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Theoretical and model analysis of the unreliability of cardiac output measurement by means of the thermodilution method

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Abstract. Thermodilution is the clinically most often applied method of cardiac output measurements. This method is based on thermal indicator (iced isotonic salt solution) variation measurements by a Swan-Ganz catheter located inside the pulmonary artery. The unreliability of thermodilution should be estimated theoretically because of the lack of references. In this paper an attempt has been made to estimate theoretically the unreliability of thermodilution cardiac output measurements.

Key words: cardiac output measurement, thermodilution method.

1. Introduction

Cardiac output (defined as average blood flow caused by the function of the heart) is the fundamental hemodynamic parameter. It is monitored in the course of intensive therapy in order to check the progress and treatment of illness [1–26]. Cardiac output is also estimated during mechanical heart supporting therapy [16, 18, 19, 22–24]. In other applications this parameter is used for numerical and physical modeling of the human circulatory system [17].

Nowadays there are several clinically utilized cardiac output measurement methods [3]. Among non-invasive methods the most popular one is echocardiography, which is based on the analysis of the shape of heart ventricles or Doppler blood velocity measurements [3, 4, 21, 22]. The primary method of invasive measurements is pulmonary artery catheterization by means of a Swan-Ganz catheter [5, 6, 21, 22]. This method is considered to be the "gold clinical standard" and in many cases it is treated as a reference for other methods of cardiac output measurements [3, 5]. In spite of invasiveness this treatment is safe for the patient and does not cause any risk of death or serious side-effects [7].

Usually, the Swan-Ganz catheter is inserted into the pulmonary artery through the right atrium and right ventricle (Fig. 1) [2]. A thermal sensitive resistor (which detects local changes of the blood temperature) is located at the distal part of the catheter (Fig. 1). The indicator (iced or room-temperature isotonic salt solution) is injected through a special canal, which is located at the proximal part of the catheter. After injection of indicator the changes of blood temperature drop *vs.* time (*IDC – indicator dilution curve*) is registered by means of an external computer. The value of the cardiac output is calculated by integrating of *IDC*.

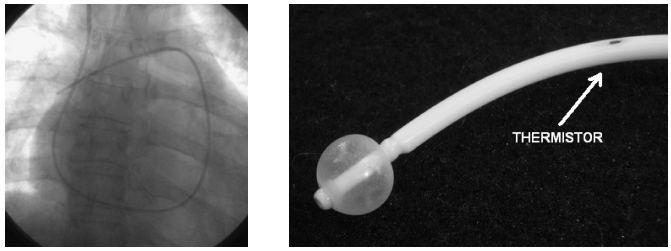

Fig. 1. Swan-Ganz catheter: intraoperative X-ray and device scheme

The unreliability of thermodilution cardiac output measurements is difficult to estimate experimentally, due to the lack of references [2–6, 8]. Available flow measurement methods (e.g. transit time ultrasound flow meter equipped with a vascular probe) are not accurate enough (the unreliability of Transonic TS420 reaches 5% after *in-situ* calibration [9, 16, 19, 22, 23]). Moreover, the measurement itself requires serious interference in the measured object (intubation, anesthesia and thoracotomy). Therefore thermodilution is usually compared with the Fick method, whose unreliability is estimated only theoretically [6, 15]. It should be emphasized, that the real accuracy of the thermodilution method, determined experimentally, is unknown.

Goal. The goal of this work was to estimate the typical and maximum unreliability of cardiac output measurements by means of the thermodilution method. Theoretical studies were supplemented and supported by investigations and measurements performed on a physical model.

2. Material and methods

2.1. Initial assumptions. In the course of theoretical analysis the following assumptions concerning the examined thermodilution method were made:

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- indicator: 0.9%NaCl, iced (1.5...4.5°C) or room temperature (20...23°C), injection volume 10 mL,
- catheter: size 7 F, volume of the indicator duct about 0.5 mL,
- thermodynamic parameters of liquids: specific heat = 3528 J/kg·K, mass density = 1065 kg/m^3 for blood and specific heat = 4180 J/kg·K, mass density = 996 kg/m^3 for indicator.

The following mathematical models of the dilution phenomenon are known: heat balance [10, 15], the stochastic local diffusion random walk model [11] and the Stewart-Hamilton equation [5, 6, 10, 15]. In the presented paper the Stewart-Hamilton model Eq. (1) for the thermal indicator was theoretically examined. The estimation of the unreliability of the cardiac output measurement was accomplished by means of the sensitivity analysis method.

$$Q = \frac{c_i \cdot \sigma_i}{c_b \cdot \sigma_b} \cdot \frac{V_i \cdot (T_b - T_i)}{S_c}, \tag{1}$$

where c_b, c_i – specific heat of blood and the indicator; ρ_b, ρ_i – mass density of blood and the indicator; V_i – volume of the indicator; T_b, T_i – temperature of blood and the indicator; S_c – integral of the IDC curve.

2.2. Sensitivity analysis. Sensitivity analysis allows to determine the individual disturbing factors influencing the transmittance of the system or process [12]. The T function, which describes the investigated process depends on n parameters: $T = f(Y_1, Y_2, \ldots Y_n)$. If $\delta T = \dfrac{\Delta T}{T}$ denotes the relative increment of the T function and $\delta Y_i = \dfrac{\Delta Y_i}{Y_i}$ denotes the relative increment of parameter, then:

$$\delta T = \sum_{i=0}^{n} S_{Y_i}^T \cdot \delta Y_i, \tag{2}$$

where S_{Yi}^T – relative sensitivity index of the function T on the parameter Y_i.

The relative sensitivity index is defined by the following equation:

$$S_{Y_i}^T = \frac{Y_i}{T} \frac{\partial T}{\partial Y_i}, \tag{3}$$

where ∂T/∂Y$_i$ – partial derivative of the function T.

Equation (3) defines the low-incremental relative sensitivity index. It means, that the relative increment of Y_i must be about 10%. [12]. The value of S_{Yi}^T may be understood as the force of the variation Y_i influence the total modification of the function T, therefore $1 > S_{Yi}^T > 1$ causes an amplification and $1 < S_{Yi}^T < 1$ causes the attenuation of the mentioned effect. The maximum deviation of the function T is given by the equation:

$$\delta T_{\max} = \pm \sum_{i=1}^{n} \left| S_{Y_i}^T \cdot \delta Y_i \right|. \tag{4}$$

2.3. Estimation of the relative increment of the parameters. There are eight parameters in the analyzed function T, given by Stewart-Hamilton's model Eq. (1). The methods of estimating its relative increment are described below:

- c_i, ρ_i (specific heat and mass density of the indicator): these parameters are constant because of the stable chemical constitution of the indicator.
- c_b, ρ_b (specific heat and mass density of blood): these parameters are variable and their values depend on the hematological properties of blood. Blood consists of plasma (solution of water, albumins and other organic and inorganic compounds) and cellular components. The hematocrit level determines the ratio of cellular components to the whole blood volume and it may be variable. The thermodynamic features of the diphase mixture are given by Eq. (5):

$$c_{F12} = (1 - n) \cdot c_{F1} + n \cdot c_{F2}. \tag{5}$$

- V_i (volume of the indicator): the relative increment of this parameter is difficult to estimate. Typically, the indicator is injected with a medical syringe, therefore most probably the volume of the indicator may be underrated. Moreover, a small portion of the indicator injected previously remains in the catheter canal. In a 7F size catheter the volume of the canal amounts to 0.5 mL.
- T_i (temperature of the indicator): the relative increment of this parameter consists of two components: the first one is due to the unreliability of the thermistor, the second one is due to the heating of the indicator during its flow through the canal by the thermal energy of blood. The method of estimating the unreliability of the thermistor will be discussed further. The heating up of the indicator can be defined by Newton's empirical theory [13] given by the following equation:

$$Q = \alpha \cdot A \cdot (T_2 - T_1), \tag{6}$$

where Q– heat flux density; α – surface film conductance; A – heat exchange surface; T_1, T_2 – temperatures on both sides of the exchanging surface.

In the definition of the specific heat, Eq. (6) may be rearranged to Eq. (7):

$$\Delta T_i = t \cdot \frac{\alpha \cdot A \cdot (T_b - T_i)}{\sigma_i \cdot c_i \cdot V_i}, \tag{7}$$

where α – surface film conductance; A– heat exchange surface; T_b – temperature of blood; T_i – temperature of the indicator; ρ_i – mass density of the indicator; c_i – specific heat of the indicator; V_i – volume of the indicator.

The surface film conductance depends on the physical features of the liquid and the way of its flow. It can be estimated by the equation:

$$\alpha = \frac{\lambda_i}{d} \cdot 0.023 \cdot \mathrm{Re}^{0.8} \cdot \left(\frac{c_i \cdot \mu_i}{\lambda_i} \right), \tag{8}$$

where λ_i – thermal conductivity coefficient; Re – Reynolds number; μ_i – absolute viscosity of the indicator; c_i – specific heat of the indicator; d – diameter of the canal.

- T_b (temperature of blood): the relative increment of this parameter is directly connected with the accuracy of the thermistor located at the tip of the catheter. Six catheters (manufactured by Becton-Dickinson, Edwards Lifescience and Burron Medical) were examined. The catheters were connected to a patient monitor (PM9000, Mindray) equipped with cardiac output measurement function. As a reference a high precision (0.0011°C) thermometer (Fluke 1532 equipped with a PRT probe) was used. The thermistors of the catheters and the probe of the thermometer were located inside a water bath (Fig. 2). The temperature was measured within the range of 33...38°C. The regression method was applied to analyze the results.
- S_c (indicator dilution curve integral): in essence, the indicator dilution curve is determined by measurements of the blood temperature T_b by a non-ideal detector (slope of transfer function $k \neq 1$ and offset $T_0 \neq 0$). This kind of detector may be defined by the equation:

$$\Delta T_b^*(t) = k \cdot [\Delta T_b(t) + T_0]\,, \tag{9}$$

where k – slope of transfer function; T_0 – offset.

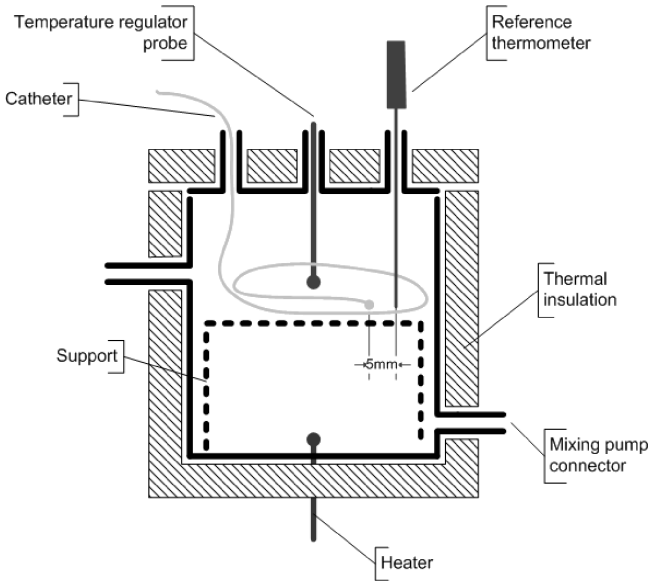

Fig. 2. Scheme of the laboratory stand for the examination of the Swan-Ganz catheter thermistors

Let S_c^* and S_c denote the integral of the indicator dilution curve measured by ideal and non-ideal detectors, respectively. Because:

$$S_c^* = \int_0^{t_{pom}} \Delta T_b^*(t)\; dt \tag{10}$$

therefore:

$$S_c = \int_0^{t_{pom}} k \cdot [\Delta T_b(t) + T_0] dt = \tag{11}$$
$$= k \cdot \left[\int_0^{t_{pom}} \Delta T_b(t)\; dt + \int_0^{t_{pom}} T_0\; dt \right] = k \cdot (S_c^* + T_0 \cdot t_{pom})\,.$$

The measurement method realized by the patient monitor eliminates the offset T_0, therefore the relative increment of the indicator dilution integral depends merely on the slope of the temperature detector.

3. Results

3.1. Sensitivity analysis. The values of relative sensitivity indices calculated from Eq. (3) have been presented in Table 1.

Table 1
Relative values of the sensitivity indices

Parameters	Relative sensitivity index	
	symbol	value
specific heat of the indicator	$S_{c_i}^Q$	1
mass density of the indicator	$S_{\rho_i}^Q$	1
specific heat of blood	$S_{c_b}^Q$	-1
mass density of blood	$S_{\rho_b}^Q$	-1
volume of the indicator	$S_{V_i}^Q$	1
temperature of blood	$S_{T_b}^Q$	$\frac{T_b}{T_b - T_i}$
temperature of the indicator	$S_{T_i}^Q$	$-\frac{T_i}{T_b - T_i}$
indicator dilution curve integral	$S_{S_c}^Q$	-1

The relative sensitivity indices of the temperature of blood T_b and the indicator T_i depend on absolute values of these temperatures. Both of them are variables. The indicator temperature depends on the kind of the dilution method (iced or room-temperature). The temperature of the blood is quite often reduced (even to 25°C) during cardiosurgical operations [14]. In consequence the relative sensitivity indices of the mentioned temperatures may differ as shown in the table below:

Table 2
Relative sensitivity index values for different blood and indicator temperature

Indicator	Patient condition	T_i [°C]	T_b [°C]	$S_{T_i}^Q$	$S_{T_b}^Q$
iced	physiological condition	5	36.6	-0.15	1.15
	hypothermia		30.0	-0.20	1.20
	inflammatory condition		38.0	-0.15	1.15
room temp.	physiological condition	23	36.6	-1.69	2.69
	hypothermia		30.0	-3.28	4.28
	inflammatory condition		38.0	-1.53	2.53

3.2. Relative increment of the parameters.

- δc_i, $\delta \rho_i$: relative increments of the specific heat δc_i, and mass density of the indicator $\delta \rho_i$ equals zero.

- δc_b, $\delta \rho_b$: it is known [10], that the specific heat of cellular components and plasma amounts to 3.52 J/mL·K and 4.03 J/mL·K, respectively. Assuming a hematocrit level in the range of 25...60% [1, 2], the relative increment of the specific heat of blood δc_b calculated from Eq. (5) amounts to 2.5%. In the same way, assuming that the mass density of the plasma and cellular components amounts to 1027 kg/m^3 and 1095 kg/m^3, respectively, the relative increment of the mass density of blood $\delta \rho_b$ equals 1.3%.
- δT_i: a refillable indicator temperature probe may be mounted at the outlet of the syringe or in the reference container, located in the same thermal condition as the sterile one, designed for injection. Neither of the presented solutions takes into account the heating effect of the indicator due to the thermal energy of the blood. The rise of the temperature of the indicator can be calculated from Eqs. (7) and (8). For 110 cm of the catheter length and 0.4 mm of the diameter of the canal the heat exchange surface A amounts to 14 cm^2. The measured injection time for 10 cm^3 of indicator was about 3 s which gives a Reynolds number of the order of 10000. Assuming the following parameters of the indicator: thermal conductivity coefficient $\lambda_i = 0.591$ W/m·K [13], absolute viscosity at 0°C $\mu_i = 1.79 \cdot 10^3$ Pa·s [6, 10], the surface film conductance calculated from Eq. (8) amounts to $\alpha \approx 90$ W/K·m^2. Taking into account Eq. (7) and typical temperature of blood (37°C) and the iced indicator (2°C), the temperature rise of the indicator caused by its heating amounts to 0.2°C (relative increment of indicator temperature $\delta T_i = 3\%$).
- δT_b: six catheters originated from different lots were examined. For each of them $N = 20$ measurements were performed. The value of the regression coefficient ($Y = mx + b$), R^2 and the maximum δT_b have been compared in Table 3.
- δS_c: taking into account the typical slope of the thermistor transfer function (see Table 3), the relative increment of the indicator dilution integral calculated from Eq. (11) equals to $\delta S_c = 6\%$.

Table 3
Results of the regression analysis and maximum relative increment of blood temperature measurements

Catheter type	Size	m	b	R^2	$\delta T_{b\,\max}$ %
B2254	7F	1.069	−3.197	0.9997	**2.73**
B2269	7F	1.062	−1.675	0.9981	**−1.72**
EDW	5F	0.980	3.295	0.9996	**−7.83**
BD1	7F	1.164	−9.846	0.9965	**13.55**
BD2	7F	1.027	−1.019	0.9982	**0.27**

3.3. Maximum T function deviation. The relative sensitivity indices and respective relative increments of the parameters were compared and presented in Table 4. The unreliability of cardiac output measurements defined as the maximum deviation of the T function was calculated from Eq. (4). Its typical and maximum value for different types of the indicator are compared in Table 5.

Table 4
Comparison of relative sensitivity indices and relative increment of the parameters

Parameter	Relative sensitivity index [–]	Relative increment of the parameter [%]
c_i	1	**0**
ρ_i	1	**0**
c_b	−1	**2.5**
ρ_b	−1	**1.3**
V_i	1	**2.0**
T_b	$\frac{T_b}{T_b - T_i}$	**5.3** (average) **13.0** (max.)
T_i	$-\frac{T_i}{T_b - T_i}$	**3.0** (iced) **0.5** (room temp.)
S_c	−1	**6.0** (average) **16.0** (max.)

Table 5
Unreliability of cardiac output measurements estimated by means of the transfer function sensitivity analysis

Deviation of the function T (unreliability of cardiac output measurements):	Indicator	
	iced	room temperature
typical:	18.3%	26.9%
the worst case:	34.2%	54.7%

4. Discussion

Many papers [2, 3, 5, 6, 8, 10, 14, 20, 21] maintain, that iced thermodilution is more reliable than room temperature. In the presented work this thesis was confirmed theoretically (see Table 2) – relative sensitivity indices concerning the room-temperature indicator are 3–10 times bigger than in the case of iced ones. However, a cold indicator seems to be more accurate, but a room-temperature indicator is more convenient for the patient and does not cause any side effects, like arrhythmia [5].

It should be noticed, that relative sensitivity indices for blood-temperature measurements are significantly larger than those for indicator temperature (see Table 2). In consequence, in order to obtain a low unreliability of cardiac output measurements the temperature of blood must be measured with a high accuracy. The presented papers dealing with the thermodilution method [5, 8, 10] are focused on the precision of measurements of the indicator temperature.

In spite of pre-standardization (made during manufacturing by built-in precise resistors) the accuracy of temperature probes utilized in catheters is low (see Table 3). This fact seems to be the most important component of the unreliability of the thermodilution method, because it directly influences the indicator dilution curve integral (see Eq. (11)).

In the case of an iced indicator, the typical unreliability of thermodilution cardiac output measurement is **18...34%** (see Table 5). It should be considered to be a low value, moreover that this method is utilized as a reference [5, 8]. In the case of the room-temperature indicator the unreliability may exceed **50%**, which makes the obtained results useless in practical application.

In the presented paper some phenomena and effects have not been taken into consideration in the theoretical analysis. It is known, that the following components may influence the results obtained by the thermodilution method: spontaneous respiration [5, 20], indicator injection rate [5, 15] and hypothermia [14, 15, 20]. In the analysis the dynamic features of the thermistor were omitted.

5. Conclusions

Basing on the performed theoretical analysis and experimental investigations the following conclusions may be formulated:

- room-temperature thermodilution is more susceptible to thermal disturbances than the iced one,
- the precision of measurements of blood temperature is more significant than the temperature of the indicator. In order to obtain precise results of the cardiac output estimation the blood temperature should be measured with a high accuracy. The thermistor transfer function slope should be close to 1,
- in spite of pre-standardization the accuracy of thermistors mounted in catheters is low. A significant influence of this effect on the total unreliability of thermodilution method is to be expected,
- in the case of iced and room-temperature indicators, the typical unreliability of the method amounts to 18% and 27%, respectively.

As the unreliability of the thermodilution method cannot be determined experimentally, the presented results and conclusions may constitute a valuable contribution to the development of cardiac output measurement methods.

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