

Yevtushenko V.¹, Shadrin V.¹, Kramarov S.¹, Voronov A.¹, Kyrytsia N.¹, Kaminska T.²

¹ Bogomolets National Medical University, Kyiv, Ukraine

² Kyiv City Children's Clinical Infectious Diseases Hospital, Kyiv, Ukraine

Евтушенко В.В.¹, Шадрин В.О.¹, Крамарев С.А.¹, Воронов А.А.¹, Кирица Н.С.¹, Каминская Т.Н.²

¹ Национальный медицинский университет имени А.А. Богомольца, Киев, Украина

² Киевская городская детская клиническая инфекционная больница, Киев, Украина

Predictive Value of the Temperature Gradient Regarding the Parameters of Peripheral Hemodynamics in Children with Severe Forms of Infectious Diseases

Прогностическое значение градиента температуры в отношении параметров периферической гемодинамики у детей с тяжелыми формами инфекционных заболеваний

Abstract

Introduction. Skin temperature measurement is one of traditional tools used by physicians for a long time to evaluate blood circulation. Despite the long history of use, this method is still not standardized. The objective of this study was to evaluate the predictive value of skin thermometry to determine the parameters of peripheral hemodynamics in children with severe infectious disease.

Materials and methods. The study is prospective, observational. The study covers patients aged between 1 month and 18 years, who were treated in the intensive care unit of pediatric infectious diseases hospital. We analyzed patients' parameters of central and peripheral hemodynamics using echocardiography and Doppler ultrasound; the skin temperature gradients were measured (simultaneously) within the first 24 hours of stay in the ICU. Absolute measures of temperature are used then to calculate temperature gradients: knee-air (KAG)=TK-TA, foot-air (FAG)=TF-TA, knee-foot (KFG)=TK-TF.

Results. We conducted 74 comprehensive hemodynamic studies among 57 patients aged from 1 month to 18 years. Based on the regression analysis of mean linear velocity in the posterior tibial artery and the temperature gradient between the knee and the foot, the F index was 25.730 ($p < 0.001$). The linear correlation was also observed between the knee-air gradient and average velocity in the abdominal aorta; the F index was 26.282 ($p < 0.001$). The F index was 22.472 ($p < 0.001$) between the foot-air temperature gradient and the average velocity in the posterior tibial artery. The temperature gradients demonstrated good prediction abilities for both increased and decreased systemic vascular resistance. The mathematically determined threshold for increased SVR for FAG was about 10.0°C (sensitivity – 79.5%, specificity – 65.4%), KAG – 10.0°C (sensitivity – 61.5%, specificity – 69.2%), KFG – 2.5°C (sensitivity – 33.3%, specificity – 96.2%). Reduced vascular resistance was associated with calculated threshold for FAG at 12.5°C (sensitivity – 80.0%, specificity – 96.7%), KAG – 12.5°C (sensitivity – 80.0%, specificity – 93.3%), KFG – –2.5°C (sensitivity – 80.0%, specificity – 71.7%).

Conclusion. These results support the use of skin temperature as a noninvasive marker of peripheral hemodynamics among children with severe infectious diseases.

Keywords: skin temperature gradient, hemodynamics, infectious diseases, children.

Резюме

Введение. Измерение температуры кожи – один из традиционных клинических методов, который давно используют врачи для оценки кровообращения. Несмотря на долгую историю использования, этот метод до сих пор не стандартизирован.

Цель. Оценить прогностическую ценность термометрии кожи для определения параметров периферической гемодинамики у детей с тяжелыми инфекционными заболеваниями.

Материалы и методы. Исследование проспективное, обсервационное. В исследование включены пациенты в возрасте от 1 месяца до 18 лет, находящиеся на лечении в отделении интенсивной терапии детской инфекционной больницы. Мы проанализировали параметры центральной и периферической гемодинамики пациентов с помощью эхокардиографии и ультразвуковой доплерографии, а также измеряли градиенты температуры кожи (одновременно) в течение первых 24 часов пребывания в отделении интенсивной терапии. Абсолютные значения температуры были затем использованы для расчета температурных градиентов: колено – воздух (KAG) = TK-TA, стопа – воздух (FAG) = TF-TA, колено – стопа (KFG) = TK-TF.

Результаты. Мы провели 74 комплексных гемодинамических исследования среди 57 пациентов в возрасте от 1 месяца до 18 лет. На основании регрессионного анализа средней линейной скорости в задней большеберцовой артерии и градиента температуры между коленом и стопой индекс F составил 25,730 ($p < 0,001$). Также наблюдалась линейная корреляция между градиентом колено – воздух и средней скоростью в брюшной аорте, индекс F составил 26,282 ($p < 0,001$). Индекс F составил 22,472 ($p < 0,001$) между градиентом температуры стопы и воздуха и средней скоростью в задней большеберцовой артерии. Градиенты температуры продемонстрировали хорошие возможности прогнозирования как повышенного, так и пониженного системного сосудистого сопротивления (ССС). Математически определенный порог увеличения СССР для FAG составил около 10,0 °C (чувствительность – 79,5%, специфичность – 65,4%), KAG – 10,0 °C (чувствительность – 61,5%, специфичность – 69,2%), KFG – 2,5 °C (чувствительность – 33,3%, специфичность – 96,2%). Снижение сосудистого сопротивления было связано с рассчитанным порогом FAG 12,5 °C (чувствительность – 80,0%, специфичность – 96,7%), KAG – 12,5 °C (чувствительность – 80,0%, специфичность – 93,3%), KFG – –2,5 °C (чувствительность – 80,0%, специфичность – 71,7%).

Заключение. Эти результаты подтверждают использование температуры кожи в качестве неинвазивного маркера периферической гемодинамики у детей с тяжелыми формами инфекционных заболеваний.

Ключевые слова: градиент температуры кожи, гемодинамика, инфекционные заболевания, дети.

■ INTRODUCTION

Infectious diseases are the major cause of mortality among pediatric population [1]. The serious course of infectious disease is associated with disorders of the haemocirculation, which lead to a decrease in cardiac output and insufficient perfusion of tissues and organs. In the absence of timely diagnosis and correction, a complex of multiple organ failure develops with a high likelihood of unfavorable outcome [2]. The study of peripheral blood

flow is an important component of assessing the severity of hemodynamic disorders and monitoring treatment effectiveness [3]. To determine the characteristics of peripheral hemodynamics, both physical examination methods (skin color and temperature, capillary filling time) and instrumental techniques (plethysmography, Doppler ultrasound, laser Doppler flowmetry, determination of oxygen and carbon dioxide concentration in the peripheral vessels, videomicroscopy, infrared spectroscopy) are used [4, 5]. In the absence of a commonly recommended method for the study of peripheral hemodynamics, doctors often prefer using traditional methods in their practice. Control of peripheral areas' skin temperature is one of such traditional tools that has been used by physicians for a long time to evaluate hemodynamics. Despite the long history of use, this method is still not standardized and there is no clear idea with which parameters of peripheral hemodynamics it correlates.

■ PURPOSE OF THE STUDY

Of this study was to evaluate the predictive value of skin thermometry to determine the parameters of peripheral hemodynamics in children with severe infectious disease.

■ MATERIALS AND METHODS

The study is prospective, observational. Because it was a pilot study, the minimum sample size was not calculated. The study covered patients aged between 1 month and 18 years who were treated in the intensive care unit of the Kyiv City Children's Clinical Infectious Diseases Hospital (KCCIDH) in 2010–2016 for infectious pathology. The exclusion criteria were the non-infectious nature of the disease and concomitant pathology of the cardiovascular system in the past medical history.

During the first 12 hours of stay in the ICU patients' parameters of central and peripheral hemodynamics were measured using echocardiography and Doppler ultrasound. The measurements were performed using a Siemens Sonoline Sienna Ultrasound system with 5–7.5 MHz and 3.5–5 MHz convex transducer and a 7.5 MHz linear transducer. The second test was performed in 24 hours after the previous one. The afterload was evaluated by the Systemic Vascular Resistance (SVR), which was calculated using the simplified SVR formula as the ratio of the Mean Arterial Pressure (MAP) to the Cardiac Index (CIx) [6]. SVR levels considered normal were within the range of 1200–2400 dyn*s*cm⁻⁵*m² (800–1200 for children from 1 month to 12 months) [7]. The characteristics of blood flow in the abdominal aorta, renal arteries, upper mesenteric artery, femoral and posterior tibial arteries were examined with Doppler ultrasound. The ultrasound test was performed according to the standard procedure with the determination of linear velocity characteristics of blood flow. For further analysis, the average linear blood flow rate (TAMx) was used, which is known to correlate better with bulk perfusion [8].

Skin thermometry was performed during the same period of time as hemodynamic parameters were investigated by the Doppler ultrasound. A non-contact Maniquick MQ160 infrared thermometer with a measuring range of 0–100.0 °C was used for thermometry. The resolution of the thermometer is: 0.1 °C, measurement accuracy: ±0.2 °C (according to

the operating instructions). The temperature in the foot area (TF) was determined on the dorsal surface in the projection zone a. dorsalis pedis, skin temperature in the knee area (TK) was determined on the anterior surface. Indoor air temperature (TA) was measured using a Wendox w2040 thermometer with a measurement range of -50°C to $+70^{\circ}\text{C}$, which was located near the patient's bed. The resolution of the thermometer is: 0.1°C , measurement accuracy: $\pm 1.0^{\circ}\text{C}$ in the range of 0°C to $+40^{\circ}\text{C}$. Then the gradients between ambient and skin temperatures were calculated: knee-air (KAG)=TK-TA, foot-air (FAG)=TF-TA, knee-foot (KFG)=TK-TF.

Standard descriptive statistics tools were used to present the data. When studying the relationship of quantitative indicators, Pearson's correlation coefficient and regression analysis for quantitative data were used. For non-parametric data, the Chi-square test, the Fisher exact test and the Mann-Whitney test were used. The difference of $p < 0.05$ was considered statistically significant. All data were collected by one researcher.

Ethical approval

The study was assessed and approved by the KCCIDH's Bioethics Commission. Privacy was ensured by the irreversible removal of identifying information as soon as the data collection and analysis were completed.

■ RESULTS

The results of 57 patients' examinations were selected for the analysis. In total, 74 comprehensive hemodynamic studies were conducted in this group of patients. Among these 57 patients 43 was underwent hemodynamic study once and another 14 children was examined 2 or more times. Secondary exams were performed especially in cases when patient's hemodynamic status apparently deteriorated or improved. Intervals between separate hemodynamic studies ranged from 4 hours till 72 hours. Age of patients ranged from 1 month to 18 years (median – 2 years 6 months). There were 23 girls (40.4%) and 34 boys (59.6%). None of the patients had significant medical history prior to the disease.

Among the studied patients, 42 (73.7%) were diagnosed with sepsis (meningococemia with meningitis – 11, meningococemia – 6, bacterial meningitis – 11, sepsis – 14), 11 (19.3%) – with viral meningoencephalitis, 2 (3.5%) – with severe form of acute viral hepatitis B, 2 (3.5%) – with acute infectious diarrhea. In 11 patients with sepsis, the course of the disease was complicated by septic shock.

All patients underwent medical care according to current local protocols. Mechanical ventilation of the lungs with sodium thiopental sedation was performed in 36 patients at the ICU. Prompt volume resuscitation with crystalloid solutions (0.9% sodium chloride) was used in all cases of septic shock. 6 patients, who did not answer adequately for volumetric therapy, received sympathomimetic support (dopamine 5–20 mcg/kg/min, norepinephrine 1–2 mcg/kg/min). In 5 patients (8.8%) the disease was fatal, in particular: 3 children with meningococemia, 1 patient with sepsis and 1 patient with fulminant viral hepatitis B. Circulatory shock and multiple organ failure developed in all lethal cases.

The room temperature was stable during the survey and in all cases was in the range of $21-23^{\circ}\text{C}$. During the studies in 24 of 74 cases, patients had an

increase in body temperature to more than 37 °C as per results of a routine monitoring in the axillary area. Among these 24 cases, which simultaneous routine measurement of body temperature showed elevated result, 19 cases were within 37–38.0 °C and 5 – within 38.1–39.0 °C.

The thermometry and hemodynamic parameters are presented in the Table 1. Cardiac index was within the normal range (3.3–5.5 l/min/m²) in 22 cases, below 3.3 l/min/m² in 49 cases and above 5.5 l/min/m² in 3 cases. Tachycardia was observed in 14 cases, in the other 60 cases heart rate was within normal limits. The decrease in the mean arterial pressure was observed in 13 studies, in other 61 cases blood pressure was within normal limits.

The calculated systemic vascular resistance was low in 5 cases, within the normal range in 28 cases and increased in 41 cases. In all cases of the low SVR, cardiac output was within the normal range or slightly increased. The average level of Clx in children with the low SVR was 5.1 l/min/m² (4.3 to 5.7 l/min/m²). In the vast majority of cases with increased SVR (85.5%), cardiac output was below normal. The average level of Clx in patients with elevated SVR was 1.9 l/min/m² (0.8 to 4.2 l/min/m²).

We have examined the relationship between the temperature gradients and peripheral hemodynamics. To do this, we have reviewed the scatterplots to detect linear dependence. We have also determined the correlation coefficients between values of the temperature gradients and peripheral hemodynamics (Table 2).

Among the considered parameters, a moderate correlation was noticed between the KFG and FAG gradients and the average linear velocity in the posterior tibial artery. A moderate correlation was also observed between the KAG and the average linear velocity in the abdominal aorta. For the pairs of parameters that had a linear orientation on the scatterplots and a correlation coefficient level above 0.5, we have conducted a further regression analysis (Fig. 1).

Table 1
The thermometry and hemodynamic parameters in the studied patients [1]

Parameter	Min	Max	Mean (SD)	95% CI
KAG (°C)	4.7	17.3	9.9 (2.7)	9.3–10.5
FAG (°C)	0.3	17.6	8.5 (3.5)	7.6–9.3
KFG (°C)	–8.8	8.3	0.7 (2.7)	0.1–1.4
Clx (l/min/m ²)	0.80	5.63	2.65 (1.26)	2.34–2.96
SVR, dyn*s*cm ⁻⁵ *m ²	777.2	8688.9	2818.9 (1683.3)	2403.3–3234.6
HR (beat/min)	56	200	121.8 (30.6)	114.7–128.8
MAP (mmHg)	46.0	113.3	73.0 (14.7)	69.6–76.4
Abdominal aorta TAMx, m/s	0.08	1.26	0.47 (0.19)	0.42–0.51
Renal artery TAMx, m/s	0.11	0.69	0.35 (0.14)	0.32–0.39
Upper mesenteric artery TAMx, m/s	0.18	2.13	0.55 (0.35)	0.47–0.64
Femoral artery TAMx, m/s	0.03	0.35	0.17 (0.09)	0.15–0.19
Posterior tibial artery TAMx, m/s	0.01	0.40	0.09 (0.09)	0.06–0.11

Notes: KAG – knee-air temperature gradient, FAG – foot-air temperature gradient, KFG – knee-foot temperature gradient, Clx – cardiac index, SVR – systemic vascular resistance, HR – heart rate, MAP – mean arterial pressure, TAMx – average linear speed, SD – standard deviation, CI – confidence interval.

Table 2**Correlation coefficients between the temperature gradients and parameters of hemodynamics [2]**

Parameter	KFG		KAG		FAG	
	r	p	r	p	r	p
Abdominal aorta TAMx	-0.008	0.944	0.522	<0.001	0.403	<0.001
Kidney artery TAMx	-0.066	0.596	0.305	0.008	0.195	0.114
Upper mesenteric artery TAMx	-0.046	0.723	0.217	0.093	-0.111	0.936
Femoral artery TAMx	-0.170	0.168	0.433	<0.001	0.480	<0.001
Posterior tibial artery TAMx	-0.542	<0.001	0.194	0.121	0.516	<0.001
Systemic vascular resistance (SVR)	-0.098	0.437	-0.357	0.003	-0.229	0.067

Based on the regression analysis of TAMx in the posterior tibial artery and the temperature gradient between the knee and the foot, the F index was 25.730 ($p < 0.001$). The dependence equation was: $TAMx = 0.108 - 0.021 \cdot KFG$. The dependence of a linear nature was also observed between KAG and average velocity in the abdominal aorta. The F index was 26.282 ($p < 0.001$). The dependence equation was: $TAMx = 0.078 + 0.039 \cdot KAG$. The F index was 22.472 ($p < 0.001$) between the foot-air temperature gradient and the average velocity in the posterior tibial artery. The equation for this dependence was as follows: $TAMx = -0.03 + 0.013 \cdot FAG$.

We have also investigated dependence between the thermometry parameters and the direction of changes in the SVR: with reduced or increased vascular resistance. To determine the possibility of using the temperature gradient to predict increased or decreased peripheral resistance, we have used ROC analysis for each of the temperature gradients investigated (Fig. 2, 3).

Reduced vascular resistance was noted in 5 cases. The analysis of the foot-air gradient with respect to the prediction of reduced vascular resistance showed that the area under the ROC curve (AUC) was 0.903 (Confidence interval (CI): 0.722–1.085, $p = 0.092$). The threshold value calculated using the Youden's index was around 12.5 °C. At this level sensitivity and specificity values were 80.0% and 96.7%, respectively. For the KAG, the AUC was 0.845 (CI: 0.626–1.064, $p = 0.112$). The threshold, calculated mathematically, was also close to the level of 12.5 °C. The sensitivity and specificity levels for this threshold were 80.0% and 93.3%, respectively. For KFG, the AUC was 0.762 (CI: 0.510–1.013, $p = 0.128$). The calculated threshold was at the level -2.5 °C, the sensitivity level was 80.0%, specificity – 71.7%.

Similarly, we have analyzed the predictive capabilities of temperature gradients for the increased vascular resistance (Fig. 3). In general, elevated vascular resistance was observed in 41 measurements within this study.

Regarding the increased SVR for the FAG, the area under the ROC curve (AUC) was 0.769 (Confidence interval (CI): 0.656–0.882, $p = 0.058$). The calculated threshold for the prediction of increased SVR was about 10.0 °C. The sensitivity and specificity values were 79.5% and 65.4%, respectively. In addition, with FAG values less than 2.5 °C, we have observed increased SVR in all cases. When analyzing the KAG gradient, the AUC was 0.714 (CI:

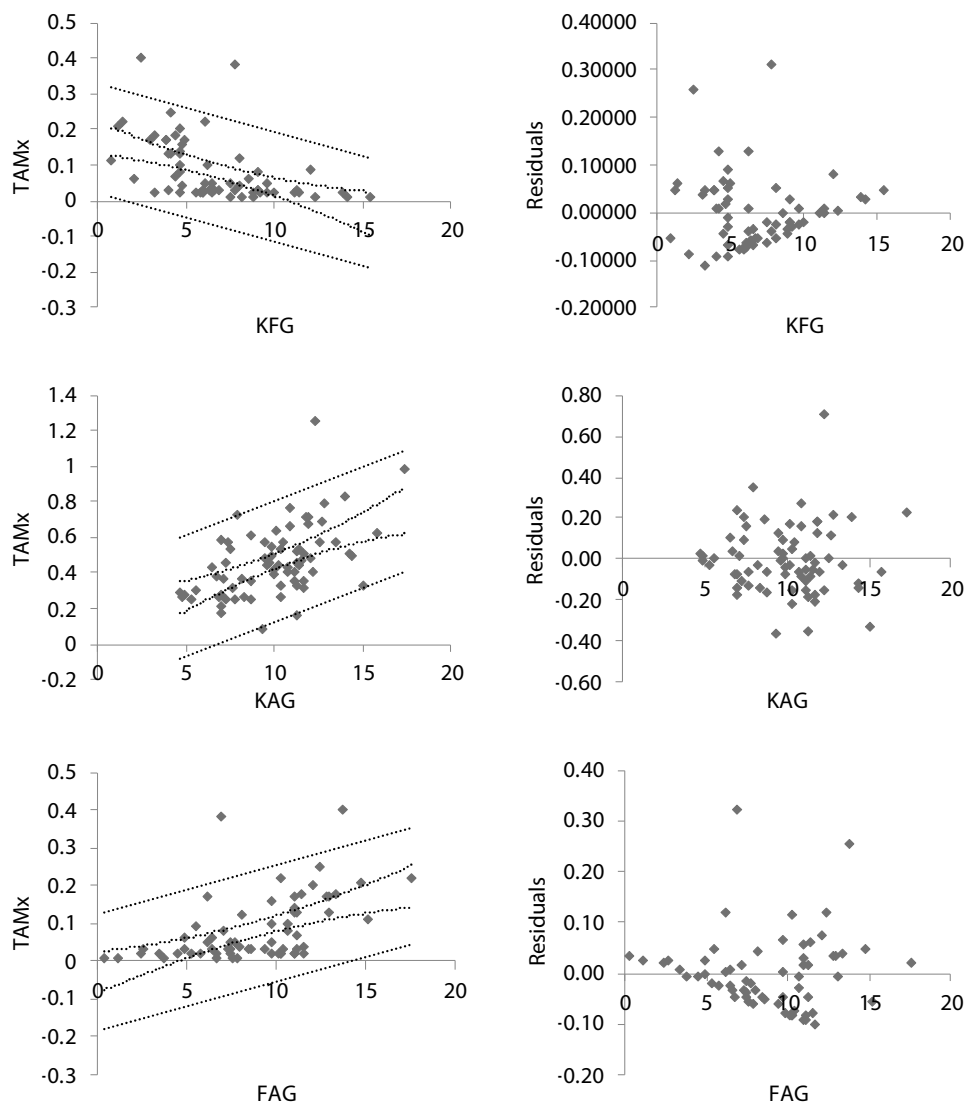


Fig. 1. Interdependence between KFG and the average velocity of blood flow in the posterior tibial artery (A) and residuals in the regression analysis (B); interdependence between KAG and the average velocity of blood flow in the abdominal aorta (C) and residuals in the regression analysis (D); interdependence between FAG and the average velocity of blood flow in the posterior tibial artery (E) and residuals in the regression analysis (F)

0.590–0.838, $p=0.063$). The mathematically determined threshold was 10.0 °C. For this level, the calculated values of sensitivity and specificity were 61.5% and 69.2%, respectively. The KAG value below 5.0°C was associated with the increased vascular resistance in all cases. For the KFG,

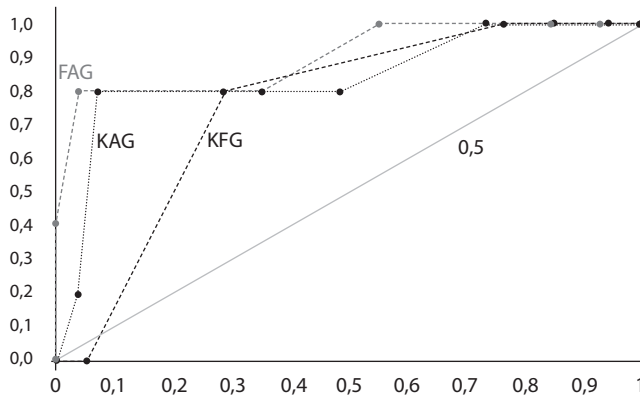


Fig. 2. ROC curve of the predictive value of the temperature gradient relative to the reduced vascular resistance

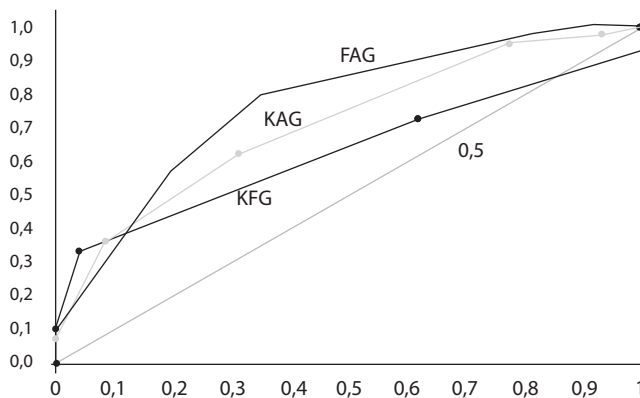


Fig. 3. ROC curve of the predictive value of the temperature gradient relative to the increased vascular resistance.

the AUC was 0.627 (CI: 0.491–0.763, $p=0.070$). The KFG threshold calculated mathematically was 2.5 °C. At this level, sensitivity value was 33.3%, specificity – 96.2%. In addition, in all cases, the KFG gradient above 5.0°C was associated with the elevated SVR.

■ DISCUSSION

As it is known, skin temperature in general is regulated by blood flow. Peripheral vessels dilatation is associated with warming and spasm makes skin colder. In case of neutral ambient temperature and absence of other outer physical impact like radiation and mechanical effect skin temperature reflects inner mechanism of blood supply. Fever, that often accompanies inflammatory diseases and associated with increased core temperature, usually turn on thermoregulatory mechanisms that lead to

skin vessels dilatation and redistribution of blood flow from splanchnic organs for heat removal. This thermoregulation may be affected by deterioration of blood circulatory system in such cases like severe dehydration and shock or may be affected by some toxins or medicines. Regardless of compound inner mechanisms we may expect that skin temperature reflects regional and, perhaps, central hemodynamic. Some surrounded factors like ambient temperature, humidity, presence of sweat or fluid on the skin surface, hot or cold objects are located close to skin may affect local skin temperature. Blood flow also may be impaired because of local vascular or neural abnormalities. It should be appreciated during the skin temperature measurement and results interpretation. Using of temperature gradient instead of absolute temperature is also believed to improve accuracy. Among different temperature gradients for hemodynamic indication long time in medical practice is used core to peripheral gradient. Core temperature in general is taken from rectal measurement. Despite known accuracy rectal thermometry is associated with some disadvantages especially like lag core temperature changes, variable readings depending on depth of insertion and presence of stool in rectum, risk of contagious illness spread, discomfort for both the patient and the parent, risk of intestinal wall damage. By that there is interest of clinicians to use other points of temperature measurement that are easier to test.

The obtained results indicate a sufficiently high correlation between the temperature gradient and the parameters of blood flow in the peripheral vessels. In particular, the temperature gradients between the skin of the foot and the surrounding air and the skin of the foot and knee showed a linear relationship with the average blood flow velocity in the posterior tibial artery. And the temperature gradient between the skin of the knee and the surrounding air had a linear relationship with the average blood flow velocity in the abdominal aorta. At the same time, we have not identified a clear correlation between the temperature gradients and blood flow in the renal and upper mesenteric arteries.

The results show that skin temperature in the distal lower extremities reflects regional hemodynamics in the thigh region. This makes it possible to consider the temperature gradients of the skin of the foot as a means of early diagnosis of circulatory disorders such as hypotension and shock, since it is known that the skin and soft tissues are the first to take part in the compensation mechanism by providing, through vasoconstriction, the redistribution of blood flow to vital organs [9]. Disruption of regional blood flow in the extremities may also be caused, for example in case of septic shock, by vascular thrombosis due to the activation of coagulation hemostasis and DIC. Disruption of blood flow in these cases is often associated with shock damage to the liver and impaired production of antithrombin and protein C [10].

It should be noted that in the literature available to us we have found only a few studies devoted to the study of the prognostic value of thermometry for the evaluation of hemodynamics and their results do not always have unambiguous conclusions. Currently, there are convincing enough evidences to suggest a relationship between peripheral temperature and blood flow. In particular, in a study of adult patients after

abdominal surgery, it was also observed that the temperature gradient between the finger and forearm correlated with the peripheral perfusion index [3]. The authors of another study did not find a correlation between the foot-to-central temperature gradient and changes in microcirculation when examining microcirculation parameters in the sublingual zone among adult patients with severe sepsis and septic shock [11].

Our results also indicate a sufficiently high diagnostic value of the temperature gradients to predict the direction of changes in the systemic vascular resistance. Better diagnostic features for the prediction of reduced or increased vascular resistance were obtained by analyzing the temperature gradient between the temperature of the skin of the foot and the surrounding air.

Peripheral resistance is an important parameter of hemodynamics that depends on the ratio of cardiac output to blood pressure and is used in practice for the overall assessment of vasoconstriction and peripheral perfusion. Among the published studies on the use of thermometry for the evaluation of hemodynamics, there are reports that also confirm that temperature gradients can have a prognostic value for perfusion parameters. For example, in one study in an adult intensive care unit, the temperature gradient between the distal lower extremity and the ambient temperature was correlated with the following perfusion markers: lactate, diuresis and capillary filling time [12]. At the same time, in another study in patients with cardiosurgical pathology, the authors found that the foot temperature and the gradient between the foot and the central temperature had a significant correlation with cardiac output and blood pressure but did not find a significant relationship between thermometry and vascular resistance [13].

The limitation of interpreting the results of this study is a small number of studied cases. Further studies will help to determine the optimal zones for thermometry and to create a standardized hemodynamic monitoring technique.

■ CONCLUSION

In children with severe infectious diseases, temperature gradients of the foot correlate with the blood flow velocity in the tibial artery, and the temperature gradient of the knee area with the blood flow velocity in the abdominal aorta. The temperature gradients of the skin of the foot and knee correlate with the direction of changes in peripheral resistance. The contactless thermometry method can be considered as a simple tool for non-invasive evaluation of the parameters of peripheral hemodynamics.

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Contacts/Контакты: evv1972@gmail.com

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