Hemodynamic Modelling in the Calf – A Pilot Study

Magdalena Matejkova[1], Pavel Jurak[1,2], Ladislav Soukup[1], Josef Halamek[1,2], Ivo Viscor[2], Peter Langer[1], Vlastimil Vondra[1,2]

[1]International Clinical Research Center, St. Anne's University Hospital Brno, Brno, Czech Republic
[2]Institute of Scientific Instruments of the ASCR, Brno, Czech Republic

Abstract

With increasing age, the cardiovascular system loses its efficiency. The goal of this work was to investigate the hemodynamic system response to a head-up tilt test in two groups of different aged people. We used a model for describing this response in the right calf based on a non-invasive, non-occlusive, bioimpedance signal measurement technique. A decrease in the bioimpedance value in the calf during the head-up tilt test is associated with the accumulation of blood in the calf, which can be expressed by a model parameter.

Subjects were examined in both a head-up tilt test and a supine position. 50 healthy non–smoking volunteers were divided into two groups according to age.

The impedance signal during the tilt test for each subject was fitted by a model exponential function: $Z_{0\,model\,EF}(t) = A*exp(-t/B)+C$*, where* $Z_{0\,model\,EF}(t)$ *is the calculated model of electrical impedance in the calf by an exponential function, A is the amplitude of impedance change, B is the time constant of the impedance decrease, C is the value of the steady state after the tilt test and t denotes time. A lower time constant B shows a faster filling of the vascular system in the investigated part.*

The Mann-Whitney test (p-value<0.005) revealed that the time constant B for the older group was significantly lower than for the young group (145.24± 80.28 vs. 239.23±136.59 sec.). A lower time constant value means a faster response to blood filling in the lower limbs and directly reflects decreased vessel elasticity. This time constant was lower in the older group. The results show increased vessel stiffness in old age and could lead to a non-invasive evaluating the cardiovascular system state.

1. Introduction

Cardiovascular complications are the leading causes of morbidity and mortality [1]. Describing their causes is necessary for improving the health of the population [2]. A decrease of arterial compliance, depending on age, is accelerated in varied cardiovascular disorders [3]. With increasing age, the cardiovascular system loses its efficiency and large arteries dilate and stiffen as a result of changes in the vessel wall [4], [5].

The head-up tilt test is a frequently performed cardiovascular test of sympathetic nervous system function. Head-up tilting from the supine position results in a pooling of blood in the sub-diaphragmatic venous system and legs, which results in a decrease in ventricular filling and stroke volume [6].

Thoracic bioimpedance measurement is most often considered as a non-invasive measurement of cardiac output [7]. It is a non-occlusive and patient-friendly method and consists of two main parts. First, $\Delta Z(t)$ responds to the impedance of pulsatile blood flow [8]. And secondly, 'static' low frequency impedance $Z_0(t)$ was used for this study. This part of the impedance signal responds to the impedance of tissue and residual blood in vessels [9], [10]. A decrease of the calf impedance value $Z_0(t)$ during a head-up tilt test is associated with the accumulation of blood in the calf. The dynamic properties of blood distribution can be expressed by a time constant of this decrease.

The purpose of this work was to investigate the hemodynamic system's response to a head-up tilt test in two groups of different aged people. This study was focused on investigating the lower limbs where there is an assumption of an early manifestation of the disease caused by risk factors such as atherosclerosis, diabetes and smoking. We developed a model ($Z_{0\,model}(t)$) for describing this hemodynamic response in the lower limbs based on measuring bioimpedance signals.

Calculating this simple time constant could lead to a non-invasive valuation of the cardiovascular system state and could be used in clinical care as a diagnostic marker.

2. Methods

2.1. Subjects and the study protocol

All participants gave written informed consent and the study was approved by the ethics committee of St. Anne's University Hospital in Brno. All participants were asked

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about their anamnesis, age and height. A technician measured the weight and arm span of each subject.

Study groups: a young group (20 women and 18 men) and an older group (6 women and 6 men). All members were non-smokers. Table 1 shows a description of these groups.

Measurements were taken at International Clinical Research Center at St. Anne's University Hospital, Brno, Czech Republic.

Table 1. A description of the subjects. BP means blood pressure.

		Young group		Older group	
		mean	standard deviation	mean	standard deviation
Age	[years]	23.40	2.80	65.33	8.65
Height	[m]	1.74	0.09	1.69	0.11
Arm span	[m]	1.77	0.11	1.73	0.15
Weight	[kg]	68.10	12.15	79.48	13.58
Systolic BP	[mmHg]	109.39	8.08	129.83	13.72
Diastolic BP	[mmHg]	65.05	7.59	75.00	10.13
Mean BP	[mmHg]	79.83	6.03	93.28	10.28
Pulse Pressure	[mmHg]	44.34	10.35	54.83	10.68

Study protocol: 2 minute supine position, followed by 5 minutes of the head-up tilt test at 70 degrees and then again in the supine position for 10 minutes.

Electrocardiography (ECG), continuous blood pressure and phonocardiography (PCG) were simultaneously measured with impedance signals. Blood pressure (BP) measurement was provided by patient monitor at the beginning of the study protocol.

2.2. Impedance measurement

Continuous impedance signal Z(t) measurements were provided by a Multichannel Bioimpedance Monitor (ISI Brno), which used a four-electrode method for measuring the bioimpedance signal from the desired part of the body [11]. For this study, an alternating sine wave current source I(t) with a frequency of 50 kHz and an amplitude of 1 mA was used.

Standard Ag/AgCl electrodes placed on the body surface were used. An electrical source was connected to the electrodes placed on the right part of the neck (carotid) and the right foot. Two voltage-sensing electrodes (E+ and E-) were placed on the right calf (Figure 1).

The impedance Z(t) of the calf between the two electrodes E+ and E- was calculated according Ohm's law equation:

$$Z(t) = \frac{U(t)}{I(t)} [\Omega], \quad (1)$$

where U(t) is the voltage measured between electrodes E+ and E-, and I(t) is the current.

The change in blood volume of the lower limbs caused by the head-up tilt test is reflected by the change in impedance and can be calculated as follow:

$$Z(t) = \frac{\rho(t) * l^2}{V(t)} [\Omega], \quad (2)$$

where ρ(t) is the specific resistivity of the tissue forming the cylinder, l is the length of the segment of the limb and V(t) is the volume [12].

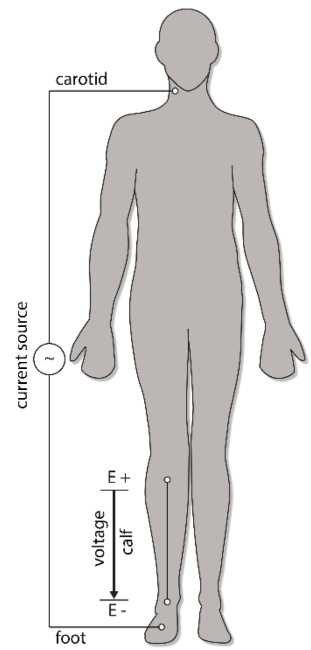

Figure 1. A placement of the current and voltage-sensing electrodes.

2.3. Signal analysis

A lowpass filter (0.8 Hz) was used to obtain 'static' low frequency impedance $Z_0(t)$ from the measured bioimpedance signal Z(t). A time interval of the tilt test was manually selected from the whole protocol record by the technician. The beginning of the head-up tilt test was marked after the end of tilt table movement. Figure 2 shows an example of measured signals with a marked investigation part of record.

A selected impedance signal interval during the tilt test was fitted: $Z_{0\ model\ LR}(t)$ for each subject by linear regression (3) and $Z_{0\ model\ EF}(t)$ for each subject by the exponential function (4) as follows:

$$Z_{0\ model\ LR}(t) = a * t + b\ [\Omega] \qquad (3)$$

and

$$Z_{0\ model\ EF}(t) = A * e^{-\frac{t}{B}} + C[\Omega], \qquad (4)$$

where $Z_{0\ model\ LR}(t)$ is a calculated model of electrical impedance in the calf by linear regression, $Z_{0\ model\ EF}(t)$ is a calculated model of electrical impedance in the calf by the exponential function, *a* is the slope and *b* is the amplitude of impedance at the beginning of the head-up tilt test, *A* is the amplitude of impedance change, *B* is the time constant of impedance decrease, *C* is the value of the steady state after the tilt test and *t* denotes time.

The root mean square error (RMSE) was calculated for both functions. This value shows an error between the measured signal and the calculated function (Equation 1 and Equation 2).

A lower RMSE value was used for choosing a better description of the measured signals by the calculated function.

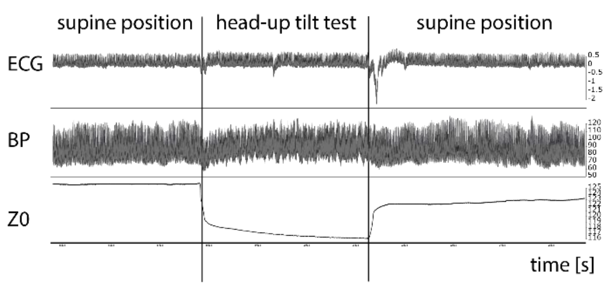

Figure 2. An example of the decreasing impedance Z_0(t) during the head-up tilt test. The beginning of the head-up tilt test was marked after the end of tilt table movement. The image was generated by SignalPlant software [13]. ECG means electrocardiography, BP means blood pressure and Z_0 means the absolute value of 'static' low frequency impedance.

2.4. Statistical analysis

A non-parametric statistical analysis was chosen due to the small size of the study groups. The Mann-Whitney test was used for making a statistical analysis of the time constant *B* difference between the younger and the older groups.

3. Results

The parameters of the fitting function were computed for each subject and visualized with the impedance signal.

The exponential fitting function was selected for analysing the next data due to a better description of the measured signals using the RMSE calculation (Table 2).

Table 2. The RMSE of the used models. LR means linear regression, EF means exponential function.

RMSE		Young group		Older group	
		mean	standard deviation	mean	standard deviation
LR	[Ω]	0.23	0.12	0.27	0.10
EF	[Ω]	0.12	0.07	0.13	0.06

Examples of impedance signals $Z_0(t)$ during the head-up tilt test and fitting by the exponential function $Z_{0\ model\ EF}(t)$ are shown in Figure 3 for the young group and in Figure 4 for the older group. There is an obvious difference between time constant *B* in the sample of subjects from the young group and the older group.

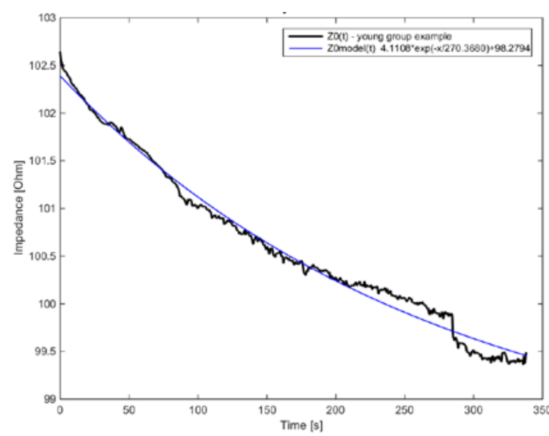

Figure 3. An example of one subject of fitting in the young group using a decreased exponential function. Time constant *B* = 270.4 s.

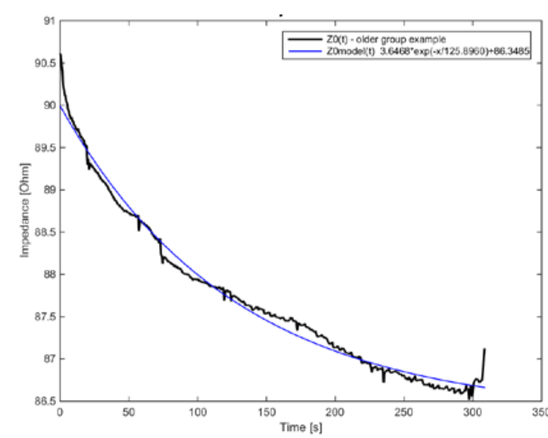

Figure 4. An example of one subject of fitting in the older group using a decreased exponential function. Time constant *B* = 125.9 s.

The Mann-Whitney test revealed that time constant *B* of the older group was significantly lower than time constant *B* of the young group ($p< 0.005$).

Table 3. A description of the parameters of the exponential function model.

		Young group		Older group	
		mean	standard deviation	mean	standard deviation
A	[Ω]	4.03	1.74	3.12	0.66
B	[s]	239.23	136.59	145.24	80.00
C	[Ω]	104.39	18.94	97.97	16.61

The variance of values was higher in the young group for each parameter, which could have been caused by the different group sizes (Table.3). The rate of vessel filling was approximately 1.65 times faster in the older group.

Finally, no statistical significant difference between parameters *A* and *C* were observed in the analyses.

4. Discussion and conclusion

As shown in Table 2, Figure 3 and in Figure 4, the $Z_0(t)$ decrease during tilting was well approximated by the exponential function $Z_{0\ model\ EF}(t)$.

The chosen function models show changes in impedance, which corresponds to vessel filling. A lower time constant *B* should indicated a faster filling of the vascular system.

These results show a decrease in cardiovascular system efficiency to deal with hemodynamic changes with increasing age and could lead to a non-invasive evaluation of the cardiovascular system state. Nevertheless, in order to clinically use this method, it would be desirable to verify it through an extended study group, especially older healthy subjects and should be used for special groups of subjects such as hypertensive and diabetic patients or smokers.

Eventually, this method should be used with more impedance channels and should be compared with different investigative methods.

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Address for correspondence.

Magdalena Matejkova
International Clinical Research Center
St. Anne's University Hospital Brno
Pekarska 53, 656 91 Brno, Czech Republic
magdalena.matejkova@fnusa.cz