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Can Partial Oxygen Pressure of Urine be an Indicator for Tissue Perfusion?

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Abstract

Objective: None of the advanced monitorisation procedures, which are focusing only on the haemodynamic and blood gas parameters, are sufficient to estimate tissue perfusion adequately. The search for new parameters that are non-invasive and reliable to provide information about tissue hypoperfusion is significant. The purpose of the present study was to evaluate the relationship between urine partial pressure of oxygen (PuO_2) and routine systemic tissue perfusion parameters in patients with sepsis-like syndrome and impaired cardiac pressure–volume relationship after an open cardiac surgery.

Methods: The study was designed in 50 patients who had elective coronary bypass surgery. Patients were assessed for arterial lactate levels, arterial partial oxygen pressure (PaO_2), cardiac output (CO) and PuO_2 in bladder urine at 180, 360 and 540 min postoperatively.

Results: Tissue perfusion parameters were found to be similar throughout the surgery in addition to no significant rise in plasma creatinine levels. PuO_2 was found to be 91±22, 99±22 and 97±13 mmHg, respectively, at the time points described above. Any correlation between PuO_2 and other measurements was not determined at any time points.

Conclusion: The present study suggests that urine PuO_2 has no relationship with routine systemic tissue perfusion parameters, such as PaO_2, lactate levels and CO. In our opinion, since the COs of the patients were within the normal limits, and none of the patients developed renal injury, the present study might have been unable to determine any correlation. Further studies focused on patients with transient renal ischaemia are needed.

Keywords: Cardiac surgery, renal blood flow, urinary oxygen pressure

Introduction

The undetected circulatory perfusion disorders, improper delivery of oxygen or impaired oxygen utilisation may lead to irreversible organ damage or even death. High-risk surgeries, such as cardiac surgery, require advanced monitoring to predict disturbances in haemodynamics and oxygenation to provide the appropriate treatment. However, the mortality and morbidity rates in patients with sepsis and multiorgan failure remain quite high (1). It appears that none of the advanced monitorisation procedures focusing only on the haemodynamics and blood gas parameters are sufficient to estimate tissue perfusion adequately (2). As a result, new parameters to predict tissue perfusion are needed.

The renal medulla of healthy kidneys is high in blood supply with 15%-20% of total renal blood flow and has a very low oxygen extraction ratio of approximately 16%. However, the renal medulla is highly sensitive to perfusion failure and is one of the first tissues to be affected in hypoperfusion (3-5). It was shown that urine partial pressure of oxygen (PuO_2) is affected by renal arterial flow, hence renal medullary oxygen pressure (6, 7).

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The aim of the present study was to evaluate the relationship between urinary PuO_2 and invasive indirect systemic tissue perfusion parameters and also to investigate if the measurement of PuO_2 may be useful as an early tissue perfusion parameter among patients with sepsis-like syndrome and impaired cardiac pressure-volume relationship after open cardiac surgery.

Methods

The Ethics Committee of Acıbadem Mehmet Ali Aydınlar University approved the study. Informed consent was obtained from the patients. A total of 50 patients who were undergoing routine, elective coronary artery bypass graft surgery were included in the study. Alprazolam (0.5 mg kg^{-1} po^{-1}) and midazolam (125 µg kg^{-1} im^{-1}) were administered to all patients at the night before and 30 min before the operation. Isotonic saline infusion was started at a rate of 100 mL h^{-1} via a 16G cannula. All patients were monitored by two-lead electrocardiography (DII, V5), invasive arterial pressure (via 18G pressure cannula) and central venous pressure (CVP) (via the right internal jugular vein) with 8F introducer under local anaesthesia.

Anaesthesia was induced with midazolam (50 µg kg^{-1} iv^{-1}) and fentanyl (25-35 µg kg^{-1} iv^{-1}). Muscle relaxation was obtained with a pancuronium bolus (2 mg kg^{-1} iv), and in total, 0.1 mg kg^{-1} iv pancuronium was administered. All patients were given 20 mg furosemide after the induction. Through extracorporeal circulation (ECC), haematocrit was kept at 23%-30% as mean arterial blood pressure (ABP) was between 50 and 80 mmHg. The pump flow rate was maintained >2 L m^{-1} during ECC. Moderate hypothermia (32°C) was administered to all patients.

Postoperative follow-up

In the intensive care unit, patients were warmed up by heating blankets, and axillary body temperature was kept at 37°C. Meperidine (0.4 mg kg^{-1} iv) was administered to patients with severe shivering. The mechanical ventilation protocol was performed as SIMV+PS mode, 0.5% FiO_2, 3-5 cm H_2O positive end-expiratory pressure, 10 cm H_2O pressure support, −2 cm H_2O trigger sensitivity, 12 pm respiratory rate and 8 mL kg^{-1} tidal volume. Necessary adjustments were performed according to arterial blood gas analysis. After the patients could spontaneously breathe, the mechanical respiratory rate was reduced by 8 and 4 sequentially. According to the respiratory effort and the patients could maintain the tidal volume, the pressure support was decreased to 4 cm H_2O preferably. When extubation was done, all the patients had been conscious, haemodynamically stable, had no drainage and had <48 mmHg as $PaCO_2$, had a pH >7.30, >250 arterial partial oxygen pressure (PaO_2)/FiO_2 and had been administering dopamine <5 µg kg^{-1} min^{-1}. The patient's fluid balance was monitored for as long as they stayed in the intensive care unit.

Blood and urine sampling

Routine arterial blood gas analysis and electrolyte analysis measurements were performed at the post-extubation period. In addition to the routine blood gas analysis and electrolyte measurements, cardiac output (CO), Pv-aCO_2 and blood-urine gas analysis were performed at 180 (T0), 360 (T1) and 540 (T2) min post-extubation. Urine was collected through a silicone urine catheter inside the bladder into a 27G blood gas analysing syringe to avoid air aspiration. The measurement was immediately performed after sampling using a blood gas analyser (4, 8). Serial creatinine measurements were performed preoperatively and postoperatively at 1 and 5 days to follow-up the renal functions after surgery.

Measurement of CO

CO measurement was performed by using a finger cuff method (Nexfin; BMEYE B.V, Amsterdam, Netherlands). The current method is based on the development of the pulsatile unloading of the finger arterial walls using an inflatable finger cuff with a built-in photoelectric plethysmograph. While continuously measuring ABP, the monitor also calculates CO. The cuffs were placed in the middle phalanx of the second finger of the patients' left hand.

Statistical analysis

Data were presented as mean±SEM. Statistical analysis was performed using GraphPad Prism v5.0 (GraphPad Software, La Jolla, CA, USA). A comparative analysis of the values obtained at various time points was performed using one-way ANOVA test. Pearson correlation was used for comparison of the data sets. A p value <0.05 was considered statistically significant.

Results

Demographic data of the current study are shown in Table 1. Blood gas and chemistry results at post-extubation 180 (T0), 360 (T1) and 540 (T2) min are shown in Table 2. The results related with cardiovascular parameters are presented in Table 3. The relationship between urine PuO_2 and PaO_2 with lactate levels and also CO at the same time points is represented in Figures 1-3.

The patients were haemodynamically stable throughout the surgery and post-extubation period in terms of heart rate, mean arterial pressure (MAP), CVP and CO (p>0.05). Additionally, blood gas analyses and electrolyte concentrations were also found within the normal limits (p>0.05).

Tissue perfusion parameters were similar with T0 with no significant difference. Postoperative PuO_2 was measured as

Table 1. Demographic data

Age (years)	63±5
Gender (male/female)	29/21
BMI (kg m^{-2})	27.3±3.9
Diabetes (%)	26.4
Hypertension (%)	50.4
EuroScore	3±2.5
Duration of CBP (min)	72±35
Duration of cross-clamp (min)	38±18
Postoperative fluid balance (mL)	635±773
Postoperative extubation time (min)	378±113

BMI: body mass index; CBP: coronary artery bypass graft surgery

Table 2. Blood gas parameters, urine partial pressure of oxygen and fluid balance

	T0	T1	T2
Pv-aCO_2 (mmHg)	7.96±1.6	6.35±2.4	7.41±1.1
pH	7.38±0.01	7.36±0.03	7.41±0.04
PCO_2 (mmHg)	35±6	37±8	35±9
HCO_3^- (mmol L^{-1})	25±1.7	26±1.7	25±1.2
BE	0.2±2	2±1.6	1±1.7
PuO_2 (mmHg)	91±22	99±22	97±13
Fluid balance (mL)	760±382	555±425*	562±402*

*p<0.05 versus T0. Pv-aCO_2: venous-to-arterial carbon dioxide difference; PCO_2: partial pressure of carbon dioxide; BE: base excess; PuO_2: urine partial pressure of oxygen

Table 3. Cardiovascular parameters

	T0	T1	T2
CO (L min^{-1})	5.64±1.63	6.11±1.40	6.21±1.58
HR (bpm)	94±8	89±6	81±6
MAP (mmHg)	74±14	76±11	75±13
CVP (mmHg)	9±3	7±2	10±4

CO: cardiac output; HR: heart rate; MAP: mean arterial pressure; CVP: central venous pressure.

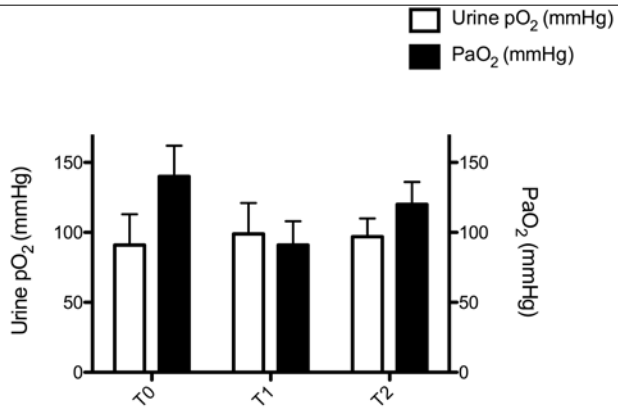

Figure 1. Urine pO_2 and PaO_2 levels through the periods

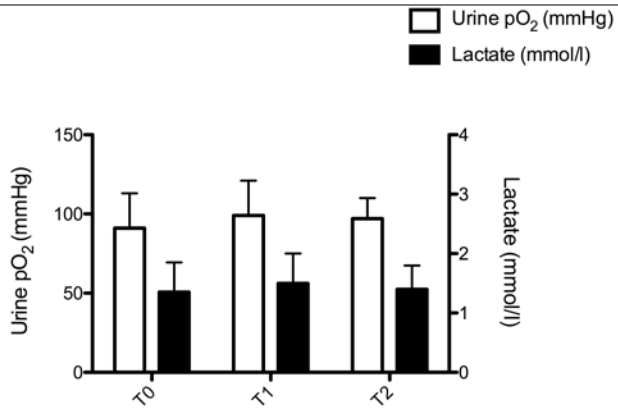

Figure 2. Urine pO_2 and lactate concentrations through the periods

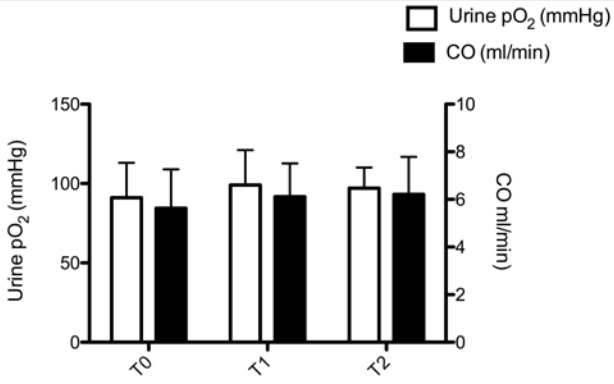

Figure 3. Urine pO_2 and cardiac output concentrations through the periods

91±22, 99±22 and 97±13 mm Hg, respectively, and no significant difference was determined at any post-extubation time points. Moreover, there were no significant correlations between PuO_2 and other tissue oxygenation parameters, such as CO, arterial oxygen pressure and lactate levels (p>0.05).

Fluid balances at the given times were 760±382, 555±425 and 562±402 mL, respectively. Statistically, at time points T1 and T2, fluid balances were closer to the equilibrium state with respect to T0 (p<0.05), but this was not clinically significant.

For the evaluation of renal functions, serum creatinine measurements were performed preoperatively and postoperatively at 1 and 5 days as 0.92±0.5, 0.93±0.5 and 0.85±0.5 mg dL^{-1}, respectively, and no significant difference was found.

Discussion

In patients undergoing open cardiac surgery with ECC, a sepsis-like condition (sepsis-like syndrome) may occur due to major surgical stress, contact of the blood cells to foreign surfaces, cross-clamping of the aorta, non-pulsatile blood flow and body temperature variations (9, 10). As the end-organ damage secondary to impaired microcirculation is one of the main determinants of postoperative mortality, ensuring the adequacy of the microcirculation should be the main focus. With the impaired cardiac pressure-volume relationship, deteriorated microcirculation due to the sepsis-like syndrome makes the routine evaluation of postoperative tissue perfusion difficult to interpret.

Limited information obtained by routine tissue perfusion parameters has led to the need for new research. New techniques have been tending to be non-invasive, easy to perform, safe, low-priced and capable of giving information on the early stages of hypoperfusion. As the renal medulla is one the first affected tissues from hypoperfusion and urine can be sampled by a semi-invasive route, the kidneys are one of the promising organs that can be studied for this purpose.

The renal medulla will be the first affected part of the kidneys in the case of disrupted renal blood flow, and it is known that renal medullary oxygen tension is decisive for PuO_2 (6). Urinary partial oxygen pressure in the collecting tubules is a marker for medullary oxygenation, and it is related to the partial oxygen pressure of the medullary tissue (11, 12).

There are some animal studies that had suggested a relationship between PuO_2 and renal medullary oxygenation. Kitashiro et al. (8) research investigating the relationship between PuO_2 changes and CO had shown a significant correlation between the two and also MAP in dogs with impaired CO.

Wang et al. (13) measured renal pelvic PuO_2 in healthy volunteers using magnetic resonance imaging (MRI) and had found that changes in renal pelvic PuO_2 are compatible with renal medullary ischaemic changes. Despite this, since MRI has a high cost and clinically impractical, this method has limited implementation in clinical practice.

Based on the limitations in our study, we compared PuO_2 of semi-invasively collected urine samples instead of renal medullary or pelvic urine with the most routinely used tissue perfusion parameters, such as CO, plasma lactate levels and mean ABP. Although some studies had shown a correlation between these parameters (6, 13), it could not be demonstrated in our study.

Valente et al. (7) have noted the promising relationship between PuO_2 and systemic oxygenation by demonstrating the decrement of PuO_2 in the cases of decreased renal oxygen delivery associated with anaemia and subsequent increment after transfusion due to increased renal oxygen delivery. However, there are some limitations on the correct interpretation of the literature. It is not fully revealed how much PuO_2 is affected by the large number of variables, such as total renal blood flow or medullary metabolic activity.

In our study, we believe that urine PuO_2 showed no correlation with tissue perfusion parameters because of a large range of urine PuO_2 variations due to renal perfusion alterations or even renal microvascular alterations that change the renal medullary oxygen demand. Meanwhile, none of the patients who participated in the present study had undergone a low CO syndrome or a renal ischaemic condition, which would be quite demonstrative for the sepsis-like syndrome and usefulness of urine PuO_2 among those patients.

Conclusion

Therefore, the normal ranges of renal medullary, renal pelvic and urine PO_2 should be found by studying larger patient groups. Animal studies should be performed to determine the factors affecting PuO_2 while urine is both passing through the urinary tract and waiting in the bladder, thus the factors adversely affecting the measurement could be understood. Additionally, further studies focused on patients with transient renal ischaemia risk or who will undergo surgery with high risk for renal ischaemia are needed to determine the cut-off levels for renal oxygen delivery.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Acıbadem Mehmet Ali Aydınlar University (2017-13/40).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.T.; Design – F.T.; Supervision – F.T.; Data Collection and/or Processing – U.A., H.U.; Surgery – M.O., C.A., H.K.; Writing Manuscript – M.T., U.A., F.T.; Critical Review – F.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

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