease Control and Prevention (June 16, 2016 update), Heart Failure Fact Sheet from: https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_failure.htm
- [3] Roger VL, Weston SA, Redfield MM, et al. Trends in heart failure incidence and survival in a community-based population. JAMA. 2004; 292(3): 344-350.

- [4] American Heart Association (May 2017): http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Types-of-Heart-Failure_UCM_306323_Article.jsp#.Wpbm82pubIU
- [5] Ursino, Mauro. Interaction between carotid baroregulation and the pulsating heart: a mathematical model. Am. J. Physiol. 275 (Heart Circ. Physiol. 44): H1733–H1747, 1998.
- [6] A. Ferreira, S. Chen, M.A. Simaan, J.R. Boston, and J.F. Antaki. A nonlinear state-space model of a combined cardiovascular system and a rotary pump. In Proceedings of the 44th IEEE Conference on Decision and Control and European Control Conference (CDC-ECC'05), pages 897–902, Seville, Spain, December 2005.
- [7] Garcia D, Barenbrug PJ, Pibarot P, Dekker AL, van der Veen FH, Maessen JG, Dumesnil JG, Durand LG. A ventricular-vascular coupling model in presence of aortic stenosis. Am J Physiol Heart Circ Physiol 288: H1874–H1884. 2005.
- [8] Wu Y, Allaire PE, Tao G, Olsen DB. Modeling, Estimation and Control of Cardiovascular Systems with A Left Ventricular Assist Device, Proceeding of American Control Conference 2005: 3841-46, Portland, OR. June 2005
- [9] Hassanain Ali Lefta Mossa: Engineering Modeling of Human Cardiovascular System. The 1st Regional Conference of Eng. Sci. NUCEJ Spatial ISSUE vol.11,No.2, 2008 pp 307-314
- [10] Deepa P. Ramachandran, Chuan Luo, Tony S. Ma, and John W. Clark Jr. Modeling Study of the Failing Heart and its Interaction with an Implantable Rotary Blood Pump. Conf Proc IEEE Eng Med Biol Soc. 2011; 2011: 2403–2409.
- [11] Wang Y, Loghmanpour N, Vandenberghe S, Ferreira A, Keller B, et al. Simulation of Dilated Heart Failure with Continuous Flow Circulatory Support. PLoS ONE 9(1): e85234, 2014. doi:10.1371/journal.pone.0085234.
- [12] American Heart Association (May 2017): http://www.heart.org/HEARTORG/Conditions/HeartFailure/CausesAnd RisksForHeartFailure/Causes-of-Heart-Failure_UCM_477643_Article.jsp#.WxDoPe6FPIV
- [13] Allen P. Burke, Fabio Tavora: Practical Cardiovascular Pathology, Lippincott Williams & Wilkins, chapter 13, pp 148-157, Nov.2010.
- [14] American Heart Association (March 2016): http://www.heart.org/HEARTORG/Conditions/More/Cardiomyopathy/ Dilated-Cardiomyopathy_UCM_444187_Article.jsp#.WxHmse6FPIV
- [15] American Heart Association (May 2017): http://www.heart.org/HEARTORG/Conditions/HeartFailure/Diagnosing HeartFailure/Ejection-Fraction-Heart-Failure-Measurement UCM 306339 Article.jsp#.WoJsNSWxXIU
- [16] Richard Lehman, Jenny Doust, Paul Glasziou: Cardiac impairment or heart failure? "Heart failure" confuses doctors and patients and needs renaming. BMJ VOLUME 331 20-27 AUGUST 2005
- [17] Suga H, Sagawa K, Shoukas AA: Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res 1973, 32:314-322
- [18] Shishido T, Hayashi K, Shigemi K, Sato T, Sugimachi M, Sunagawa K: Single-beat estimation of end-systolic elastance using bilinearly approximated time-varying elastance curve. Circulation 2000, 102:1983-1989
- [19] A. Kiani, J. Gilani Shakibi: Normal Value of Left Ventricular End-Systolic Elastance in Infants and Children. IJMS Vol 28, No.4, December 2003
- [20] Shihara H, Yokoda M, Sobue T, Saito H: Relation between ventriculoarterial coupling and myocardial energetics in patients with idiopath-ic dilated cardiomyopathy. J Am Coll Cardiol 1994;23: 406-16
- [21] American Heart Association (May 2017): http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeart Failure/What-is-Heart-Failure_UCM_002044_Article.jsp#.WttjQS5ubIX