Noninvasive evaluation of cardiac output based on various biosignals

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Abstract: A convenient and reliable enough method of cardiac output monitoring is still of interest. The following article presents a comparison of selected methods of noninvasive evaluation of this parameter. It considers the analysis of signals measured from the thorax (blood impedance change) and from distal locations like signals from a photoplethysmographic sensor or blood pressure from a limb. All of the analyses contained in this article were performed on the same set of biosignals. The paper shows the advantages and constraints of the methods used. The relation between the cardiac output and signals coming from distal parts of the body has been particularly closely investigated.

1. Introduction

Cardiac output (CO) is one of the most important and most frequently analyzed parameters in hospitalized patients. It reflects the average amount of blood being ejected from the left heart ventricle during the period of one minute. In males this value is usually about 5.5 L/min, whereas in females it is usually 10% lower. When cardiac output goes beyond the range between 4 and 8 L/min, it is a strong trace of possible cardiovascular health problems of a subject.

The importance of CO monitoring could be evidenced in the following examples. Cardiac output is an indicator of the level of body blood supply and an important determinant of oxygen transport. Naturally, it is correlated with the blood pressure, which gives a quick feedback on the general health of a patient. There are some cases where standard monitoring signals are associated with cardiac output as in high-risk postsurgical patients and in patients after refractory or cardiogenic shock (Lopes et al., 2007; García et al., 2011). Maintaining CO at an appropriate level during surgeries increases the chance to reduce potential complications (Garcia et al., 2011; Pöllönen et al., 2000). It is also one of the key factors while monitoring elders and children with circulatory failures (Lemson, 2008).

There are invasive methods of measuring CO, which are good, but reliable, less troublesome and easy to apply methods are of interest. These methods are not as accurate as the gold standard invasive measurement methods like the thermodilution method, but they are much more convenient (Geerts et al., 2011). They are easily
applicable even by the patients themselves and they do not present a risk of infection or any other health risks.

The following article presents selected methods of noninvasive cardiac output estimation. Each of them bases on a different set of biosignals and has different kinds of limitations. The methods have been discussed, and the CO estimations (basing on the theories) have been calculated in MATLAB. The biosignals were measured on a 24-year-old healthy male volunteer.

2. Classification of noninvasive cardiac output monitoring methods

Due to the origin of the biosignals an elementary division of cardiac output estimation methods was performed. They contain calculations based on signals from regions proximal to heart, distant from heart, and mixed.

2.1. Bioimpedance – signals from regions proximal to heart

The volume of blood flowing through the thorax changes over every single cardiac cycle. Blood is a good current conductor, hence its impedance change in time could be relatively easily measured. As in every medical measurement of immittance, two pairs of electrodes are required. A current pair is used for introducing the current into the body and a voltage pair is used for measuring the resulting voltage signal. This is a kind of plethysmography which allows us to measure the change of tissue volume inside the body basing only on the measurement performed at the surface of the skin. This particular manner is called the impedance waveform method or thoracic electrical bioimpedance. It was first proposed by Nyboer (1950) and further developed by Kubicek et al. (1966).

This method requires a low frequency (20-100 kHz), low amplitude alternating current (1 mA) which flows through the section of the lowest value of available impedance in the volume. That, in the human thorax, is the blood which has less resistivity than the surrounding tissues, bones and muscles.

The magnitude and the rate of impedance change is a direct reflection of left ventricular contractility. The measured impedance signal generally reflects total thoracic fluid volume. The change in this signal, related to time, generates a waveform that is similar to the aortic flow curve. The first derivative $dZ/dt$ of the obtained impedance waveform is related linearly to aortic blood flow (Lavdaniti, 2008). Therefore, Kubicek has proposed a formula to calculate a single stroke volume (SV) of the heart:

$$SV = \rho \cdot \frac{L^2}{Z_0^2} \cdot \frac{dZ}{dt_{\text{max}}} \cdot LVET$$

\[\rho\] – blood resistivity $[\Omega \cdot \text{cm}]$,
\[L\] – distance between voltage electrodes $[\text{cm}]$,
\[Z_0\] – base thoracic impedance $[\Omega]$,
\[\frac{dZ}{dt_{\text{max}}}\] – minimum signal derivation within a cardiac cycle $[\Omega/s]$,
\[LVET\] – left ventricle ejection time $[\text{s}]$. 
Having that value, in order to obtain the cardiac output, one has to multiply it by the number of heart cycles in one minute (heart rate – HR), hence the simple formula:

\[ CO = SV \cdot HR \] (2)

An illustration of how the above variables are extracted from the signal of impedance is demonstrated in Fig. 1. The green signal is impedance and the black one is its hardware derivative over time. \( LVET \) time could be better extracted if the ECG signal was measured additionally. \( L \) is the height of a geometry which represents a simplified model of the thorax, taken into account in this method. The inner cylinder is a blood compartment while the surrounding pipe shape reflects a tissue compartment.

In (1) it is assumed that the rate of cardiac ejection of blood is constant during the systolic period, which is a rough approximation. The formula has also other simplifications, some of which are enlisted below:

- the two-compartment model which is a severe simplification;
- the assumed cylindrical geometry is a greatly simplified approximation;
- blood conductivity variations with a change in velocity have been entirely neglected in that model.

On the other hand, the method is very convenient and does not harm the patient in any way. It requires only collecting the signals from the thorax by pairs of electrodes, which, after a few minutes after sticking them to the skin, are hardly noticeable by the subject.

2.2. Systolic pulse contour analysis – mixed signals, proximal and distal to the heart

This is a solution for the method of pulse contour analysis. Its reliability has been widely analyzed and compared with invasive and noninvasive methods revealing its high accuracy (Gödje et al., 2002; Laleg-Kirati et al., 2009; Linton and Linton, 2001).
Its assumption is that blood flow in the thorax is correlated with the level of arterial pressure giving the possibility of tracking the stroke volume.

Human circulatory system can be modeled using the RLC circuit. In such a system, the aortic blood pressure \( P \) is represented by the voltage and flow rate \( Q \) of the current. In this example a modified three element Windkessel model was designed to demonstrate the shapes of electrical signals which are similar to real, biological waveforms. This is because RLC elements play the role of an arterial compliance \( C \), vascular resistance \( R \), blood inertia \( L \) and \( Z \) of aortic impedance (Mathews and Singh, 2008). The pumping function of the heart is simulated by the pulse current source.

This method is about estimating the area under the curve of blood pressure waveform during a specific period. The aortic pressure waveform (AO) in the systolic area, subtracted by the end diastolic (ED) pressure is the area of interest. That is expressed in the equation 3 and the pulsatile systolic area \( PSA \) is presented in Fig. 2.

\[
PSA = \int_{ejection} \{ P_{AO} (t) - P_{ED} \} \, dt
\]  

(3)

Fig. 2. Windkessel model circuit and its signals (left) and the \( PSA \) area (right).

The circuit respects the proximal and distal arterial compliance \( C2 \) and \( C1 \) respectively), arterial pulse propagation effects \( L1 \), and total peripheral resistance \( R1 \). The obtained pulsatile systolic area is related to single stroke volume by the mean impedance of the thorax, which results in:

\[
SV = \frac{PSA}{Z_a}
\]  

(4)

where \( Z_a \) is the characteristic impedance of the aorta. The pressure signal can be taken from a catheter inserted into an artery, which would give a direct pressure trace. Due to the convenience requirement, the approximation of continuous blood pressure signal could be taken from a pulse contour monitor like CNAP 500, which was used in this research. Although \( PSA \) can be found from the area under the curve, there are no simple direct methods to establish the appropriate value of \( Z_a \) without taking a
measurement. In the survey the thorax impedance signal was collected simultaneously with the pressure waveform.

The blood pressure curve profile changes significantly passing through the arterial tree. It is caused by the changing elasticity function of the arterial walls, the diameter of the vessel and many bifurcations. Blood pressure transmittance from the aortic arch to peripheral limbs function changes with age and is vulnerable to some cardiovascular diseases. Additionally, this method is based on electrical models which neglect some physiological phenomena or do not include the whole arterial tree. The PSA method requires calibration due to the usually unknown $Z_a$ value. Also the noninvasive continuous blood pressure signal is not easy to obtain.

2.3. PPG based – signals from regions distal to the heart

The attempts at extracting vascular dynamics and cardiac output basing on photoplethysmographic (PPG) signals were also performed (McCombie et al., 2005). The PPG signal reflects blood volume changes under the sensor. A specific index from the PPG waveform measured in the index finger, which is well correlated with CO was proposed (Wang et al., 2009). The virtue of such solution is that it can be easily applied to many existing optical sensors because it is only a matter of proper signal computation.

The idea was to substitute well known parameters with their surrogates from a PPG signal. It was proved that total peripheral resistance ($TPR$) could be well extracted from a PPG signal (Wang and Zhang, 2008). According to the two-element Windkessel model, the CO is the mean amount of current passing through the $TPR$ and is equal to the mean blood pressure ($MBP$), hence:

$$CO = \frac{MBP}{TPR}$$ (5)

Recalling the wave theory and analyzing the PPG profile it is clear that it is composed of two components: progressive and reflected waves. The first of them is associated with arterial blood pressure, while the second is related to arterial stiffness. The inflection point area ratio ($IPA$ – (6)) is influenced mainly by reflections. The $S1$ is the area under the systolic phase, while $S2$ in diastolic one (Fig. 3). The majority of $TPR$ comes from small blood vessels and it influences the $IPA$ index.

$$IPA = \frac{S2}{S1}$$ (6)

Changes caused by the $TPR$ are revealed not only in the time domain but in the frequency domain as well (Yan and Zhang, 2005). The proposed index, a normalized harmonic area ($NHA$) is strongly correlated with systolic and diastolic blood pressure.

$$NHA = \left(1 - \frac{\sum_{n=2}^{N} FFT^2(f_n)}{\sum_{n=1}^{N} FFT^2(f_n)}\right)$$ (7)

The $FFT^2(f_n)$ is the square of a value at the $n^{th}$ harmonic of a spectrum of a PPG signal. The inflection and harmonic area ratio, which bounds the $NHA$ and $IPA$, was proposed as an indicator of CO.

$$IHAR = \frac{NHA}{IPA}$$ (8)
Its changes are associated with the variability of CO but it has to be leveled by some mathematicians in order to scale it to an appropriate range.

The disadvantage of this method is that the PPG signal is often inconsistent and prone to hand movements. Additionally, the optical waveform depends on the health of the vascular tree and aging, which is a significant constraint. The stiffening of arterial walls or the impact of cholesterol would make it harder to detect the dicrotic notch (notch at the waveform where the systolic phase ends and the diastolic begins) so the inflection point would be hardly recognizable. The proposed IHAR index is well associated with blood pressure and cardiac output but it needs to be calibrated in order to reflect the SV changes (Wang et al., 2009).

3. Results

The formulas discussed in the previous section have been implemented and calculated using MATLAB. The biosignals were collected simultaneously from a 24-year-old healthy male. They were recorded with the sampling frequency of 2500 Hz, for 30 s at rest. The bioimpedance analysis showed that blood resistivity \( \rho \) was equal to 1.60 \( \Omega/m \), the distance \( L \) between voltage electrodes was 0.33 m. The recording contained 41 cardiac cycles.

The formulas from bioimpedance and PSA methods contain a variable related with the value of blood impedance. It is often troublesome to extract, it is not always included in standard measurement; it and its value are modified in order to calibrate the method. The reason why two ways of analysis were used was the need to compare impedance extraction. First of them assumed constant values of \( Z_0 \) and \( Z_a \), variables for bioimpedance and PSA methods. They were set to 0.15 and 0.23 \( \Omega \) respectively. In the second path of analysis, the mean values of a measured impedance signal, in the analyzed time windows in the following cardiac cycles, were taken.

The IHAR index from the PPG signal was calibrated using linear regression, with both SV estimation methods of both analysis paths, what results in 8 different set of results. The comparison of the received results is presented in Tab. 1.

The PPG rows contain results from the IHAR index calibrated with respect to the PSA and bioimpedance methods as reference. The IHAR was put into a linear

![Fig. 3. Areas under the curve of the PPG waveform (left) and the FFT signal of a waveform (right).](image-url)
Tab. 1. Cardiac output estimation methods – a comparison.

<table>
<thead>
<tr>
<th>$Z_0$, $Z_a$</th>
<th>method</th>
<th>average SV [mL]</th>
<th>median SV [mL]</th>
<th>std. dev. [mL]</th>
<th>CO [L/min]</th>
<th>error cycles [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>constant</td>
<td>PPG (PSA)</td>
<td>66.83</td>
<td>65.75</td>
<td>6.32</td>
<td>5.48</td>
<td>4.87</td>
</tr>
<tr>
<td></td>
<td>PPG (BIO)</td>
<td>62.69</td>
<td>57.03</td>
<td>33.02</td>
<td>5.14</td>
<td>4.87</td>
</tr>
<tr>
<td></td>
<td>PSA</td>
<td>67.64</td>
<td>68.21</td>
<td>7.35</td>
<td>5.54</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Bioimpedance</td>
<td>62.34</td>
<td>67.21</td>
<td>26.57</td>
<td>5.11</td>
<td>7.31</td>
</tr>
<tr>
<td>variable</td>
<td>PPG (PSA)</td>
<td>62.35</td>
<td>59.89</td>
<td>14.35</td>
<td>5.11</td>
<td>4.87</td>
</tr>
<tr>
<td></td>
<td>PPG (BIO)</td>
<td>64.27</td>
<td>53.66</td>
<td>61.93</td>
<td>5.27</td>
<td>4.87</td>
</tr>
<tr>
<td></td>
<td>PSA</td>
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<td>62.16</td>
<td>17.58</td>
<td>5.11</td>
<td>14.63</td>
</tr>
<tr>
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<td>64.32</td>
<td>61.88</td>
<td>60.75</td>
<td>5.27</td>
<td>12</td>
</tr>
</tbody>
</table>

function as proposed in (Wang et al., 2009). The results in the first group, where the impedances were set as constant are more consistent. The error cycles column shows how much of the calculated stroke volumes were far beyond the double standard deviation error range. They were corrected by substituting the values by the median of a given data vector.

The application of changing $Z_0$ and $Z_a$ impedances in time led to increased standard deviation and cycle errors of the computed stroke volumes. That was an additional source of potential errors caused by algorithms fed by locally disturbed data from the measurements.

![Fig. 4. Plots of SV agreement when calculating with different methods. Bioimpedance (rhombus) and PSA (circles) as functions of PPG (left) and PSA as a function of Bioimpedance (right). Variant with constant impedances.](image-url)

The figures show the relations between stroke volumes computed for every cardiac cycle during the measurement. A good agreement between methods means that the
measurement points are arranged along a straight dashed line (Fig. 4 and Fig. 5). It means that a certain value of SV computed with one method, basing on a biosignals from one cardiac cycle, is exactly the same as for the one computed with another method. From these plots it is clear that although methods give very similar numbers after calibrating, they are far from being equivalent with respect to a single cardiac cycle.

Normalized stroke volumes along the whole analyzed period are presented in Fig. 6.
They were all divided by the median value of each vector in order to level them to unity and emphasize monotonicity and a general trend agreement.

4. Discussion

The bioimpedance and PSA methods strongly depend on the applied impedance value. Results show a significant increase in the standard deviation of a stroke volume and error cycles when the impedances where extracted from each cardiac cycle.

Although the CO values are very similar for all the methods and impedance variants, it does not mean that they are equally reliable. The great variability of the obtained stroke volume values could be partially explained by the imperfect signal shape during the examination. It is easy to calibrate the period of a few cardiac cycles to obtain the desired CO but it does not mean that separate SV values would be reliable. One highly overestimated or underestimated SV value in the period could affect such calibration significantly. If the median value is very close to the mean (±5%) and standard deviation is low (less than 10 mL) that could indicate a stable and a reliable measurement.

The SV values for Bioimpedance and PSA methods were applied to calibrate the IHAR index. This index has the lowest error rate (under 5 %) and the smallest variability (difference between the mean and the median) which is its clear advantage. If the measurement is stable, that could be a good indicator of CO.

5. Conclusions

Noninvasive and reliable cardiac output monitoring is still an important issue in medicine and biomedical engineering.

All of the presented methods provide convenient stroke volume monitoring, and allow us to estimate the cardiac output. The least troublesome are the bioimpedance and PPG methods. Collecting this kind of biosignals noninvasively is relatively easy unlike collecting the blood pressure signal. The impedance method measures the signal which is the least affected by the transmission function because it is obtained directly from the thorax.

These methods do not give very similar results considering only the SV variability along the analyzed period. Joining some of them could possibly improve the CO estimation correctness. The combination of bioimpedance and PPG would be the easiest to obtain and could be developed in further research.

Despite the fact that the presented methods look promising, all of them should be compared with the invasive gold standard method, e.g. thermodilution, in order to find out how accurate they really are.

References


