Mathematical Biosciences xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Modeling of cardiovascular circulation for the early detection of coronary arterial blockage

Karan Jain*, Srinivasu Maka, Amit Patra

Department of Electrical Engineering, Indian Institute of Technology Kharagpur 721302, India

ARTICLE INFO

Keywords:
Blood pressure
Cardiovascular model
Coronary arterial blockage
Ejection fraction
Heart
Nonlinear system

ABSTRACT

Coronary arteries are responsible for maintaining blood supply to the heart. When these arteries get blocked due to plaque deposition, the corresponding pathological condition is referred to as coronary artery disease. This disease develops gradually over the years and consequently, the function of the heart deteriorates, leading to a heart attack in many cases. As the symptoms manifest themselves only when it has become severe, detection of the disease often gets delayed. In order to detect it early and take preventive action, this work is aimed at detecting the arterial blockage in its early stage via cardiovascular modeling. To achieve this, the cardiovascular circulation has been modeled as a sixth order nonlinear system. Blood circulation in a body is viewed as an electrical system using the pressure-voltage analogy. In this case, the heart is considered as a self-excited generator. The rest of the body tissues form a systemic load. In the models reported in the literature, coronary circulation has been assumed to be a part of the systemic load. However, this circulation path has its own importance as it is responsible for the blood supply to the heart. Therefore, in our work, the coronary path is separated out from the rest of the body tissues. This enables us to explicitly model the coronary arterial resistance and thereby helps us to detect coronary arterial blockage condition by estimating this parameter from blood pressure measurements. Increase in the coronary resistance is found to reduce the left ventricular ejection fraction; this information can therefore be used as an index for coronary arterial blockage. It has been shown that the systolic function of the heart deteriorates when the resistance of the coronary path increases beyond a critical value; the situation can be related to a severe blockage condition. The model has been tested on a chosen sample of 20 subjects suffering from coronary artery disease and the results are found to be quite promising.

1. Introduction

Coronary arteries play an important role in maintaining blood supply to the heart. The coronary artery disease (CAD) develops when these arteries get damaged or blocked due to deposition of plaque on the inner walls of the arteries. As the plaque deposition increases, the blood supply to the heart starts decreasing, which eventually leads to the deterioration of the function of the heart. This may even lead to a heart attack. Further, the traditional approach to diagnose CAD has been ECG measurement followed by echocardiography and then coronary angiography, as needed. However, usually these diagnostic tests are recommended, only when there are symptomatic changes, and the disease has already become very severe. Some of the previous works attempted to detect CAD using fingertip Photoplethysmogram (PPG) and/or Phonocardiogram (PCG) signals [1,2]. They could produce a binary prediction whether a subject is suffering from coronary artery disease or not with reasonable accuracy. However, these approaches do not reveal much about the severity of the blockage; thereby lack wide acceptability by the medical fraternity. *This work* is aimed at detecting the arterial blockage in its early stage via cardiovascular modeling.

In the literature, many cardiovascular models have been reported. Grodin analyzed the cardiovascular system as a feedback regulator [3]. The controlling system comprised the medullary cardiovascular centers as well as endocrine glands which operate upon the heart and blood vessels. The controlled system comprised the mechanical and gas exchanger elements of the cardiovascular system. Guyton et al. proposed a detailed model for overall circulation that was composed of 354 blocks, each of which represented one or more mathematical equations describing some physiological facet of circulatory function [4]. Suga and Sagawa's model [5] is also among the classical models that highlight instantaneous left intra-ventricular pressure and volume ratio as an index to measure the contractile state of the ventricular chamber. Also, heart's system of self-regulation is analyzed via concepts of automatic control theory as reported in literature [6].

---

* Corresponding author.

E-mail addresses: karanjain@ee.iitkgp.ernet.in (K. Jain), maka@ee.iitkgp.ernet.in (S. Maka), amit@ee.iitkgp.ernet.in (A. Patra).

https://doi.org/10.1016/j.mbs.2018.08.002
Received 16 December 2016; Received in revised form 27 February 2018; Accepted 1 August 2018

Please cite this article as: Jain, K., Mathematical Biosciences (2018), https://doi.org/10.1016/j.mbs.2018.08.002

The models can be grouped into two categories, namely, lumped and distributed models. Lumped models are mathematically represented using ordinary differential equations (ODE); dependent variables are just the time-varying entities. On the other hand, distributed models are mathematically represented by partial differential equations (PDE). Here, the dependent variables are functions of time and one or more spatial variables. In physiological models, the spatial variable could be the anatomical geometry. The present work is based upon lumped models and in this context the literature is reviewed below.

Kappel and Peer modeled the cardiovascular circulation as a compartmental model; the ventricles were modeled by their contractilities using second order ODEs [7]. Ottesen's model is a minimal order model having only three state variables- the arterial and venous pressures and the heart rate [8]. Ursino modeled cardiovascular circulation as a 15th order system; the objective was to model the control of short-term arterial pressure by the carotid baroreceptors in pulsatile conditions [9].

Danielsen and Ottesen described the pumping heart as a pressure source depending on time, volume and flow [10]. Their approach allowed a separation between isovolumic and ejecting heart properties. They extended their approach by modeling ventricular contractions for arbitrary heart rates and could show the subsequent variations in stroke volume and cardiac output with heart rate [11].

Williams et al. [12] proposed a patient-specific model to study complex cardiovascular regulation occurring in response to head-up tilt (HUT), so that the blood pressure is maintained at homeostatic levels. The model comprises five compartments, namely, the arterial and the venous chambers in upper and lower extremities of the body, in together, accounting for the systemic circulation, along with the left ventricular chamber of the heart. The pressures in the arterial and the venous chambers along with the ventricular volume become the dynamic variables to be modeled. The model uses heart rate as an input to fit the dynamic changes in the arterial blood pressure data during supine as well as HUT positions. The estimation part begins with sensitivity analysis (classical) and subset selection (based upon singular value decomposition and QR factorization) to identify the parameters that would be optimized. This follows the nonlinear least squares based estimation (using Levenberg–Marquardt algorithm) of the parameters so that the model output fits the arterial blood pressure data observed at the level of carotid arteries. Then the simulations are performed with these optimized parameters to obtain the pulsatile pressures, volumes and flows. Two different residuals are chosen for the supine and the HUT position; hence different set of identifiable parameters in the two cases. In the supine position, vascular resistance and compliance along with the cardiac contractility are the relatively more sensitive parameters whereas in the HUT position, vascular compliance is not in the subset.

A few more examples from recent times are [13,14] that illustrate cardiovascular models in depth and highlight their applications.

Some recent works on the parameter estimation and the sensitivity analysis of cardiovascular models are demonstrated in [15–18] where standard techniques such as- Unscented Kalman Filter, Extended Kalman Filter and non-linear least squares estimation techniques have been used. Then, physiological concepts are explained well in [19,20].

The coronary circulation has been modeled by various research groups and some of the literature in this context is reviewed as follows. Roberto et al. proposed a lumped model of the coronary arterial system on the basis of the waterfall mechanisms [21]. It consisted of an epicardial compliance, a coronary resistance, and an intramyocardial compliance. Garcia et al. developed a mathematical model to show the effect of aortic stenosis on left coronary inflow patterns and coronary flow reserves [22]. Kim et al. have developed a patient-specific model that predicts the coronary flow and the pressure of three-dimensional epicardial coronary arteries by considering models of the heart and arterial system and the interactions between the two models [23]. Some more works on modeling of the coronary circulation have been explored in [24–26].

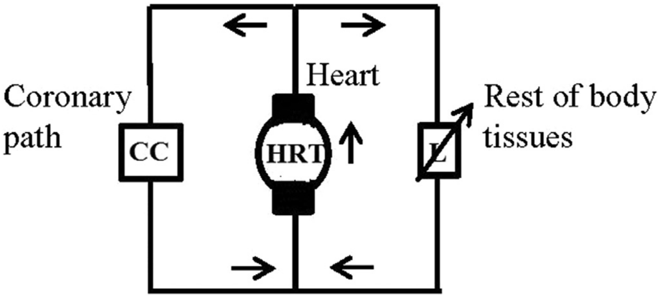

Fig. 1. A block diagram for cardiovascular circulation.

We made a few attempts to detect CAD while utilizing a state-of-the-art compartmental model [12]. However, this model was not suitable for detecting CAD as it was developed with an entirely different objective. Hence, *in this work*, we explicitly try to model the coronary path. In this model, the blood circulation in the body is viewed as an electrical system using the pressure-voltage analogy. In this case, the heart is considered as a self-excited generator. The rest of the body tissues form a systemic load. In the models reported in the literature, coronary circulation has been assumed to be a part of the systemic load. However, this circulation path has its own importance as it is responsible for blood supply to the heart. Therefore, in our work, the coronary path is separated out from the rest of the body tissues as shown in Fig. 1. This enables us to explicitly model the coronary arterial resistance and thereby helps us to detect coronary arterial blockage condition by estimating this parameter from blood pressure measurements. The model has been tested on 20 CAD subjects, and the predictive accuracy of the model is then computed based upon the chosen sample. The estimation of the model with parameters having physiological interpretation is shown to be helpful in detecting the arterial blockage at an early stage.

The remainder of the research paper is organized as follows. Section 2 explains the proposed mathematical model for cardiovascular circulation. In Section 3, the technique employed for estimation of the parameters of the model is explained. Section 4 gives an illustrative study of cardiovascular dynamics for young healthy subjects using the proposed model. Section 5 estimates the pathological conditions with subjects having high blood pressure and high heart rate. This section also shows how the left ventricular ejection fraction decreases with increase in the resistance of the coronary path, thereby, estimating the pathological condition of coronary arterial blockage. Furthermore, this section includes the analysis done for 20 CAD subjects; the predictive accuracy of the model is then computed. Section 6 makes some concluding remarks on the work and also proposes a mechanism which can be used for early detection of the coronary arterial blockage condition.

2. Mathematical modeling

A simplified block diagram of the cardiovascular circulation system is presented in Fig. 1. The heart acts as a generator while the rest of the body tissues form the systemic load. The coronary path acts as a medium for blood supply to the heart.

The technique of compartmental modeling is employed for developing the model of cardiovascular circulation. Large vessels form the compartments and are modeled as capacitors whereas small vessels form the resistors (see Fig. 2). In the proposed cardiovascular model, large and small arteries, large and small veins, heart's left ventricular chamber along with coronary compliance form the six compartments of the model. On the other hand, arterial and venous resistances, peripheral and coronary resistances form the small vessels.

The proposed cardiovascular circulation model is shown in the form of an electrical equivalent circuit in Fig. 3. The nomenclature is given in Table 1. The electrical circuit is composed of resistors and capacitors.