Abteilung für Neurochirurgie
Krankenhaus München Bogenhausen
Akademisches Lehrkrankenhaus der Technischen Universität München
(Direktor: apl. Prof. Dr. Chr. Lumenta)

# Analysis of Different Respiratory and Blood Gas Parameters to Optimize Brain Tissue Oxygen Tension (PtiO2) in Patients with Acute Subarachnoid Hemorrhage

**Pataravit Rukskul**

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## ABBREVIATIONS

| | |
|---|---|
| CBF | Cerebral Blood Flow |
| CI | Cardiac Index |
| CPP | Cerebral Perfusion Pressure |
| CSF | Cerebrospinal Fluid |
| CT | Computed Tomography |
| FiO2 | Fraction of Inspired Oxygen |
| GCS | Glasgow Coma Scale |
| Hb | Hemoglobin |
| HCO3 | Bicarbonate |
| Hct | Hematocrit |
| HR | Heart Rate |
| ICP | Intracranial Pressure |
| ICU | Intensive Care Unit |
| MAP | Mean Arterial Pressure |
| MV | Minute Ventilation |
| O2sat | Oxygen Saturation |
| PaCO2 | Partial Pressure of Carbondioxide |
| PaO2 | Partial Pressure of Oxygen |
| PEEP | Positive End-expiratory Pressure |
| pH | Hydrogen Ion Activity |
| Pplat | Plateau Inspiratory Pressure |
| PtiO2 | Partial Pressure of Brain Tissue Oxygen |
| RR | Respiratory Rate |
| SAH | Subarachnoid Hemorrhage |

| | |
|---|---|
| SjO2 | Jugular Bulb Oxygen Saturation |
| SpO2 | Pulse Oximetry |
| SVRI | Systemic Vascular Resistance Index |
| Tblood | Blood Temperature |
| Tbrain | Brain Temperature |
| TV | Tidal volume |

# 1 INTRODUCTION

As recent technological advance in neurosurgical intensive care, brain tissue oxygen (PtiO2) monitoring has become more widespread in the recent decade as PtiO2 could be a tool for prevention and treatment of cerebral ischemia from various causes. The PtiO2 level should be optimized to the value that the cerebral cellular tissue can survive.

Tissue oxygenation is the product of blood flow and arterial oxygen content perfusing the tissue over time. Adequacy of brain oxygenation can be assessed by PtiO2 monitoring, which directly refers to the driving pressure of oxygen diffusion to mitochondria at tissue level. Therefore, PtiO2 would be a good parameter for evaluating and following cerebral tissue perfusion during the intensive care management.

While the therapeutic impact of PtiO2 supplementing neurosurgical monitoring is proven by several clinical studies, its correlation with various parameters is not well studied. Recent studies generally focused, mainly in traumatic patients, on the relation between PtiO2 value and prognostic outcome (Bardt et al., 1998; Dings et al., 1998; Valadka et al., 1998). However, there is still no apparent study on how to improve the PtiO2 level by the various parameters.

In fact, a number of factors and several parameters could directly or indirectly affect to the PtiO2 level, as well as the understandings in the relationships of these various parameters are still limited. Therefore, this research is to analyze the correlation between the PtiO2 and different parameters in practical treatments for the patients with acute subarachnoid hemorrhage (SAH).

## 1.1 Background

Delayed vasospasm is a principle cause of secondary brain damage after acute SAH. Vasospasm occurs in over half of patients and causes symptomatic ischemia in about one third (Awad et al., 1987; Dorsch et al., 2002). Ischemic vasospasm is also the major cause of death and disability after aneurysm rupture (Mayberg et al., 1994; Meyer et al., 1995; Solenski et al., 1995). For this reason, the brain oxygenation should be monitored to early detect ischemic process due to delayed vasospasm after acute SAH.

For recent decades, clinicians have improved understanding of the pathophysiology of the brain following traumatic brain injury, stroke, as well as acute SAH after the development of the continuous bedside monitoring of brain oxygenation using PtiO2 or global cerebrovenous oxygen saturation (SjO2). Both techniques have provided new knowledge on the pathophysiology of cerebral ischemia and the alteration of cerebral blood flow (CBF) in traumatic brain injury (Gopinart et al., 1999, al-Rawi et al., 2000, Kiening et al., 1996, Murr et al., 1995).

The SjO2 monitoring technique has been applied to use in traumatic head injury since the 1980s (Cruz et al, 1985; Garlick et al., 1987; Robertson et al., 1989; Hans et al., 1991; Gopinart et al, 1994), and with the development of catheters, this technique has become a practical method for monitoring the global ischemic insults.

After the development of Clark type sensor probes, PtiO2 monitoring has also become a new alternative method, and several studies have been reported on the usefulness of this monitoring technique and its correlation with various parameters (Maas et al., 1993; Dings et al., 1996; Kiening et al, 1996; Zauner et al., 1996; van Santbrink et al., 1996; Hoffman et al., 1996; Valadka et al., 2002).

The PtiO2 could be affected by several factors, such as the fractions of inspired oxygen (FiO2), pH, intracranial pressure (ICP), cerebral blood flow (CBF), oxygen saturation (O2sat) and various respiratory parameters. For example, FiO2 is one of several factors which clinicians can manipulate to improve the PtiO2 level. Up to now, there are only a few reports on how PtiO2 responses to the manipulation of FiO2 (Menzel et al.,1999; Longhi et al., 2002).

Valadka et al. suggested that the mortality rate of severe head-injured patients increased in relations to the increasing duration of time at or below a PtiO2 of 15 mmHg or with the occurrence of any PtiO2 of 6 mmHg or below (Valadka et al., 1998). Therefore, the improvement of PtiO2 level should be considered and properly maintained during the management in intensive care unit (ICU).

# 2 PURPOSE OF THE STUDY

Delayed vasospasm and cerebral ischemia remain to be the principle causes of high morbidity and mortality following SAH (Mayberg et al., 1994; Meyer et al., 1995; Solenski et al., 1995). Several monitoring devices; such as transcranial doppler (TCD), angiography, or computed tomography (CT), are currently used to assess and detect the vasospasm. However, PtiO2 monitoring is a gradually widespread indicative method to observe the driving pressure of oxygen diffusion to mitochondria at cerebral tissue level.

Apart from the standard protocol treatment, there are several factors performing the essential roles for the effective management. A large number of parameters were used to monitor and improve the treatment. Monitoring of PtiO2 is a promising modern technique that permits early detection of impending cerebral ischemia in neurosurgical patients.

While the therapeutic impact of PtiO2 supplementing neurosurgical monitoring is proven by several clinical studies, its correlation with several parameters is not well understood. Recent studies focused, mainly in traumatic patients, only on the relationship between PtiO2 and outcome (Barth et al., 1998; Dings et al., 1998; Valadka et al., 1998).

In this research, the PtiO2 and its relationships with different respiratory and blood gas parameters in practical treatment of acute SAH would be highlighted.

The purpose of the study can be concluded as follows:

- To understand the relationships between PtiO2 and various parameters during monitoring the patients in ICU;
- To be knowledgeable about how to manipulate FiO2 and various parameters in order to optimize and predict the PtiO2 value;

- To obtain experiences from the study to develop techniques of monitoring and improve means of data collecting to be more precisely in the future; and
- To improve the intensive care management for the patients with acute SAH.

# 3 MATERIALS AND METHODS

## 3.1 Patients

Data from multimodal monitoring, including $PtiO_2$, were collected retrospectively in a series of 6 patients (4 male and 2 female) with acute subarachnoid hemorrhage (Glasgow Coma Scale score (GCS) ≤ 8). They were admitted to the neurosurgical intensive care unit of Academic Hospital München-Bogenhausen, Technical University of Munich, Germany between September 2001 and October 2002.

The mean age was 54.33 years (range between 32-69 years). All patients were treated according to a standard protocol of acute subarachnoid hemorrhage, and all underwent computed tomography and cerebral arteriography. All cases were definitely diagnosed to be a cerebral aneurysm rupture. The clinical grade of each patient was analyzed at admission according to the Hunt and Hess grading system (Hunt and Hess, 1968); poor-grade patients with SAH were defined as those with a grade of III or IV. The severity of SAH was classified radiologically by CT according to Fisher's grading scale (Fisher et al., 1980).

All patients were intubated and placed on volume-controlled ventilation under sedation. They were mechanically ventilated during the whole period of study and underwent a ventriculostomy for ICP monitoring and a microcatheter for PtiO2 monitoring.

The clinical profiles of the patients who were selected to study are summarized in Table 1.

**Table 1. Clinical Characteristics of The Patients with Acute SAH**

| Patient No. | Age(yr)/Sex | Initial GCS[a] | Hunt and Hess Grade | Fisher Grade | Aneurysm Location[b] | Probe Location | Operation |
|---|---|---|---|---|---|---|---|
| 1 | 69/M | 8 | III | III | AcomA | Right | Clipped |
| 2 | 45/M | 8 | III | V | AcomA | Right | Clipped |
| 3 | 62/M | 8 | III | III | AcomA | Right | Clipped |
| 4 | 62/M | 6 | IV | III | AcomA | Right | Clipped |
| 5 | 32/F | 6 | IV | IV | PcomA | Left/Right | Clipped |
| 6 | 56/F | 7 | III | IV | AcomA | Left | Clipped |

[a]GCS, Glasgow Coma Scale
[b]Aneurysm Location; AcomA, Anterior communicating aneurysm; PcomA, Posterior communicating aneurysm.

### 3.2 Brain Tissue Oxygen Monitoring

On the arrival of the neurosurgical intensive care unit, the patients were under general anesthesia, and then a triple lumen transcranial bolt was passed through and tapped into the cranium (Zauner et al., 1993), as demonstrated in Figure 1. The PtiO2 was continuously measured by using LICOX monitoring system.

LICOX (GMS, Kiel Mielkendorf, Germany) is a system for continuous quantitative regional monitoring of dissolved oxygen and temperature in body fluids (PaO2) and tissue (PtiO2). This system operates with the microcatheter oxygen electrode, which is made of polyethylene. The LICOX Brain Tissue Oxygen Monitor, recently approved by the Federal Drug Administration, is surgically implanted through the patient's skull via small catheter probes.

For the PtiO2 monitoring, three patients were placed a microcatheter in the right frontal region. Two patient was placed a microcatheter in the left frontal region and one patient was placed microcatheters in both sides. After insertion, the probes were tunneled subgaleally and secured. Calibration of each probe was performed according to the manufacture’s specifications.

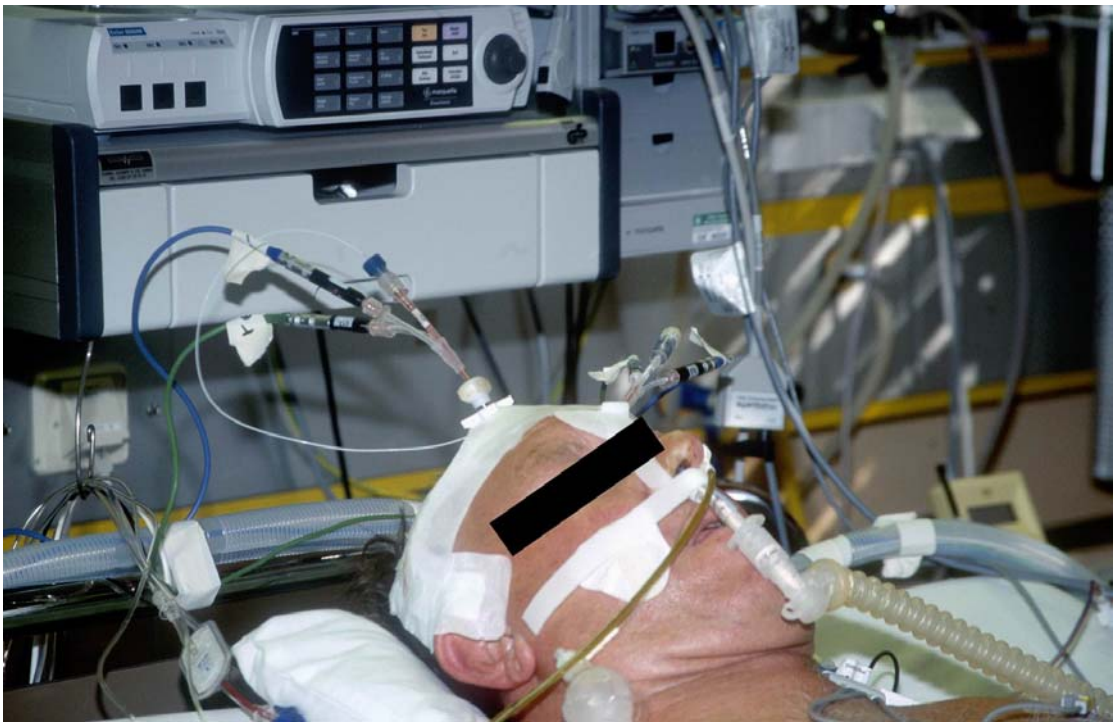


**Figure 1.** Continuous brain tissue monitoring using triple lumen transcranial microcatheter (LICOX brain tissue oxygen monitoring system).

### 3.3 ICP and CPP Monitoring

ICP was measured with an intraparenchymal sensor (ICP Express, Codman, Johnson & Johnson, UK) (Figure 2). The data was continuously monitored and stored at 1-minute interval during the time of study. All of 6 patients were monitored with Codman's ICP monitoring system.

Cerebral perfusion pressure (CPP) was calculated by subtracting ICP from mean arterial pressure (MAP), with the formula: CPP = MAP- ICP. The ICP and CPP data were collected in the computer.

### 3.4 Arterial Blood Gas and Respiratory Parameters

Bayer Rapidlab 860 blood analyser (Bayer, Germany) was routinely used to measure the arterial blood gas and electrolyte during the intensive care management. The blood gas machine is shown in Figure 3.

Blood was drawn anaerobically from a peripheral artery (radial, brachial, or femoral) via a arterial line catheter. The blood samplings were investigated for direct measurement of partial pressures of carbon dioxide (PaCO2) and oxygen (PaO2), oxygen saturation (O2sat), hydrogen ion activity (pH), bicarbonate (HCO3), hematocrit (Hct) and hemoglobin (Hb). Serial samplings of arterial blood gas were investigated for several times around the clock. Then, the results of the arterial blood gas parameters and the exact time of blood sampling were also recorded.

The values of various respiratory parameters namely, fraction of inspired oxygen (FiO2), tidal volume (TV), minute ventilation (MV), plateau inspiratory pressure (Pplat), positive end-expiratory pressure (PEEP), and respiratory rate (RR), were also routinely collected.

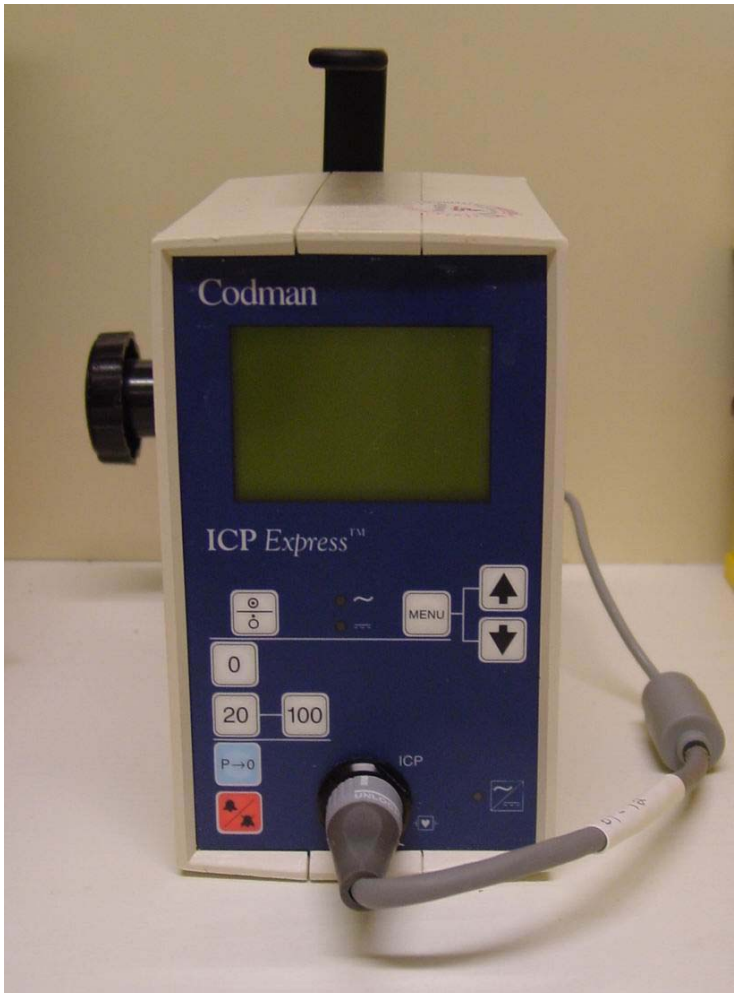



**Figure 2.** Intracranial pressure monitoring system (Codman ICP Express) was continuously used for ICP measuring during the time of study.

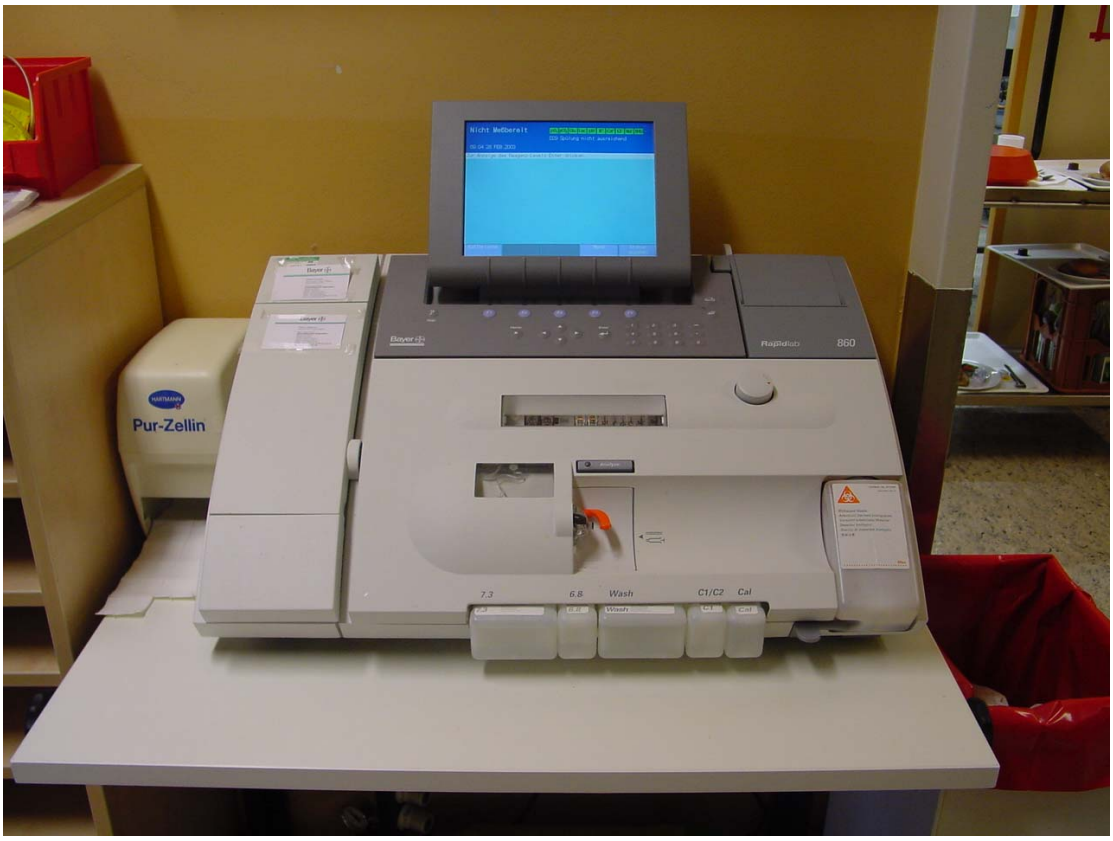



**Figure 3.** Arterial blood gas analyser (Bayer Rapidlab 860) was used to measure the arterial blood sampling (arterial blood gas, electrolyte, as well as hematocrit and hemoglobin).

### 3.5 Pulse Contour Cardiac Output Monitoring System (PiCCO®)

The PiCCO system (Pulsion Medical Systems, Munich, Germany) is a physiological device providing minimal invasive continuous monitoring of hemodynamic parameters (Figure 4). The system offers the users information to monitor and diagnose the patients' condition and, therefore, provide necessary assistance in the decision process for optimal treatment.

In this study, 2 patients were monitored by the PiCCO monitoring system. The hemodynamic parameters, namely, heart rate (HR), cardiac index (CI), blood temperature (Tblood), and systemic vascular resistance index (SVRI), were recorded and evaluated as a pilot study. The correlation between PtiO2 and various hemodynamic parameters was also assessed.

### 3.6 ICUpilot® Software

ICUpilot (CMA Microdialysis, Solna, Sweden) is a software, which was developed to assist clinicians in collecting of the data from the monitoring machines around the patients, especially in ICU. Clinicians can follow continuously the effect of various interventions.

For this study, the data from multimodal monitoring systems and PtiO2 from LICOX system were transferred to collect in the ICUpilot software. The information could be presented as trend curves; additionally, the screen was continuously updated as ICUpilot would collect the data from various monitoring instruments. Moreover, the pictures of the patients could be recorded every minute by a digital camera (Figure 5). Hence, a sudden change in ICP could be explained by, e.g. a change in the position of the patient or manipulations of the ventriculostomy tube.

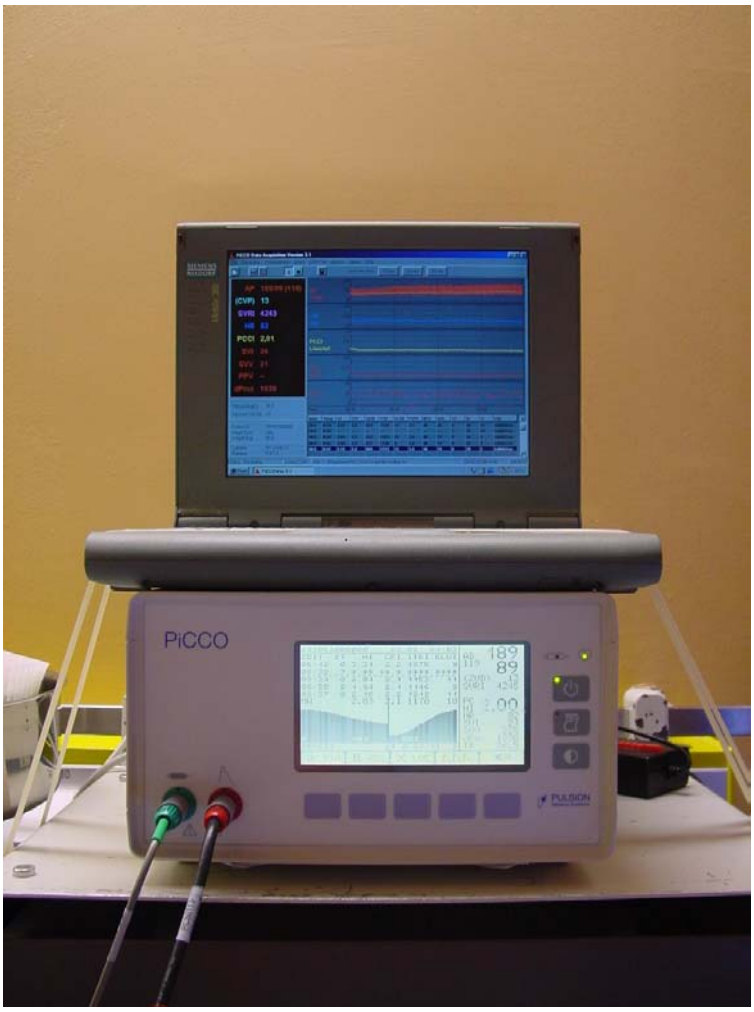
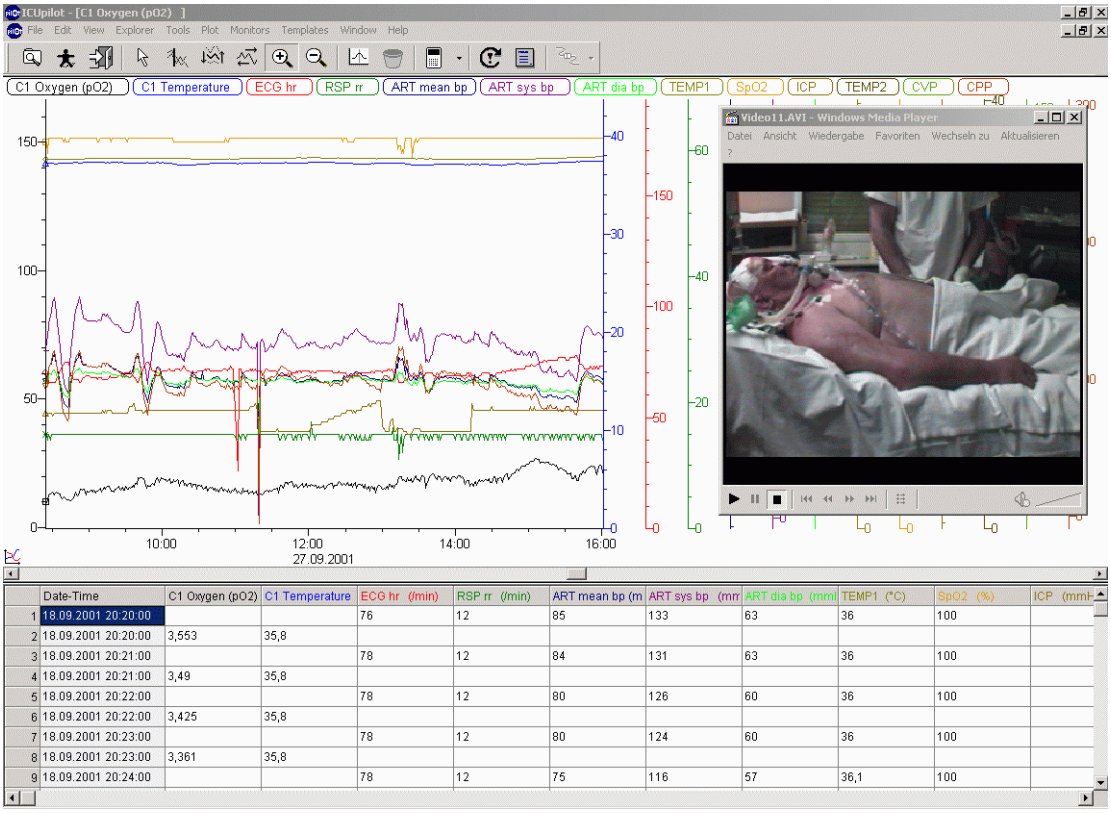



**Figure 4.** Pulse contour cardiac output monitoring system (PiCCO®) was also used to monitored hemodynamic parameters (in 2 patients).




| | Date-Time | C1 Oxygen (pO2) | C1 Temperature | ECG hr (/min) | RSP rr (/min) | ART mean bp (m | ART sys bp (mm | ART dia bp (mml | TEMP1 (°C) | SpO2 (%) | ICP (mmH |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 18.09.2001 20:20:00 | | | 76 | 12 | 85 | 133 | 63 | 36 | 100 | |
| 2 | 18.09.2001 20:20:00 | 3,553 | 35,8 | | | | | | | | |
| 3 | 18.09.2001 20:21:00 | | | 78 | 12 | 84 | 131 | 63 | 36 | 100 | |
| 4 | 18.09.2001 20:21:00 | 3,49 | 35,8 | | | | | | | | |
| 5 | 18.09.2001 20:22:00 | | | 78 | 12 | 80 | 126 | 60 | 36 | 100 | |
| 6 | 18.09.2001 20:22:00 | 3,425 | 35,8 | | | | | | | | |
| 7 | 18.09.2001 20:23:00 | | | 78 | 12 | 80 | 124 | 60 | 36 | 100 | |
| 8 | 18.09.2001 20:23:00 | 3,361 | 35,8 | | | | | | | | |
| 9 | 18.09.2001 20:24:00 | | | 78 | 12 | 75 | 116 | 57 | 36,1 | 100 | |

**Figure 5.** ICUpilot software (CMA, Microdialysis, Solna, Sweden) recorded minutely all parameters and updated continuously. The data were demonstrated in multiple trend curves. The picture of the patient can be monitored and recorded every minute by digital camera, in order to explain any artifacts from various bedside manipulations.

### 3.7 Data Evaluation

The data, chosen from the recorded data in ICUpilot at the same time as arterial blood gas sampling, would be evaluated up to 10 days after the onset of SAH. These raw data would be manually inspected all over again, with the reference to detailed plots and patients' observed images from digital video recording camera, to exclude any artifacts occurred during the monitoring from the study.

The following parameters were collected and analyzed:

1. Partial pressure of brain tissue oxygen (PtiO2)
2. Intracranial pressure (ICP)
3. Mean arterial pressure (MAP)
4. Cerebral perfusion pressure (CPP; CPP = MAP – ICP)
5. Pulse oximetry (SpO2)
6. Hydrogen ion activity (pH)
7. Partial pressures of carbon dioxide (PaCO2)
8. Partial pressures of oxygen (PaO2)
9. Bicarbonate (HCO3)
10. Oxygen saturation (O2sat)
11. Hemoglobin (Hb)
12. Hematocrit (Hct)
13. Fraction of inspired oxygen (FiO2)
14. Tidal volume (TV)
15. Minute ventilation (MV)
16. Plateau inspiratory pressure (Pplat)
17. Positive end-expiratory pressure (PEEP)
18. Brain temperature (Tbrain)

19. Respiratory rate (RR)

20. Heart rate (HR)

21. Cardiac Index (CI)

22. Blood temperature (Tblood)

23. Systemic vascular resistance index (SVRI)

### 3.8 Statistical Analysis

The statistical analysis was performed on a PC computer, using a SPSS software (version 10.0.1, SPSS Inc.,Chicago, Illinois, USA.). All data of 6 patients were analyzed together as a pooled data, as well as the data of individual patients were also analyzed.

Descriptive statistics, Pearson correlation and linear regression analysis were used in statistical analysis. Data was expressed as mean ± standard deviations. Statistical significance was set at $P < 0.05$. Pearson correlation was used to analyze the relationship between PtiO2 and each parameter. The relationship between PtiO2 and various parameters was tested by performing linear regression analysis. Overall correlations are presented in linear estimation curve and/or boxplot diagram.

In addition, multiple regression analysis with stepwise method was used to find out which valuable parameters and correlation coefficients could be helpful to predict the PtiO2 value.

# 4 RESULTS

The total of 6 selected patients with acute SAH were studied. All of them were treated with standard protocol of SAH therapy. The probes' sensors demonstrated no significant drift over the monitoring time. There was no complication associated with the use of the LICOX brain tissue oxygen monitoring device in either the brain or the artery. Remarkably, no infections, hematomas or tissue reaction were observed.

## 4.1 Pooled Data Analysis

Pooled data were recorded by ICUpilot program. The data consisted of 413 minute-points of the sampling time of blood gas analysis (n = 413) in all 6 patients and 130 minute-points recorded by PiCCO monitoring system (n = 130) in 2 of 6 patients. The data recordings of this series started an average of 15 hours (range from 5 to 26 hours) after admission.

In this study, PtiO2 value was approximately around 28.38 ± 11.02 mmHg with the range from 10 to 64.03 mmHg. The average value of ICP was 12.88 ± 7.93 mmHg and the average value of MAP was 99.02 ± 12.1 mmHg. The CPP value, calculated by the formula: CPP = MAP – ICP, was around 86.15 ± 10.76 mmHg in average with the range from 55.6 to 119.2 mmHg.

Descriptive statistical analysis of the pooled data over the entire monitoring period in all patients are summarized in Table 2.

**Table 2. Descriptive statistics of pooled data**

| Parameters | N[a] | Minimum | Maximum | Mean ± SD[b] |
|---|---|---|---|---|
| PtiO2 (mmHg) | 413 | 10 | 64.03 | 28.38 ± 11.02 |
| ICP (mmHg) | 413 | 1 | 39.6 | 12.88 ± 7.93 |
| MAP (mmHg) | 413 | 74 | 144 | 99.02 ± 12.1 |
| CPP (mmHg) | 413 | 55.6 | 119.2 | 86.15 ± 10.76 |
| SpO2 (%) | 413 | 80 | 100 | 97.6 ± 3.68 |
| Tbrain (°C) | 413 | 33.8 | 39.5 | 36.77 ± 1.157 |
| pH | 413 | 7.2 | 7.6 | 7.42 ± 0.74 |
| PCO2 (mmHg) | 413 | 27 | 60.5 | 38.97 ± 6.57 |
| PaO2 (mmHg) | 413 | 61.4 | 448 | 173 ± 68.42 |
| HCO3 (mmol/L) | 413 | 17.3 | 34.1 | 26.68 ± 3.2 |
| O2sat (%) | 413 | 91 | 99.9 | 98.83 ± 1.02 |
| Hb (g/dL) | 413 | 7.7 | 15.9 | 11.38 ± 1.56 |
| Hct (%) | 413 | 22.6 | 46 | 33.54 ± 4.63 |
| FiO2 (%) | 413 | 35 | 100 | 72.34 ± 16.35 |
| TV (mL) | 413 | 530 | 1170 | 704.28 ± 118.93 |
| MV (mL) | 413 | 6.6 | 15.6 | 11.12 ± 1.56 |
| Pplat (mmHg) | 413 | 14 | 22 | 17.78 ± 1.99 |
| PEEP (mmHg) | 413 | 2.3 | 20 | 9.94 ± 3.61 |
| RR (/min) | 413 | 11 | 20 | 16.1 ± 2.4 |
| HR (/min) | 130 | 61 | 120 | 84.14 ± 15.47 |
| CI (/min) | 130 | 1.9 | 6 | 3.83 ± 0.95 |
| Tblood (°C) | 130 | 35 | 38.5 | 37.04 ± 0.82 |
| SVRI (dyne · s · $cm^{-5}/m^2$) | 130 | 1185 | 4558 | 2000.9 ± 594.72 |

PtiO2, partial pressure of brain tissue oxygen; ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; SpO2, pulse oximetry; pH, hydrogen ion activity; PaCO2, partial pressures of carbon dioxide; PaO2, partial pressures of oxygen; HCO3, bicarbonate; O2sat ,oxygen saturation; Hb, hemoglobin; Hct, hematocrit; FiO2, fraction of inspired oxygen; TV, tidal volume; MV, minute ventilation; Pplat, plateau inspiratory pressure; PEEP, positive end-expiratory pressure; Tbrain, brain temperature; HR, heart rate; CI, cardiac index; Tblood, blood temperature; RR, respiratory rate, SVRI, systemic vascular resistance index.

[a]Numbers of minute-points.

[b]Standard deviation.

### *4.1.1 Correlations between PtiO2 and Various Parameters*

Pearson correlation was used to statistically analyze the relationship between the various data and the PtiO2 value, in order to detect which parameters influencing the PtiO2 value during the entire monitoring study.

The Pearson correlation analysis of pooled data showed good correlations between PtiO2 and several parameters. In overall correlation, positive associations were found significantly between PtiO2 and MAP ($p < 0.001$), PtiO2 and CPP ($p < 0.001$), PtiO2 and SpO2 ($p < 0.001$), PtiO2 and blood pH ($p < 0.001$), PtiO2 and HCO3 ($p < 0.001$), PtiO2 and O2sat ($p < 0.05$), PtiO2 and FiO2 ($p < 0.001$), PtiO2 and TV ($p < 0.05$),and PtiO2 and MV ($p < 0.001$). Negative associations were found

significantly between PtiO2 and Tbrain ($p < 0.05$), PtiO2 and PCO2 ($p < 0.001$), PtiO2 and Hb ($p < 0.001$), PtiO2 and Hct ($p < 0.001$), and PtiO2 and Pplat ($p < 0.001$).

For the analysis in hemodynamic monitoring (n = 130) in 2 patients, positive association was found only between PtiO2 and HR ($p < 0.05$).

The results of overall correlations were summarized in Table 3.

**Table 3. Pearson's correlation of the various parameters with PtiO2**

| | N[a] | Pearson's Correlation (r) | Significant (p) |
|---|---|---|---|
| ICP (mmHg) | 413 | 0.08 | 0.105 |
| MAP (mmHg) | 413 | 0.37** | < 0.001 |
| CPP (mmHg) | 413 | 0.357** | < 0.001 |
| SpO2 (%) | 413 | 0.212** | < 0.001 |
| Tbrain (°C) | 413 | -0.117* | 0.017 |
| pH | 413 | 0.357** | < 0.001 |
| PCO2 (mmHg) | 413 | -0.220** | < 0.001 |
| PaO2 (mmHg) | 413 | -0.005 | 0.918 |
| HCO3 (mmol/L) | 413 | 0.389** | < 0.001 |
| O2sat (%) | 413 | 0.126* | 0.11 |
| Hb (g/dL) | 413 | -0.177** | < 0.001 |
| Hct (%) | 413 | -0.180** | < 0.001 |
| FiO2 (%) | 413 | 0.387** | < 0.001 |
| TV (mL) | 413 | 0.124* | 0.012 |
| MV (mL) | 413 | 0.189** | < 0.001 |
| Pplat (mmHg) | 413 | -0.194** | < 0.001 |
| PEEP (mmHg) | 413 | -0.084 | 0.087 |
| RR (/min) | 413 | 0.094 | 0.058 |
| HR (/min) | 130 | 0.214* | 0.014 |
| CI (/min) | 130 | 0.142 | 0.108 |
| Tblood (°C) | 130 | -0.179 | 0.141 |
| SVRI (dyne · s · $cm^{-5}/m^2$) | 130 | -0.099 | 0.264 |

PtiO2, partial pressure of brain tissue oxygen; ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; SpO2, pulse oximetry; pH, hydrogen ion activity; PaCO2, partial pressures of carbon dioxide; PaO2, partial pressures of oxygen; HCO3, bicarbonate; O2sat ,oxygen saturation; Hb, hemoglobin; Hct, hematocrit; FiO2, fraction of inspired oxygen; TV, tidal volume; MV, minute ventilation; Pplat, plateau inspiratory pressure; PEEP, positive end-expiratory pressure; Tbrain, brain temperature; HR, heart rate; CI, cardiac index; Tblood, blood temperature; RR, respiratory rate, SVRI, systemic vascular resistance index.

[a] Numbers of minute-points.

** Correlation significant at 0.01 level (2-tailed).

* Correlation significant at 0.05 level (2-tailed).

### *4.1.2 Responses of PtiO2 to Changes in FiO2 and Respiratory Parameters*

In the standard practice, clinicians generally manipulates FiO2 and RR to control the oxygenation by following the various oxygen parameters, namely PaO2, O2sat, and PtiO2. For the oxygen therapy in neurosurgical patients as well as acute

SAH patients in critical status, the FiO2 is usually started at the level of 100% and decrease gradually to optimize oxygenation. The response of PtiO2 on changes of FiO2 is still questioning.

To examine the effects of changes of FiO2 level on PtiO2 value in this study, linear regression analysis was used to analyze the relationship between PtiO2 and FiO2. In this serie, the average value of FiO2 was 72.34 ± 16.35 %, by the range from 35 to 100%. Pearson correlation showed positive correlation between PtiO2 and FiO2 ($p < 0.001$). The data was then plotted to estimate the response of PtiO2 on the FiO2 at various level. The linear estimation curve of the relationship between PtiO2 and FiO2 is demonstrated in Figure 6 and boxplot diagram of the relationship is illustrated in Figure 7. The trend of changes of PtiO2 shows positive relationship with the FiO2 level.

For the PtiO2 value estimation, linear regression analysis showed that the predictive regression coefficient was 0.26 with a constant value of 9.32. Therefore, the response of PtiO2 value on changes of FiO2 value can be estimated from the regression equation : **$Y = 9.32 + 0.26X$ (Y = PtiO2; X = FiO2)**. The slope of this linear equation suggested that in every 10% change of FiO2, PtiO2 would change by 2.6 mmHg.

The parameters of respiratory setting, namely TV, MV, Pplat and PEEP were also analyzed in relationships with PtiO2 value. The results showed that the correlation between PtiO2 and TV and the correlation between PtiO2 and MV were positively significant ($p < 0.05$ and $p < 0.001$, respectively), while correlation between PtiO2 and Pplat was negatively significant ($p < 0.001$). However, in our study, the relationship between PtiO2 and PEEP was non-significantly found.

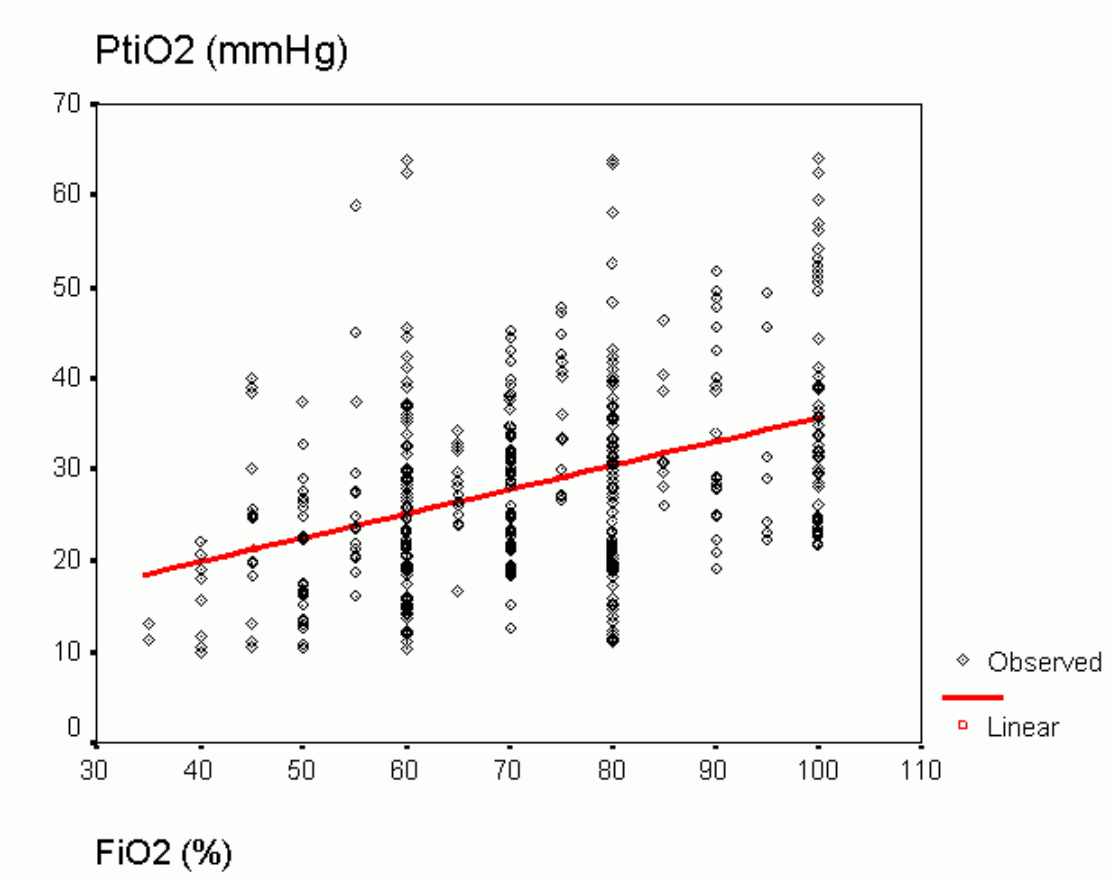



**Figure 6.** Scatterplots and linear estimation curve depicting the positive correlations between PtiO2 and FiO2 ($p < 0.001$).

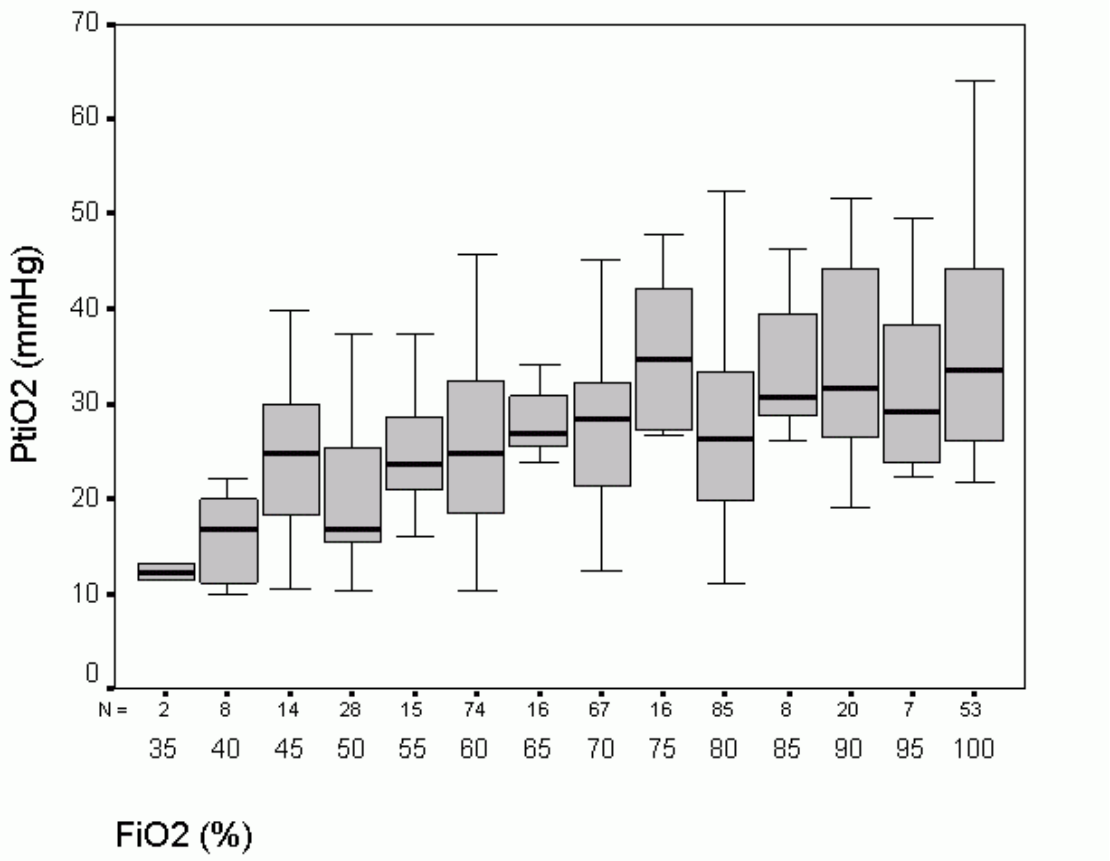



**Figure 7.** Boxplot diagram illustrating a correlation between PtiO2 and CPP in 6 patients. Horizontal bars inside the boxes indicate median levels of the PtiO2 values. Numbers (N) under the horizontal axis are the number of minute-point data at each level of FiO2.

The significant correlations between PtiO2 and these respiratory parameters are demonstrated in Figure 8, 9 and 10.

### *4.1.3 Correlations between PtiO2 and Pulse Oximetry and Arterial Blood Gas Parameters*

During the monitoring, blood gas sampling was routinely checked up to assess the patients' oxygenation. Pulse oximetry (SpO2) was also measured during the entire monitoring time. SpO2 and blood gas parameters, namely PaO2, PCO2, HCO3, O2sat, pH, including Hb and Hct, adding up from all blood gas sampling investigation, were recorded and evaluated.

In fact, blood functions as an oxygen carrier, which directly transfers oxygen, and all various blood gas components to the brain, the association between PtiO2 and these parameters could be a focus for realization. For our data analysis, good correlation was found between PtiO2 and SpO2 significantly ($p < 0.001$). The result also showed that PCO2 and O2sat are significant both in correlation with PtiO2 ($p < 0.001$ and $p < 0.05$, respectively). However, the correlation between PtiO2 and PaO2 was not significant, probably affected by various factors. The possibility on this matter will be further discussed. The estimation curves of the significant correlations are demonstrated in Figure 11, 12 and 13.

In addition, positive association was found between PtiO2 and pH and HCO3 significantly ($p < 0.001$) and negative association was found between PtiO2 and Hb and Hct significantly ($p < 0.001$). The estimation curves of the correlations are demonstrated in Figure 14-17.

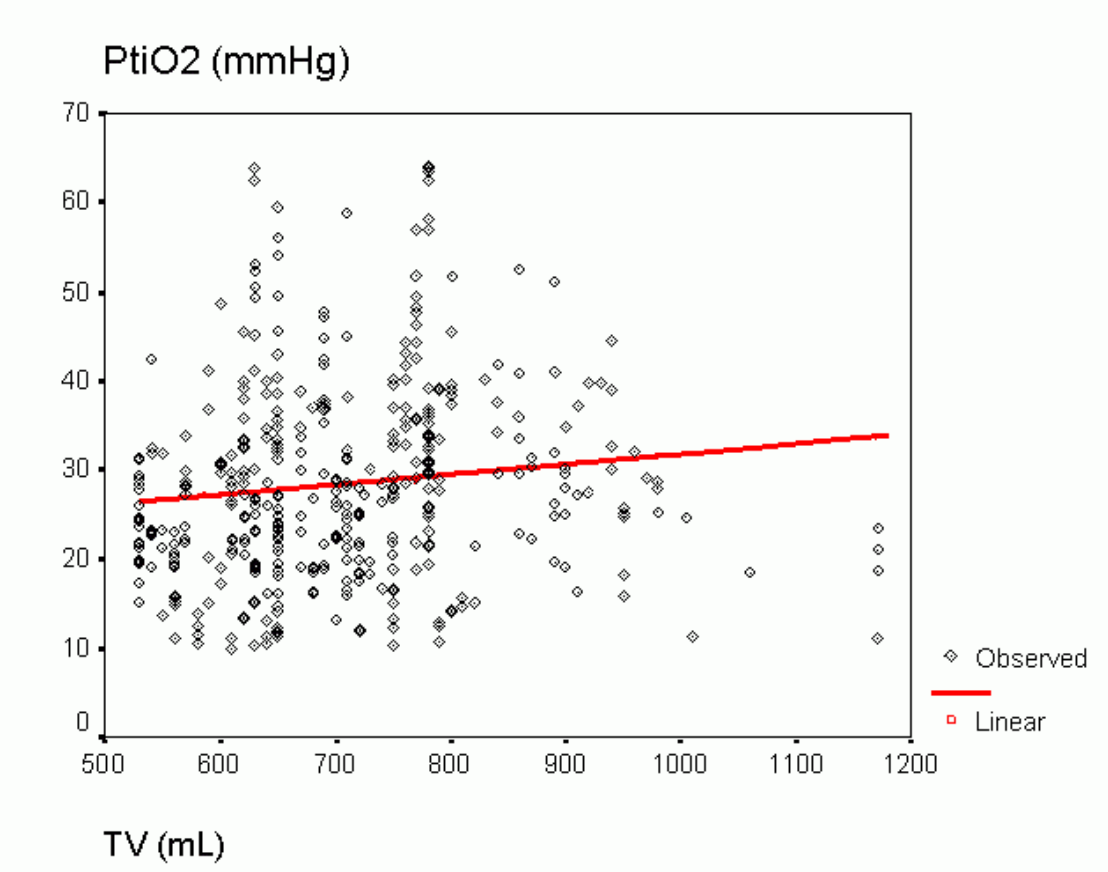



**Figure 8.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and TV ($p < 0.05$).

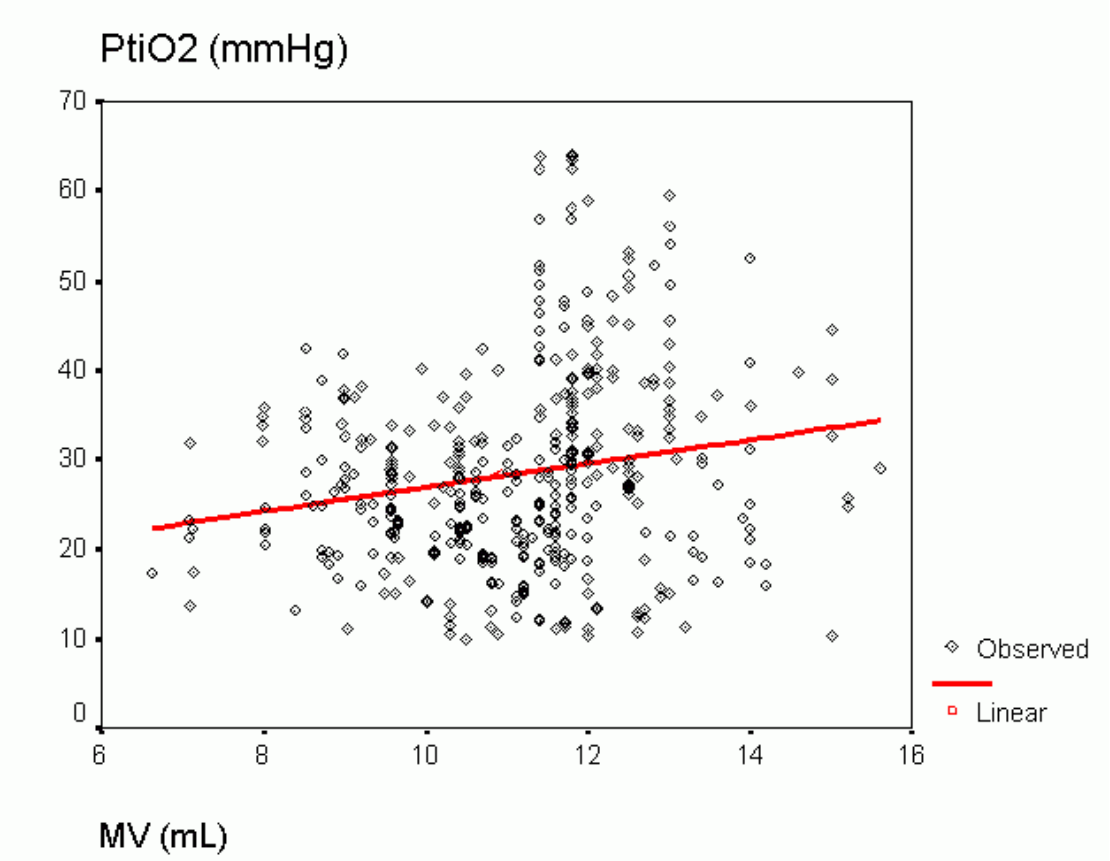



**Figure 9.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and MV ($p < 0.001$).

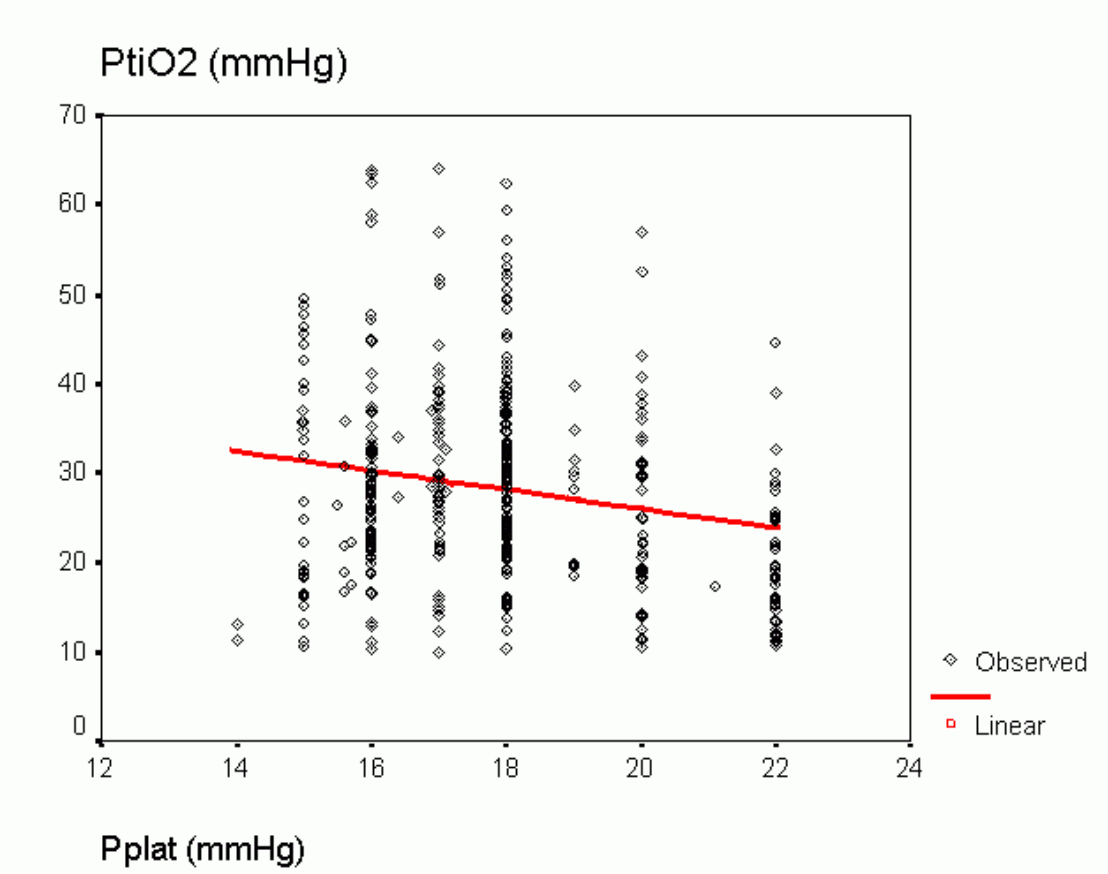



**Figure 10.** Scatterplots and linear estimation curve showing the negative correlation between PtiO2 and Pplat ($p < 0.001$).

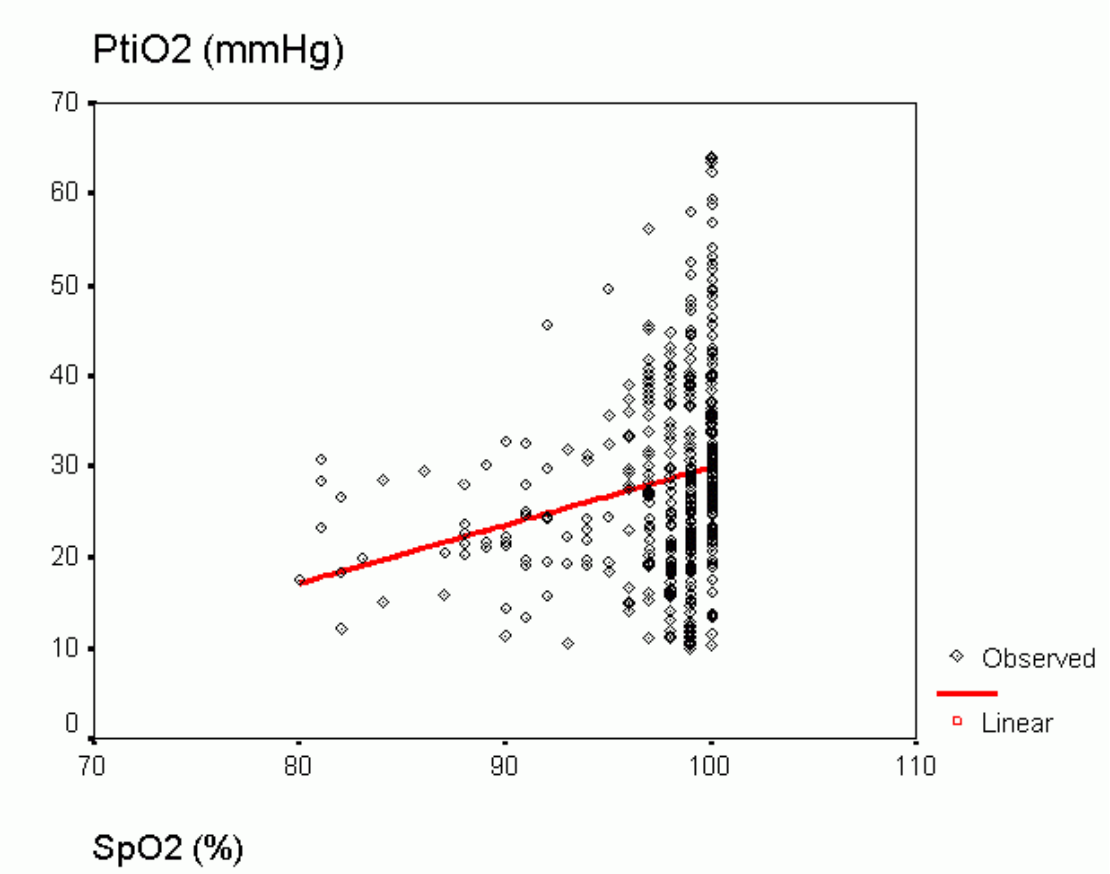



**Figure 11.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and SpO2 ($p < 0.001$).

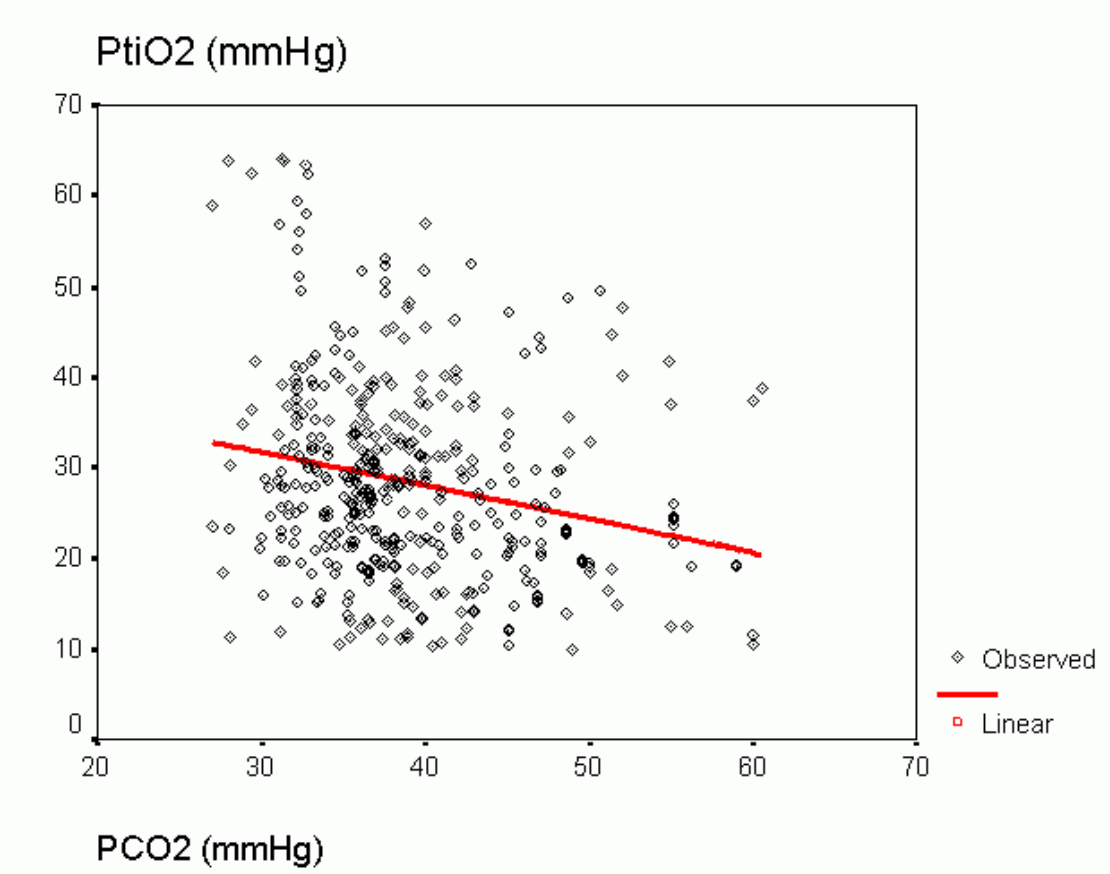



**Figure 12.** Scatterplots and linear estimation curve showing the negative correlation between PtiO2 and PCO2 ($p < 0.001$).

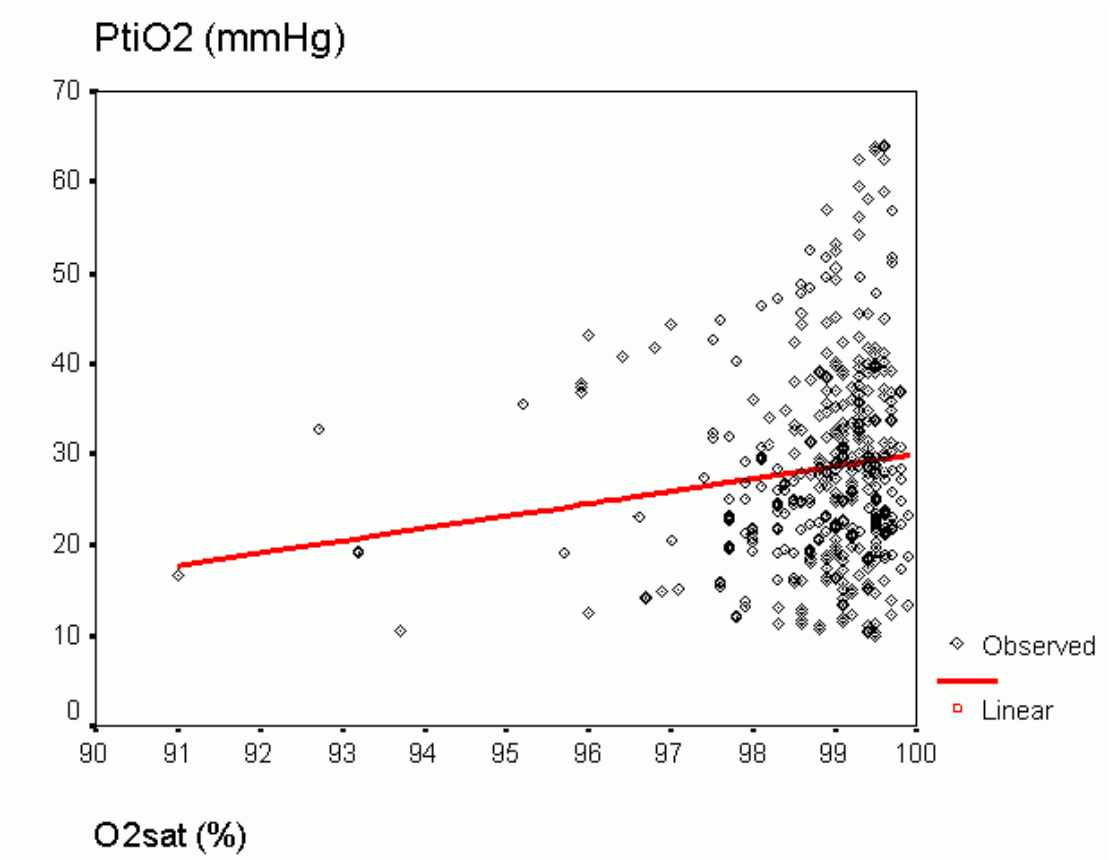



**Figure 13.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and O2sat ($p < 0.05$).

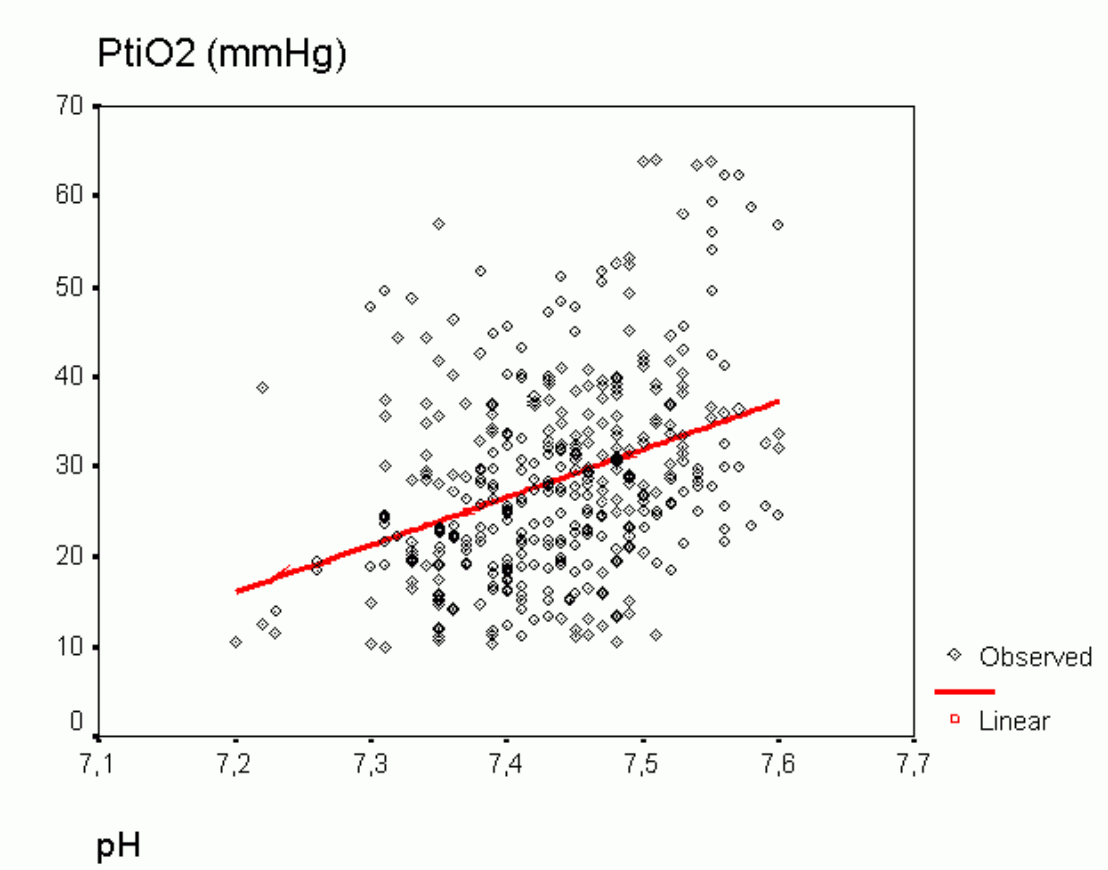



**Figure 14.** Scatterplots and linear estimation curve illustrating the positive correlation between PtiO2 and pH ($p < 0.001$).

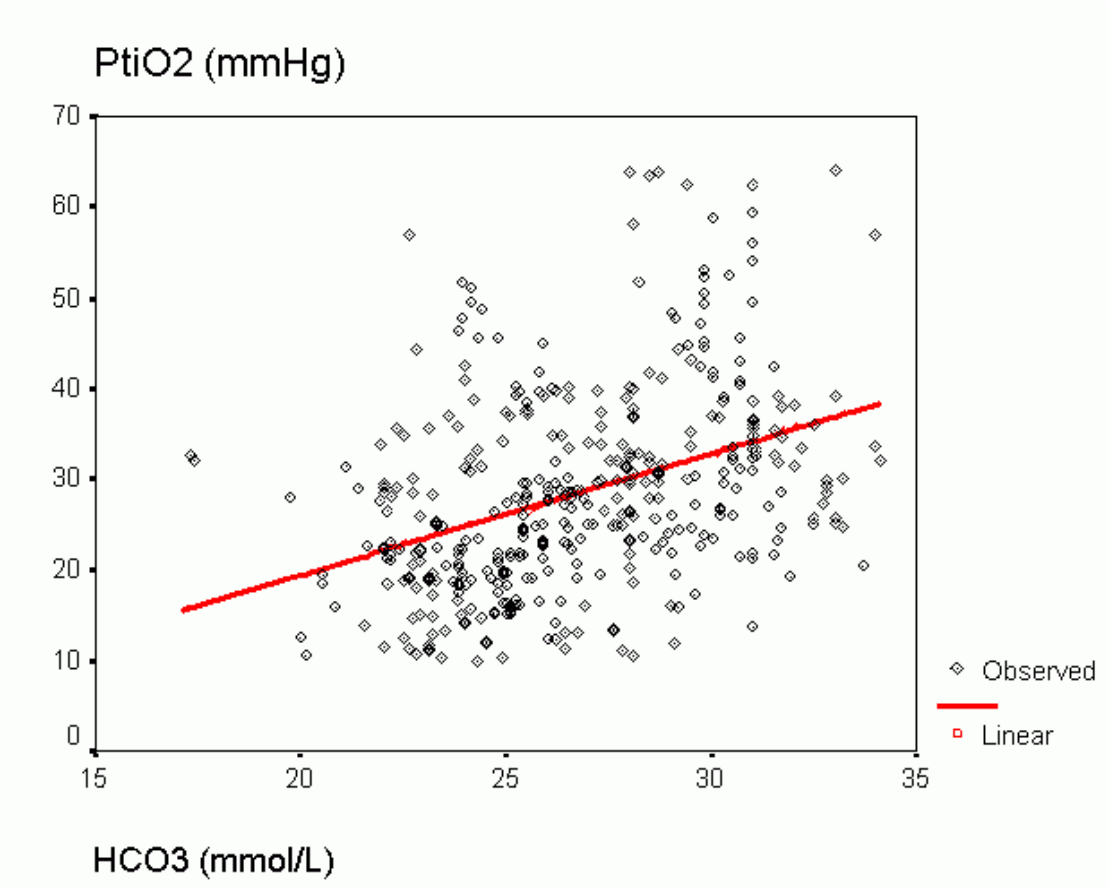



**Figure 15.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and HCO3 ($p < 0.001$).

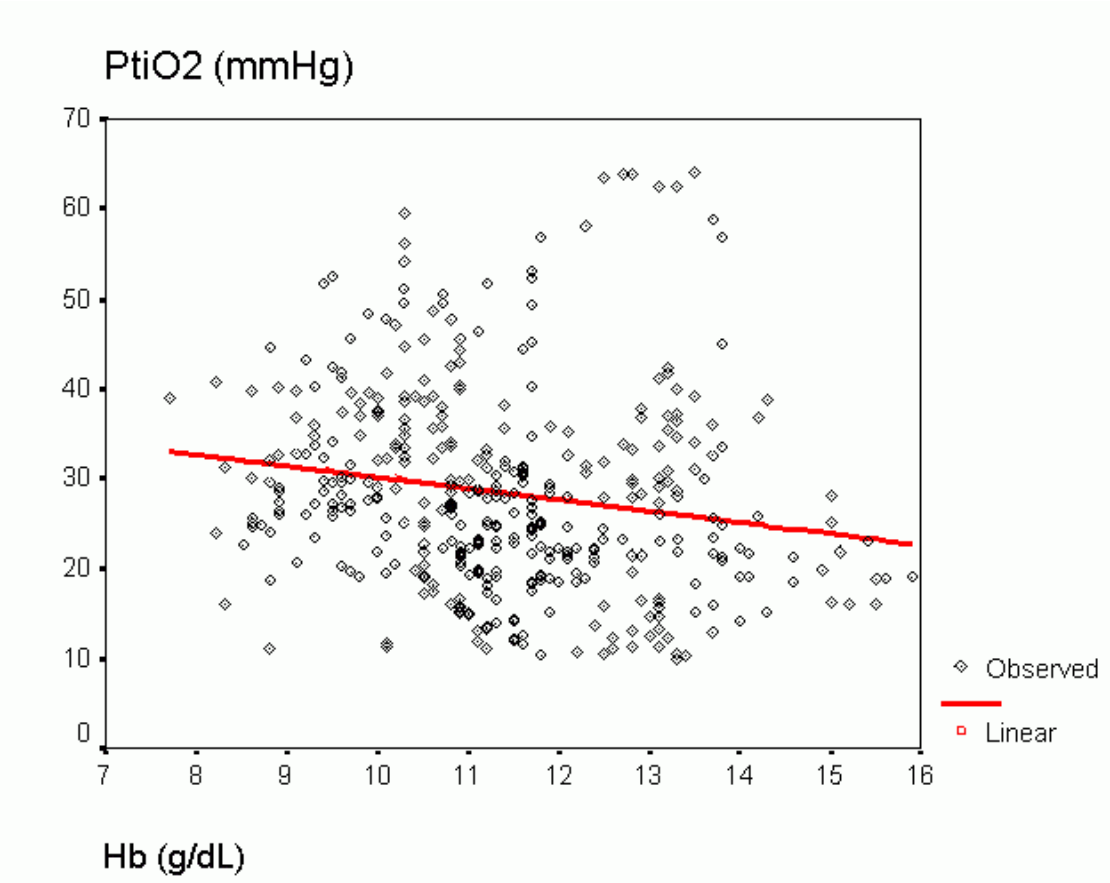



**Figure 16.** Scatterplots and linear estimation curve showing the negative correlation between PtiO2 and Hb ($p < 0.001$).

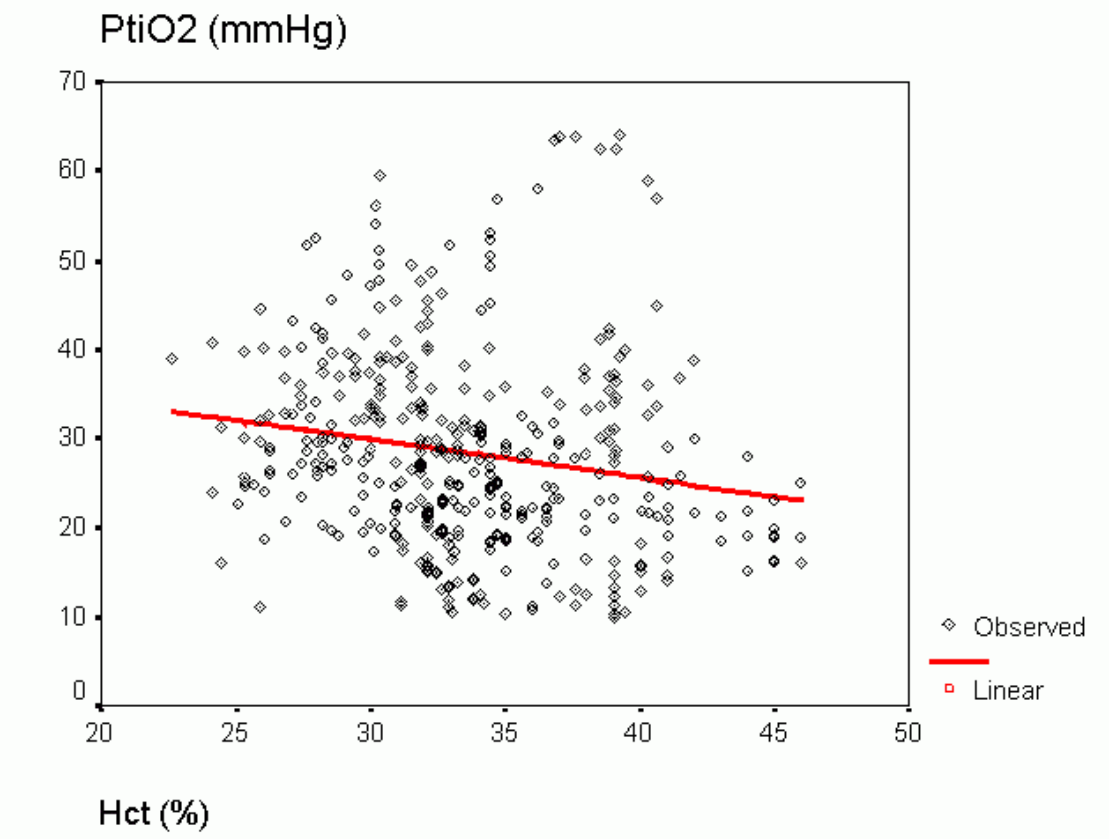



**Figure 17.** Scatterplots and linear estimation curve showing the negative correlation between PtiO2 and Hct ($p < 0.001$).

### *4.1.4 Correlations between PtiO2 and ICP, MAP and CPP*

The changes of CPP value could be affected by the changes of ICP and/or MAP value (CPP = MAP - ICP). In this study, CPP was calculated by subtracting ICP from MAP.

The mean values of ICP, MAP and CPP are 12.88 ± 7.93 mmHg, 99.02 ± 12.1 mmHg and 86.15 ± 10.76 mmHg respectively. The correlation between PtiO2 and ICP, CPP and MAP was analyzed, the results showed the relationship between PtiO2 and CPP and MAP were significant in correlation ($p < 0.001$), but the correlation between PtiO2 and ICP was not significant.

The estimation curves of these relationships are presented in Figure 18 and 19. Furthermore, the relationship between PtiO2 and CPP is also illustrated by error bar diagram in Figure 20.

### *4.1.5 Correlation between PtiO2 and Temperature*

Average brain temperature (Tbrain) of all 6 patients, measured using the probe sensor, was 36.77 ± 1.157 °C, and average blood temperature (Tblood) of 2 of 6 patients, measured using hemodynamic monitoring (PiCCO) machine, was 37.04 ± 0.82 °C.

For the correlation analysis, PtiO2 decreased significantly while Tbrain increased ($p < 0.05$) as demonstrated in Figure 21, but the correlation between PtiO2 and Tblood, analyzed in 2 of 6 patients, was not significant.

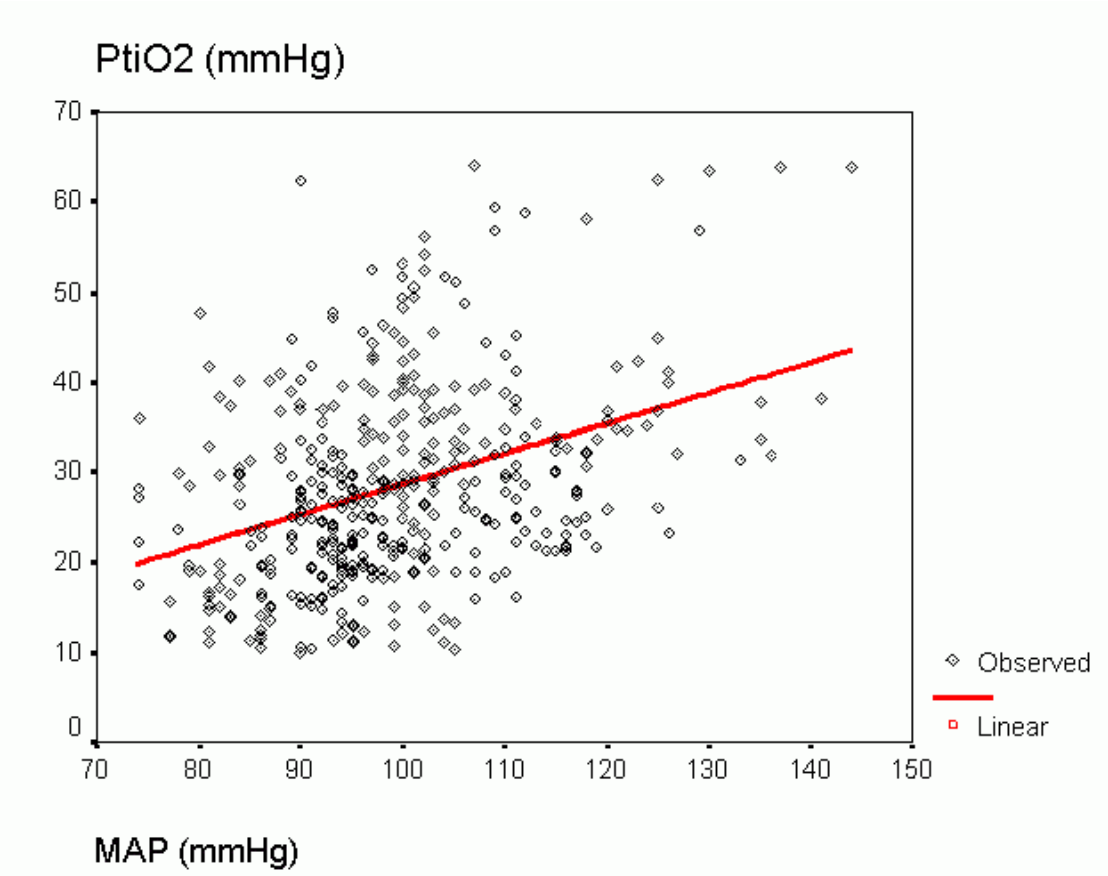



**Figure 18.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and MAP ($p < 0.001$).

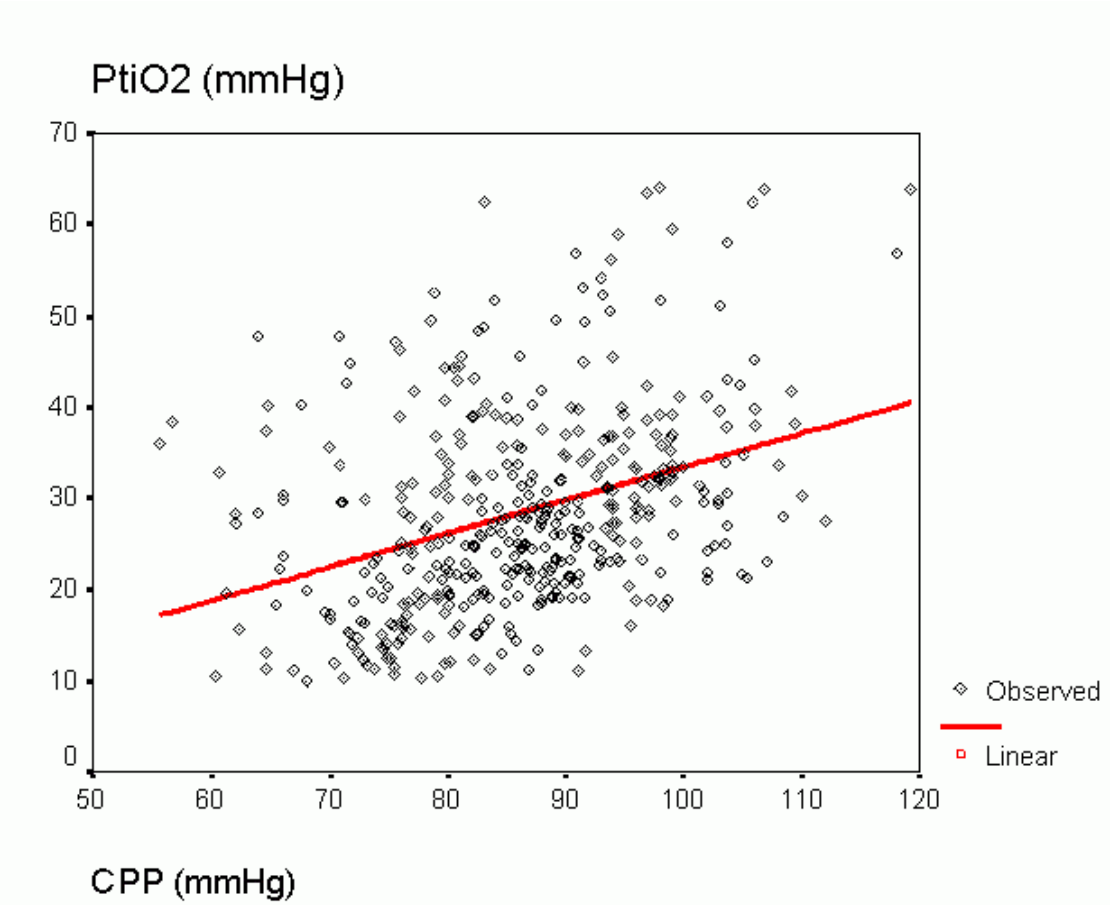



**Figure 19.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and CPP ($p < 0.001$).

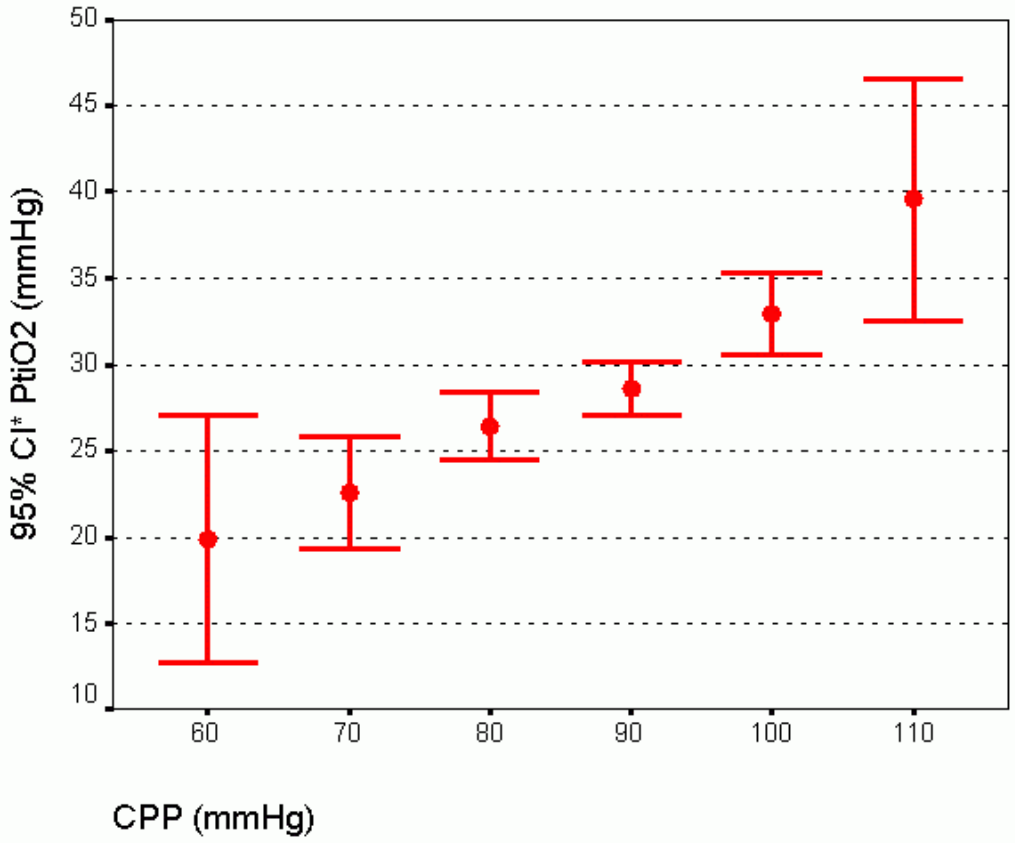



**Figure 20.** Bar diagram displaying mean values (± 95% confidence intervals) of PtiO2 level for grouped CPP value.

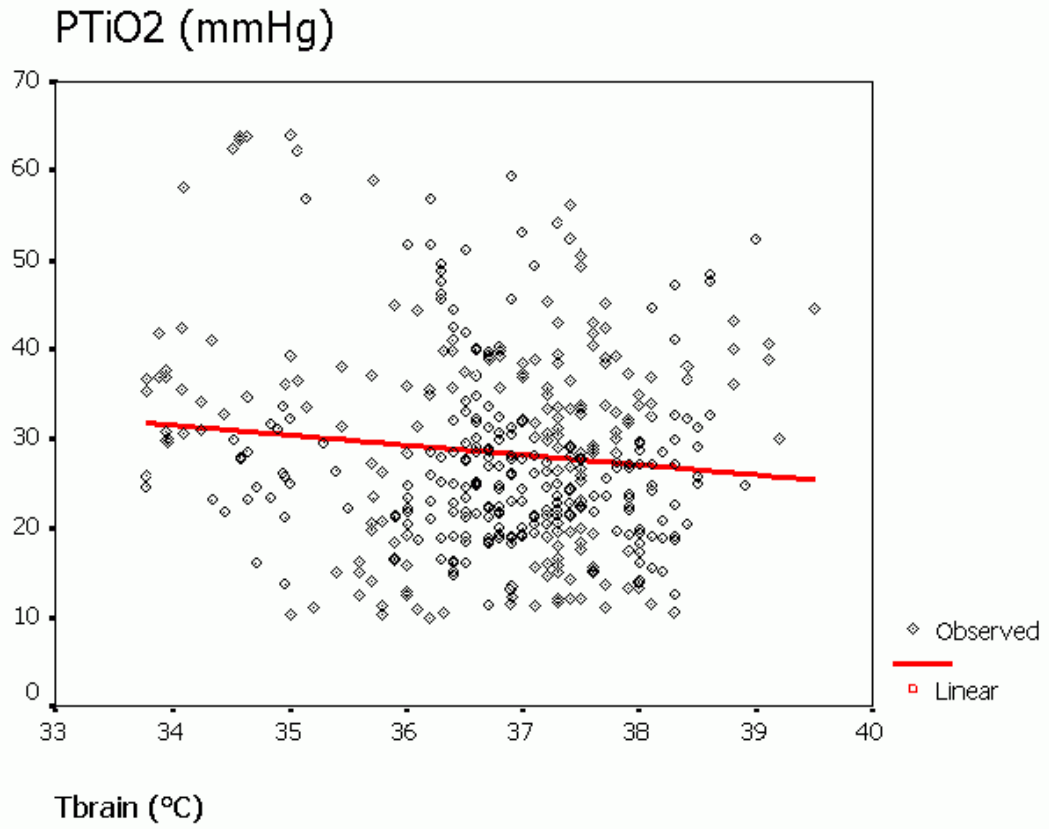



**Figure 21.** Scatterplots and linear estimation curve showing the negative correlation between PtiO2 and Tbrain ($p < 0.05$).

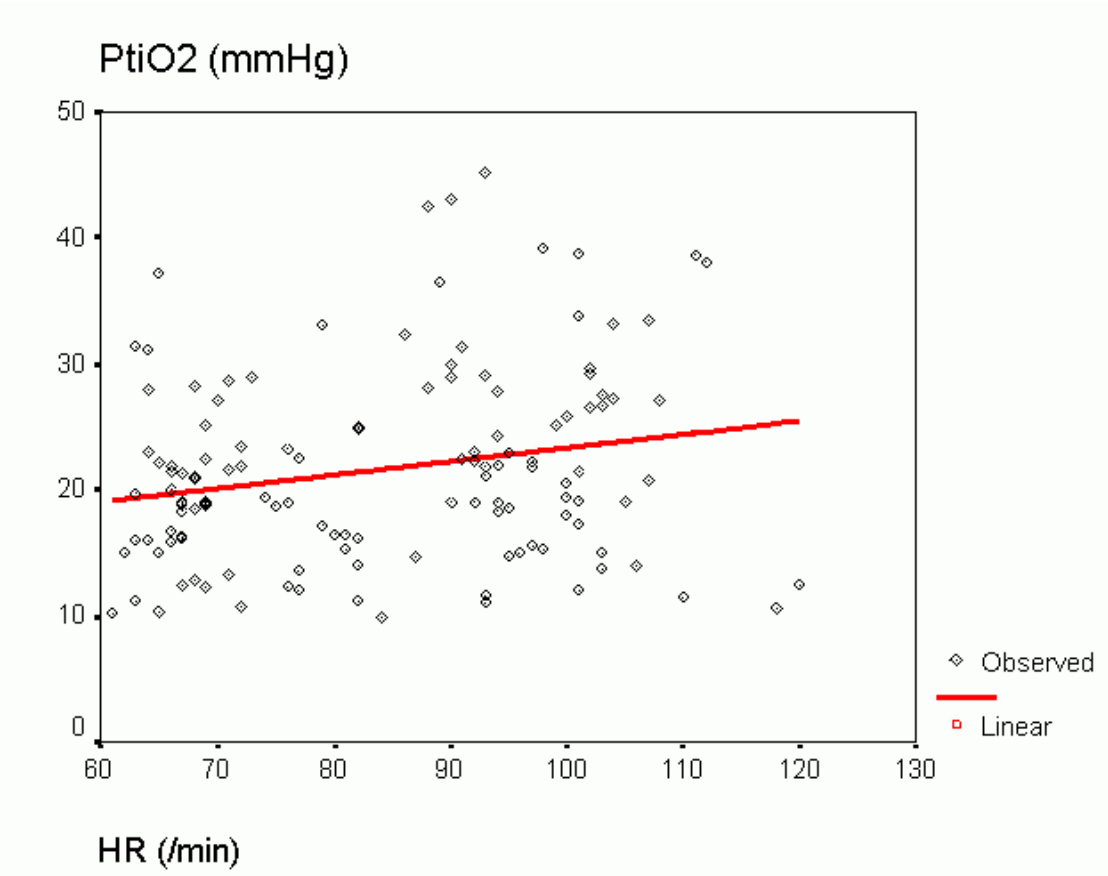



**Figure 22.** Scatterplots and linear estimation curve showing the positive correlation between PtiO2 and HR ($p < 0.05$) in 2 of 6 patients.

### *4.1.6 Correlations between PtiO2 and Hemodynamic Monitoring (PiCCO) Parameters*

At present, effects of hemodynamic changes on PtiO2 are still unknown. The study was designed to assess the hemodynamic parameters, correlated with PtiO2, as a pilot study.

In this serie, hemodynamic parameters, namely HR, Tblood, CI, and SVRI were analyzed from 2 patients, who were simultaneously monitored by PiCCO hemodynamic monitoring system.

Significant correlation was only found in relationship between PtiO2 and HR ($p < 0.05$). The estimation curve of regression analysis is shown in Figure 22.

## 4.2 Individual Patient Data Analysis

For individual patients, the changes of PtiO2 level showed large variations over 24 hours. Correlation between the PtiO2 and various parameters of individual patient were also analyzed. The mean value of PtiO2 of individual patients are shown in Table 4.

**Table 4. The values of PtiO2 of individual patients**

| Patient No. | Minimum | Maximum | Mean ± SD[b] |
|---|---|---|---|
| 1 | 10.6 | 45.14 | 23 ± 8.96 |
| 2 | 10 | 38.3 | 20.55 ± 6.59 |
| 3 | 17.48 | 56.94 | 36.18 ± 9.01 |
| 4 | 11.14 | 51.11 | 29.47 ± 7.41 |
| 5 | 10.5 / 13.19* | 39.21 / 64.03* | 27.11 ± 7.83 / 35.94 ± 14.79* |
| 6 | 11.3 | 59.39 | 28.16 ± 11.41 |

[b]Standard deviation.
*Value of PtiO2 from the monitoring of left and right side, respectively

The individual patient was evaluated, the results showed good positive correlations between PtiO2 and CPP significantly in all patients' data analysis.

Positive correlations between PtiO2 and MAP was found significantly in 5 of 6 patients. Negative correlations between PtiO2 and ICP was found significantly in 4 of 6 patients. Positive correlations between PtiO2 and SpO2 was found significantly in 3 of 6 patients. Negative correlation between PtiO2 and Tbrain was found significantly in 3 of 6 patients. Positive correlation between PtiO2 and pH and HCO3 was found significantly in 4 of 6 patients. Negative correlation between PtiO2 and PCO2 was found significantly in 3 of 6 patients, but positive correlation between PtiO2 and PCO2 was also significantly in other 2 patients. Positive correlation between PtiO2 and O2sat was found significantly in 3 of 6 patients. Positive correlation between PtiO2 and PaO2 was found significantly in only 1 patient. Negative correlation between PtiO2 and Hb and Hct was found significantly in 3 of 6 patients. Positive correlation between PtiO2 and FiO2 was found significantly in 5 of 6 patients. Positive correlation between PtiO2 and TV was found significantly in 2 of 6 patients. Positive correlation between PtiO2 and MV was found significantly in 4 of 6 patients. Negative correlation between PtiO2 and Pplat was found significantly in 2 of 6 patients. Positive correlation between PtiO2 and PEEP was found significantly in 2 of 6 patients. And positive correlation between PtiO2 and RR was found significantly in 4 of 6 patients. For an analysis on hemodynamic monitoring in 2 patients, positive correlations between PtiO2 and HR and Tblood was found significantly in only 1 patient. These results are concluded in Table 5.

In our study, one patient (no.5) was monitored bilaterally the PtiO2. The correlations between left-sided and right-sided PtiO2 values were also compared and analyzed. The difference between average value of PtiO2 from both sides was approximately 8.8 mmHg.

**Table 5. The amount of significant and non-significant correlations between PtiO2 and various parameters in individual patients analysis**

| Correlations Between | Number of Patients (Total = 6) | | |
|---|---|---|---|
| | Positive[a] | Negative[b] | Non-significant |
| PtiO2 and ICP | | 4 | 2 |
| PtiO2 and MAP | 5 | | 1 |
| PtiO2 and CPP | 6 | | |
| PtiO2 and SpO2 | 3 | | 3 |
| PtiO2 and Tbrain | 3 | | 3 |
| PtiO2 and pH | 4 | | 2 |
| PtiO2 and PCO2 | 3 | 2 | 1 |
| PtiO2 and PaO2 | 1 | | 5 |
| PtiO2 and HCO3 | 4 | | 2 |
| PtiO2 and O2sat | 3 | | 3 |
| PtiO2 and Hb | | 3 | 3 |
| PtiO2 and Hct | | 3 | 3 |
| PtiO2 and FiO2 | 5 | | 1 |
| PtiO2 and TV | 2 | | 4 |
| PtiO2 and MV | 4 | | 2 |
| PtiO2 and Pplat | | 2 | 4 |
| PtiO2 and PEEP | 2 | | 4 |
| PtiO2 and RR | 4 | | 2 |
| PtiO2 and HR* | 1 | | 1 |
| PtiO2 and CI* | | | 2 |
| PtiO2 and Tblood* | 1 | | 1 |
| PtiO2 and SVRI* | | | 2 |

[a]Significant positive correlation.
[b]Significant negative correlation.
*Total patients = 2 (hemodynamic monitoring)

The results showed a good correlation between left-sided and right-sided PtiO2 values ($p < 0.001$, $r = 0.68$), and this relationship can be seen in the monitoring tracing from ICUpilot graphic presentation as shown in Figure 23.

In addition, the correlations between PtiO2 and different parameters from both sides were found significantly together in only 2 parameters, namely CPP and MAP.

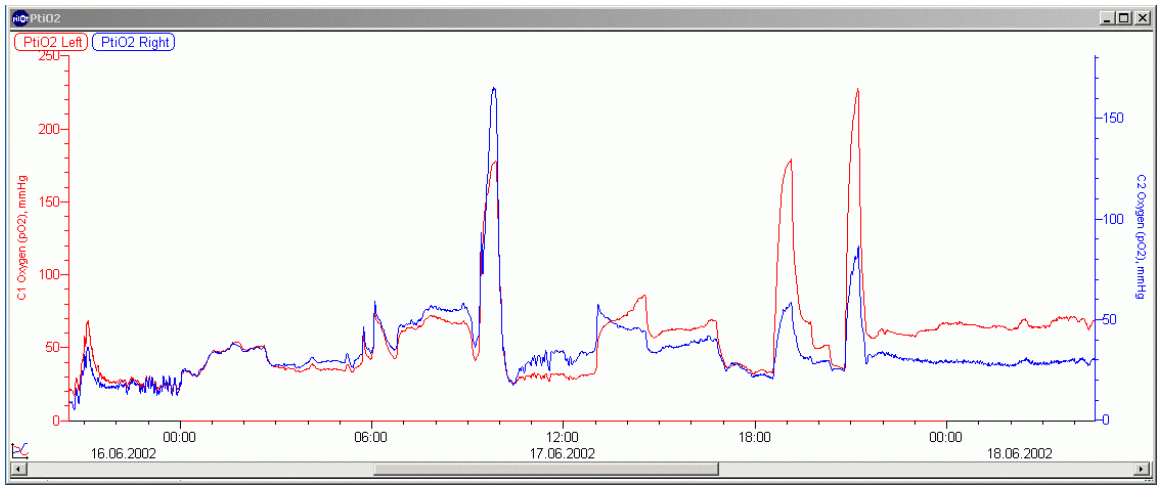



**Figure 23.** Bilateral PtiO2 monitoring graphic presentation showing the relationship between the left-sided and right-sided PtiO2 tracing curves. The red graphic tracing demonstrates PtiO2 value from the left-sided monitoring. The blue graphic tracing demonstrates PtiO2 value from the right-sided monitoring.

### 4.3 Predictive Value of PtiO2 (Multiple Regression Analysis with Stepwise Method)

In fact, the PtiO2 values are not dependent on either parameters. Therefore, multiple regression analysis was used to assess the changes of PtiO2 value, which was influenced from the various parameters.

Pearson's correlations of the pooled data were performed, only significant-correlated parameters would be selected to further analyze with multivariated analysis (multiple regression analysis). The predictive value of PtiO2 could be modified by the multiple regression analysis using the stepwise method in order to find which variables from all significant parameters were helpful to predict the PtiO2 value. The multiple regression analysis with stepwise method showed that the entered variables were CPP, HCO3, Hb, and O2sat with the coefficients of 0.463, 0.605, -1.166, and 1.204 respectively and the constant value of –138.246 (Table 6).

**Table 6. The entered parameters after linear multiple regression analysis with stepwise method**

| Entered Variables | Coefficients |
|---|---|
| CPP (mmHg) | 0.46 |
| HCO3 (mmol/L) | 0.63 |
| Hb (g/dL) | -1.17 |
| O2sat (%) | 1.20 |
| (Constant) | -138.25 |

Therefore, the predictive value of PtiO2 could be estimated by the following equation :-

$$\mathbf{PtiO2 = 0.46(CPP) + 0.63(HCO3) + 1.2(O2sat) – 1.17(Hb) – 138.25}$$

# 5 DISCUSSION

Delayed ischemic vasospasm is continuously the principle cause of mortality and morbidity after acute SAH. Therefore, the brain oxygenation should be monitored. At present, cerebral oxygenation can be monitored in two methods, namely the cerebrovenous O2 measurement in the jugular bulb (SjO2) and the local brain tissue oximetry (PtiO2) by Clark-type or multiparameter probes.

After the development of Clark-type probes and monitoring reliability of brain oxygenation by using PtiO2 value, several studies were focused on the various factors influencing the PtiO2, especially CBF, CPP, ICP, O2- and CO2-reactivity (van Santbrink et al., 1996; Artru et al., 1999; Balestreri et al., 1999; Kiening et al., 1999; Lang et al., 1999; Menzel et al., 1999; Weßling et al., 1999; Tokutomi et al., 2003). These mentioned reports showed that PtiO2 depended on multiple factors and those multiple factors influenced each others at the same time. For this reason, we purposed to consequently analyze the relationship between PtiO2 and influences from multivariated factors altogether.

## 5.1 Oxygen Therapy and Respiratory Parameters Influencing PtiO2

Besides the standard triple-H therapy in prevention of ischemic vasospasm, a goal of treatment, that is the rapid restoration and the maintainance of brain oxygenation, must be concerned especially in case of ischemic process occurrence. In practical management, blood oxygen level as well as arterial blood gas parameters are sequentially assessed by arterial blood sampling during the intensive care. Theoretically, the PtiO2 value would be influenced by the alteration of blood oxygen level and various blood gas parameters. Optimization of blood oxygen level and

various blood gas value could be routinely performed by modifications of any adjustable parameters on mechanical respirator, especially FiO2 and RR.

Therefore, we assessed responses of PtiO2 on changes of the blood gas parameters in order to know how to manipulate any adjustable parameters on the respirator in optimizing PtiO2.

There are only a few studies reported on the responses of PtiO2 value on manipulation of FiO2 and RR (Lang et al.,1999; Manley et al.,1999; Menzel et al., 1999). In the study of Menzel et al., the mean PtiO2 levels increased up to 359 ± 39% of the baseline level after raising of the FiO2 from 35 ± 5% to 100% over a period of 6 hours (Menzel et al. 1999). The relationship between PtiO2 and FiO2 was also found across a wide range of PaO2 as well as demonstrated in our study. Manley et al. observed monitoring of PtiO2 and its responses on changes of FiO2, hyperventilation and hypoventilation in swine. When FiO2 was elevated to 100%, PtiO2 increased from a baseline of 15 ± 2 mmHg to 36 ± 11 mmHg. They have found that hyperventilation while breathing 100% oxygen resulted in 40% decrease in PtiO2. Simultaneously, hypoventilation can increase PtiO2 to 88 mmHg (Manley et al.,1999).

Comparing to our study, the correlation between PtiO2 and FiO2 is also significant as demonstrated by the linear regression curve and boxplot diagram. The regression equation of the correlation could be a guideline to estimate the response of PtiO2 on manipulation of FiO2. However, in our results of respiratory parameter analysis, PtiO2 is not only influenced by FiO2 manipulation, but it is also affected by the changes of the RR and other respiratory setting factors, namely TV, MV, and Pplat. Therefore, the optimization of mechanical ventilation would be also considered for improving and maintaining the oxygenation during the intensive care.

Up to now, several studies on positive pressure ventilation, especially PEEP, influencing the ICP and CPP were performed. There is still conflicting evidence in the literature as to the potential effect of PEEP on ICP (Apuzzo et al, 1977; Feldman et al., 1997; Georgiadis et al., 2001; Videtta et al., 2002; Huynh et al., 2002). Although some reports suggested that increases in PEEP might lead to increase ICP (Apuzzo et al, 1977; Feldman et al., 1997; Videtta et al., 2002), most of the reports suggests that PEEP is not associated with reduced CPP or compromised oxygen transport (Georgiadis et al., 2001; Huynh et al., 2002; Videtta et al., 2002). However, there is still no reports on the direct responses of PtiO2 on positive pressure ventilation, such as PEEP or Pplat. Therefore, in our study, we evaluated the correlation between PtiO2 and PEEP and PtiO2 and Pplat. The results showed that the correlation between PtiO2 and PEEP is not significant in pool data analysis, while the results of individual patient analysis showed significant negative correlations between PtiO2 and PEEP in 2 of 6 patients. The correlation between PtiO2 and Pplat was also found significantly in pooled data analysis. Although the correlation between PtiO2 and PEEP showed significantly in only 2 patients, it could be suggested that the positive pressure ventilation might affected on brain oxygenation, especially in the use of Pplat. Hence, positive pressure ventilation should be considered the indications and be careful to use.

Concerning to the PaO2 value, several studies have been reported the direct dependence of the PtiO2 levels on PaO2 (van Santbrink; 1996; Roth et al., 1997; Menzel et al., 1998). However, PaO2 was not significant in association with PtiO2 value in our study. The current opinion is whether PaO2 value can reflect to PtiO2 value in practical monitoring. Because the PaO2 value is sensitive to be disturbed by several factors, such as the personal and technical errors of blood sampling, the

calibration of blood gas machine, the waiting time before checking of blood sampling. If we can improve and control the mentioned factors during the practical managements, the data might be more accurate.

For the analysis of ventilation, represented by PCO2 value, negative correlation between PtiO2 and PCO2 was seen in our results. The trends of response of PtiO2 on changes of PCO2 does not follow the theoretical concepts and several researches, which suggested that hyperventilation would improves CPP as a result of ICP reduction (Coles et al., 2002), but hyperventilation could not enhance cerebral oxygenation as demonstrated by the decreasing PtiO2. (Dings et al., 1996; Unterberg et al, 1997; Schneider et al., 1998, Imberti et al., 2002). Nevertheless, increase of PtiO2 can be seen after hyperventilation as a paradox reaction. These paradox reactions are likely the results of the local increase of local CPP without the effect of the local vasoconstriction (Dings et al., 1996). Dings et al. suggested that low PtiO2 results in vasodilatation, with the following ICP elevation. If autoregulation is still maintained, a possible reactive vasoconstrictive response might be less potent. Therefore, the vasoconstriction can be caused by hyperventilation (Dings et al., 1996). Although our results showed the significant negative correlation between PtiO2 and ventilation (PCO2), we cannot conclude at the moment that PtiO2 value would increase at the high level of PCO2 (hypoventilation) or PtiO2 would decrease at the low level of PCO2 (hyperventilation), because most of our PCO2 data extended in the range of the normal value. Hence, the response of PtiO2 on hyper- and hypoventilation should be further studied. More data should also be collected and adjusted so that it would be distributed equally in the variety range of PCO2 value.

## 5.2 Temperature

Due to reports on favourable effects of hypothermia in experiments of ischemic and traumatic brain injury (Busto et al.,1987; Clifton et al. 1991, Gupta et al., 2002, Soukup et al., 2002), several studies of therapeutic hypothermia in patients with traumatic brain injury have been performed. In 1993, the relationships between hypothermia and intracranial pressure as well as favorable outcome were also described in a few studies (Clifton et al., 1993; Marion et al., 1993; Shiozaki et al., 1993). Moreover, Tokutami et al., described the correlation between body and brain temperature and intracranial hemodynamic in severe head injury. Their results suggested that, decreasing body temperature to 35 to 35.5 °C could reduce ICP while maintaining sufficient CPP without cardiac dysfunction or brain oxygenation disturbance (Tokutami et al., 2003).

In our study, the significant negative correlation was seen between PtiO2 and Tbrain ($p < 0.05$). The higher temperature, the significant lower PtiO2. Although the range of the temperature value of almost data in the serie were still in the range of the normal value of temperature, trends of decreasing PtiO2 value during higher temperature was showed as demonstrated by the estimation curve in Figure 21. This result could be agreeable on several reports that hyperthermia is an unfavorable factor, which could significantly increase hypoxic cerebral ischemia (Laptook et al., 2002; Hickey et al., 2003; Tomimatsu et al., 2003).

For the analysis in correlation between Tblood and PtiO2 (in 2 patients), the non-significant correlation was showed. For the current opinion, this might be a small number of the data to analyze and compare with the pooled data. However, the further study should be performed to analyze the accuracy of various techniques of temperature measurement and its relationship with multiparameters and PtiO2 as well.

### 5.3 Hemoglobin and Hematocrit Concentration

Although the relative higher level of Hb concentration, related to the higher level of Hct concentration, seems to be able to bind better oxygen, the blood viscosity due to the high Hct concentration results in decreasing CBF and rate of oxygen delivery to the brain. However, not only Hct concentration influenced the blood viscosity, but several factors, such as hydration status, hyperlipidemia, hyperglycemia, and hemodilutional therapy, especially in concept of triple-H therapy, could also affect on changing of blood viscosity and CBF. Several studies reported responses of CBF on blood viscosity. Most of the studies showed that the higher blood viscosity, the lower CBF (Tomiyama et al., 1999; Eckmann et al., 2000; Ekelund et al., 2002). In addition, positive linear correlation between decrease in Hct concentration and blood viscosity was reported after experimentally induced hemodilution (Tu et al., 1988).

Our study demonstrated the higher PtiO2 inversely related to the lower concentration of Hct and Hb. However, theoretically, Hb and Hct concentration would decline to a certain level. Afterwards, Hb and Hct at the low concentration, finally resulted in an anemia stage, would not be able to bind and deliver enough oxygen to the brain, resulted in the decline of brain oxygenation as well (Morimoto et al., 2001).

The further study should be considered to find out the optimal range of Hct and Hb concentration and the hydration therapy to optimize the brain oxygenetion.

### 5.4 Hemodynamic Monitoring

In our study in hemodynamic monitoring, the result showed that only the correlation between PtiO2 and HR is significant ($p < 0.05$).

If the brain autoregulation can function and maintain the CPP, circulatory hemodynamics changes might not influence the CPP as well as cerebral oxygenation. However, there are still a small number of data in this study. Therefore, relationships between hemodynamics and brain autoregulation should be further studied.

### 5.5 How to Predict PtiO2 Value

Besides the significant linear correlation analysis in reponses of PtiO2 on the manipulation of FiO2 that would be useful to practically estimate the changes PtiO2 value in intensive care management, our study was also designed to study how to predict the PtiO2 value by using the multivariated parameters altogether. In fact, the PtiO2 value could be influenced by multiple factors and parameters. As a result, the stepwise method of multiple regression was applied to find the suitable parameters to predict the PtiO2 value. Our study shows a good relation of those parameters in a form of the equation , consisting of 4 valuable parameters, namely CPP, HCO3, O2sat and Hb, which are beneficial in PtiO2 prediction.

Although the equation of predictive value of PtiO2 seems to be helpful to estimate the PtiO2 value, it should be further analyzed as a clinical trial on its predictive accuracy. Moreover, the additional parameters might be collected and improved both quality and quantity of the pooled data, in order to improve the precision in predicting PtiO2. Unquestionably, the accurate equation of predictive value of PtiO2 would be beneficial in intensive care and also in any medical centers, in which do not have the PtiO2 monitoring machine.

Finally, further research is necessary to analyze whether managements and various parameters, aimed at optimizing PtiO2 value, will improve better treatment results.

# 6 CONCLUSION

In conclusion, the study presented the relationship between PtiO2 and multiple parameters during the practical intensive management for acute SAH patients. The results showed various parameters which significantly influenced the PtiO2 level and illustrated in linear correlation curves and boxplot diagrams. The statistical analysis showed that a number of factors might affect the PtiO2 level. We therefore proposed this study how to optimize and/or predict PtiO2 level by these various parameters.

Multivariated analysis using the multiple regression with stepwise method has been applied, we can build an equation, consisting of 4 valuable parameters, namely CPP, HCO3, O2sat, and Hb, to assist clinicians in predicting the PtiO2 value. However, this predictive value should be further evaluated and improved the accuracy and consistency for practical use. Moreover, the modification of analysis, as well as long term follow-up studies in which influence of various parameters on the PtiO2 level, improvement of ischemic detection and patient survival, should be the focus of further studies.

Finally, the physiological knowledge in the relationships between these various monitored parameters and the development of neurosurgical monitorings would hopefully be a new horizon to improve the clinical outcome for neurosurgical intensive care.

# 7 ABSTRACT

Brain tissue oxygen (PtiO2) monitoring has become more widespread as PtiO2 could be a tool for prevention and treatment of cerebral ischemia from various causes. In this research, the relationships between PtiO2 and various monitoring data; namely, intracranial pressure, respiratory, arterial blood gas, and hemodynamic parameters, would be highlighted.

These various parameters from multimodal monitoring, including $PtiO_2$, were collected retrospectively in a series of 6 patients with acute subarachnoid hemorrhage (4 male and 2 female; mean age was 54.33 years; Glasgow Coma Scale score (GCS) ≤ 8). They were admitted to the neurosurgical intensive care unit of Academic Hospital München-Bogenhausen, Technical University of Munich, Germany between September 2001 and October 2002. All data were recorded in a computer software and evaluated the correlations between PtiO2 and various respiratory and blood gas parameters using linear regression and multiple regression analysis. Moreover, in 2 of 6 patients, we also performed concurrently hemodynamic monitoring and analyzed the correlations between PtiO2 and some hemodynamic parameters. The results showed a variety of positive and negative correlations between PtiO2 and various parameters which were found significantly. In addition, from the multiple regression analysis using stepwise method, PtiO2 value might be predicted by 4 parameters; namely, cerebral perfusion pressure (CPP), serum bicarbonate (HCO3), oxygen saturation (O2sat) and hemoglobin (Hb).

***Abstract in German***

Die Verbreitung des Monitoring der hirngeweblichen Sauerstoffspannung (PtiO2) hat insoweit deutlich zugenommen, als die PtiO2 als Marker für die Vorbeugung und Behandlung von cerebraler Ischämie verschiedenster Genese genutzt werden kann.

In dieser Studie wurde besonderes Augenmerk auf die Verbindung von PtiO2 und verschiedenen Monitoring Daten, im Besonderen dem intracraniellen Druck, der Atmung, der arteriellen Blutgase, und der haemodynamischen Parameter gelegt.

Diese unterschiedlichen Betrachtungegrößen aus mutimodalem Monitoring einschliesslich PtiO2 wurden aus einer Serie von 6 Patienten mit Akuter Subarachnoidalblutung (SAH) retrospektiv gesammelt (4 Männer, 2 Frauen; Durchschnittsalter betrug 54.33 Jahre; Glasgow Koma Skala (GCS) ≤ 8). Die Patienten wurden in die neurochirurgische Intensivstation des akademischen Lehrkrankenhauses der Technischen Universität München, Deutschland im Zeitraum vom September 2001 bis Oktober 2002 eingeliefert. Alle Daten wurden computergestützt gesammelt und verwaltet. Evaluiert wurde anhand einer linearen und mehrfachen Regressionsanalyse in den Korrelationen zwischen PtiO2 und den verschieden Atmungs- und Blutgasparametern.

Darüber hinaus führten wir bei 2 der 6 Patienten gleichzeitig ein haemodynamisches Monitoring durch und analysierten die Korrelationen zwischen PtiO2 und verschiedenen haemodynamischen Meßgrößen. Die Ergebnisse zeigten eine große Bandbreite an signifikant positiven und negativen Korrelationen zwischen PtiO2 und verschiedenen Parametern. Zusätzlich ergab die schrittweise durchgeführte mehrfache Regressionsanalyse, das PtiO2 unter Zuhilfenahme von 4 Parametern vorausgesagt werden kann, welche da sind: cerebraler Perfusionsdruck (CPP), Serumbicarbonate (HCO3), Sauerstoffsättigung (O2sat) und Hämoglobingehalt (Hb).

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# 9 FIGURE LEGENDS

## 10 TABLE LEGENDS

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# PATARAVIT RUKSKUL, M.D., M.Sc.

Neurosurgical Unit, Department of Surgery, Faculty of Medicine, Thammasat University (Rangsit Campus), Klong 1, Klong-Luang, Pathumthani 12121, Thailand

**Born:** July 5, 1972

**Education:**

1987 - 1989 **High School** – Triamudomsuksa School, Bangkok, Thailand
1989 - 1995 **M.D.** – Siriraj Medical School, Mahidol University, Bangkok, Thailand
1997 - 1999 **M.Sc. (Clinical Science)** – Mahidol University, Bangkok, Thailand

**Post-doctoral Training:**

1995 - 1996 **Internship** – Faculty of Medicine, Thammasat University, Pathumthani, Thailand
1996 - 1999 **Residency Training in Neurosurgery** – Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
2000 **Fellowship** – Fellows of the Royal College of Surgeons of Thailand
2002 - 2003 **Fellowship in Minimal Invasive Neurosurgery and Spinal Surgery** – Krankenhaus München Bogenhausen, Technical University of Munich, Munich, Germany

**Licensure:**

1995 **Thailand**

**Certification:**

1999 **Diplomate Thai Board of Neurological Surgery**

**Academic Appointments:**

1999 - 2000 **Instructor** in Neurological Surgery, Faculty of Medicine, Thammasat University, Pathumthani, Thailand
2001 **Assistant Professor** in Neurological Surgery, Faculty of Medicine, Thammasat University, Pathumthani, Thailand

**Hospital Appointments:**

1999 - 2001 **Chief of the Emergency Room**, Thammasat University Hospital, Pathumthani, Thailand

**Memberships:**

Thai Medical Association
The Neurosurgical Association of Thailand
The Royal College of Surgeons of Thailand
The Parkinson's Disease Association of Thailand

**Marital Status:** Married

**Office Address:**

Neurosurgical Unit, Division of Surgery, Faculty of Medicine, Thammasat University (Rangsit Campus) Klong 1, Klong-Luang, Pathumthani 12121, Thailand

**Home Address:**
3 Sukhumvit 103 Bangna, Prakanong, Bangkok, 10260, Thailand

**Email Address:** prukskul@yahoo.com

**Representative Publications:**

**Books**

Rukskul, P. and Pao-in, W. (2000) : Transplantation. In Basic Surgery. Booknet Press. 115 pp (in Thai).

Rukskul, P : Emergency practice in neurosurgery, in preparation, approximate page volume: 150 pp (in Thai).

**Articles in journals/contributions to books**

Rukskul, P. (2000) : Parkinsonism associated with brain tumor: a case report of meningioma. The Thai Journal of Surgery, Apr – Jun; 21(2): 65-68.

Rukskul, P. and Siripakarn, Y. (2000) Prevention of adhesion using Silastic sheet in lumbosacral lipoma with tethered cord: a case report. The Thai Journal of Surgery, Oct – Dec; 21(4): 129-132

Rukskul, P. (2000) : Development of neurosurgical treatment in Parkinson's disease. The Journal of Science and Technology, 8(2): 86-93 (in Thai).

Rukskul, P. (2000) : Location and consistency of subthalamic nucleus coordinate in Thai people : a pilot study, submitted to Journal of Thai Medical Association, approximate page volume: 12 pages.

Rukskul, P. (2001) : Hydrocephalus : Development in neurosurgical practices. The Journal of Science and Technology, 9(1): 66-70 (in Thai).

Rukskul, P., Yodwisithsak, P. and Tharanon, W., Rapid prototyping and the use of customized acrylic implant for cranioplastic surgery, in preparation, approximate page volume : 12 pages.

Rukskul, P. and Chernchujit B., Ossification of posterior longitudinal ligament presented with hemiplegia : case discussion, in preparation, approximate page volume : 5 pages.

Rukskul, P. and Chernchujit, B., Hemiparesis associated with blunt cervical injury, in preparation, approximate page volume : 5 pages.

**Published contributions to academic conferences**

Rukskul, P. (1998) : Consistency of subthalamic nucleus coordinate using magnetic resonance imaging in Thai people with clinical applications. Proceeding of the Annual Meeting of Neurosurgical Association of Thailand at Central Grand Plaza Hotel, Bangkok, Thailand, 23 June 1998.

Rukskul, P.(2001) : The use of customized acrylic implant for cranioplastic surgery : experiences at Thammasat University Hospital. Proceedings of the symposium on "Applications of Rapid Prototyping in Medicine in Thailand" at Bangkok, Thailand, 18 May 2001.

Rukskul, P.(2001) : The use of customized acrylic implant for cranioplastic surgery. Proceedings of the Joint Meeting of Royal College of Surgeons of Thailand and Royal College of Surgeons of Edinburgh (2001) at Royal Cliff Beach Hotel, Cholburi, Thailand, 6 July 2001.

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