

Arterial thermodilution in burn patients suggests a more rapid fluid administration of fluids during early resuscitation

C. CSONTOS¹, V. FOLDI¹, T. FISCHER² and L. BOGAR¹

¹Department of Anaesthesia and Intensive Care and ²Department of Surgery, Faculty of Medicine, University of Pécs, Hungary

Background: A number of target points have been used for fluid replacement in severely burned patients. The aim of our prospective randomized study was to compare the effect of two different types of fluid resuscitation regimes on the multiple organ dysfunction score (MODS) and central venous oxygen saturation (ScvO₂) in the first 3 days after injury.

Methods: Twenty-four patients admitted to the critical care unit of a university hospital with the presence of burn injury affecting more than 15% of the body surface area and in-hospital fluid resuscitation started within 3 h after burn injury were included. Patients were randomized into two groups. Fluid resuscitation was guided by the hourly urine output (HUO Group, *n* = 12) or by the intrathoracic blood volume index (ITBVI Group, *n* = 12). Invasive transpulmonary hemodynamic measurements utilizing pulse contour analysis with a single dilution technique and continuous ScvO₂ measurements were performed in both groups.

Results: The mean ScvO₂ was significantly lower in the HUO Group than in the ITBVI Group (*P* = 0.024) for the first 24 h. MODS was significantly higher in the HUO Group than in the ITBVI group 48 h (*P* = 0.024) and 72 h after injury (*P* = 0.014). The two main outcome parameters, i.e., MODS calculated at 48 and 72 h after injury and ScvO₂ were negatively correlated on day 1 (*r* = −0.684, *P* = 0.004, *r* = −0.677, *P* = 0.003). There were no statistical differences in clinical outcome parameters.

Conclusion: Our data suggest that ITBVI may be a better target parameter than HOU in the fluid resuscitation of severely burned patients after injury.

Accepted for publication 24 January 2008

Key words: Burn injury; fluid resuscitation; arterial thermidilution.

© 2008 The Authors
Journal compilation © 2008 The Acta Anaesthesiologica Scandinavica Foundation

ESTIMATION of the fluid loss of severely burned patients has generated intense debate. A number of schemata have been recommended for fluid resuscitation. The Parkland formula (PF) is used most commonly, but a number of studies have proved that the PF frequently underestimates the water and electrolyte loss of burned patients (1–4). The most commonly used target parameter of fluid resuscitation is hourly urine output (HUO). The guidelines of the American Burn Association (5) and the Advanced Burn Life Support Course recommend targeting urine output between 0.5 and 1.0 ml/h/kg.

Despite adequate resuscitation based on maintaining targeted HUO an increase in base deficit (BD) can still develop, which may be associated with a higher risk of acute respiratory distress syndrome (ARDS) or multiple-organ dysfunction (6). Two publications from Holm et al. (7, 8) based

intravenous fluid resuscitation on the normal values of the intrathoracic blood volume index (ITBVI) using double indicator dilution as a method of invasive hemodynamic monitoring in resuscitation. The total circulating blood volume index (TBVI) has also been regarded as an ideal guide during resuscitation (9).

Although no study has examined the possible benefit of ScvO₂ monitoring in burn patients, it has been proven that central venous oxygen saturation of the hemoglobin (ScvO₂) reflects tissue oxygen supply in the management of early sepsis (10). Experimental studies have shown that changes in ScvO₂ closely reflect circulatory disturbances during periods of hypoxia, hemorrhage and subsequent resuscitation (11, 12). Fluctuations correlate well with those of mixed venous saturation (SvO₂), although absolute values differ (11–13). The prognostic significance of ScvO₂ reductions below 65%

has been demonstrated in trauma (14), severe sepsis (15) and myocardial infarction (16) but it has not yet been proven in fluid resuscitation of severely burned patients. For this reason, we decided to challenge the benefit of conventionally guided fluid resuscitation with an intravascular volume parameters-targeted regime.

It has already been shown that our second outcome parameter [multiple organ dysfunction score (MODS)] correlates clinically with the intensive care unit (ICU) mortality risk of burned patients (17).

The aim of our study was therefore to compare the clinical usefulness of two different target parameters (HUO and ITBVI) in the fluid resuscitation of burn patients. ScvO₂ during fluid resuscitation and MODS (18) in the first 3 days after injury were regarded as the main outcome parameters.

Materials and methods

Patients

Patients admitted with burn injury to our tertiary ICU between January 2004 and June 2006 were included in the study. After obtaining permission from the local ethics committee, informed consent was obtained from the patients, or their nearest relative. Inclusion criteria were the presence of burn injury affecting more than 15% of the body surface area (BSA) and in-hospital fluid resuscitation started within 3 h after burn injury. Burned body surface area (BBS) was estimated on the basis of the Lund-Browder chart. Exclusion criteria were chronic left heart or renal insufficiency documented in the past medical history and age under 18 years. If inhalation injury was suspected (facial burn, soot in the throat, chest X-ray), bronchoscopy was performed for verification. However, computed tomography was not used for verification, although it has been proven that peribronchial atelectasis may be a characteristic of inhalation injury (19).

Procedures

Patients were randomly assigned to two groups using the closed envelope method (Fig. 1). Intravenous fluid resuscitation was guided by HUO in the HOU Group and invasive hemodynamic monitoring in the ITBVI Group. For invasive transcatheter pulmonary haemodynamic measurements, an arterial catheter (PULSIOCATH, Pulsion Medical Systems, Munich, Germany) was inserted via the

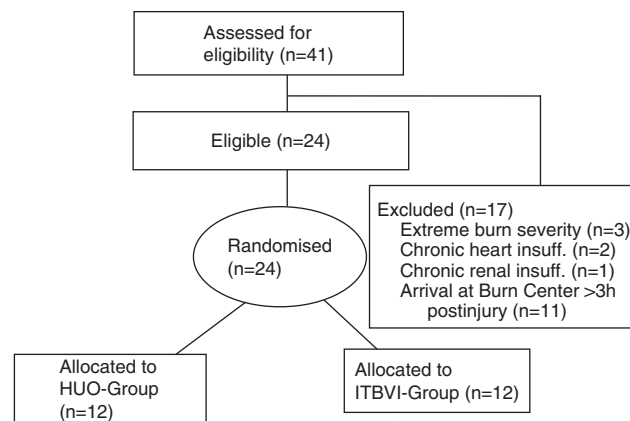


Fig. 1. Flowchart of the study.

femoral or the axillary artery, and for the continuous ScvO₂ measurement, a special fiberoptic probe (CeVOX, Pulsion Medical Systems, Munich, Germany) was introduced via the central venous line into the superior caval vein in both groups. The device for ScvO₂ measurement was calibrated *in vivo* two times daily. Blood gas analyses and measurements of serum lactate concentrations were performed with a Premier 3000 (Instrumentation Laboratory, USA) instrument.

The correct position of the central venous catheter was controlled by chest X-ray. Lactated Ringer's solution (LR) was used exclusively for intravenous fluid replacement in both groups. The initial infusion rate for the first 24 h time was set according to the PF (4 ml/kg/%) (20) in both groups. This meant that half of the calculated first day volume was administered in the first 8-h time (i.e. 0.25 kg/%/h as a starting rate that was modified according to the actual HUO or ITBVI in the HUO group or the ITBVI group, respectively).

In the HUO Group ($n = 12$), fluid resuscitation was guided by the following: if the average urine output was lower than 0.5 ml/kg/h for at least 2 h, the intravenous infusion rate was increased by 0.05 ml/kg/%/h for the next 2 h. The infusion rate was decreased by 0.05 ml/kg/%/h if the average urine output exceeded 1.0 ml/kg/h for at least 2 consecutive hours (Fig. 2). If the intravenous fluid replacement regimen had failed to maintain a mean arterial pressure (MAP) of above 70 mmHg, a norepinephrine infusion was used, with a maximum rate of 0.1 µg/kg/min. The attending physician was blinded to the results of invasive hemodynamic monitoring in the HUO group. Invasive hemodynamic measurements were performed 8 hourly for the first 3 days after injury

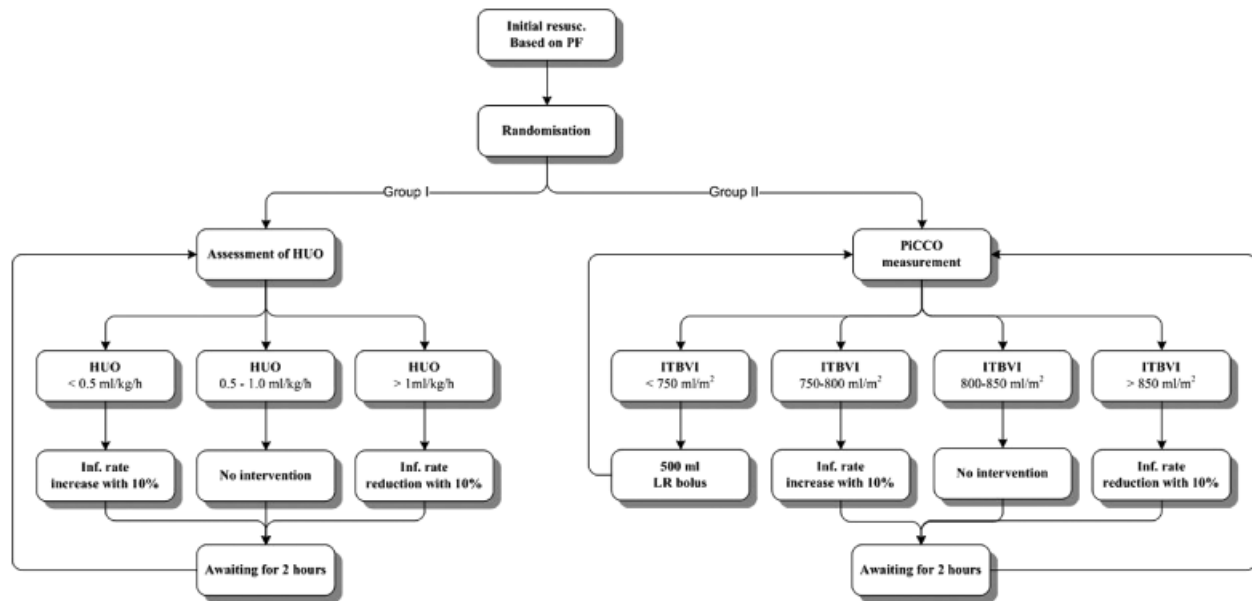


Fig. 2. Flowchart of fluid administration in both groups. PF, Parkland formula; PiCCO, transpulmonary hemodynamic measurement; ITBVI, intrathoracic blood volume index; HUO, hourly urine output.

using 20 ml cold (temperature $<4^{\circ}\text{C}$) isotonic sodium chloride solution. Three readings were taken and the mean was recorded.

The fluid resuscitation in the ITBVI group ($n = 12$) was guided by invasive transpulmonary thermodilution hemodynamic measurements and pulse contour analysis, performed every 2 h by the same method as in the HUO group. The goal of resuscitation was to maintain ITBVI between 800 and 850 ml/m^2 . The normal range for ITBVI is 850–1000 ml/m^2 . By targeting the lower limit, we tried to avoid intravenous fluid overload. If ITBVI was $<800 \text{ ml}/\text{m}^2$, the infusion rate was increased by 10%. If ITBVI was under 750 ml/m^2 , 500 ml LR was administered as an intravenous bolus, and the hemodynamic measurements were repeated. LR solution was administered until the targeted value was reached. If ITBVI was over 850 ml/m^2 , the infusion rate was decreased by 10% (Fig. 2). If the target range of ITBVI had been reached but oliguria (diuresis $<0.5 \text{ ml}/\text{kg}/\text{h}$) and/or hypotension ($\text{MAP} <70 \text{ mmHg}$) were present, norepinephrine administration was initiated on the basis of hemodynamic monitoring.

Both groups had, on days 2 and 3, background intravenous fluid replacement at 2 $\text{ml}/\text{kg}/\text{h}$ using balanced salt solutions topped with LR and hydroxyethyl starch (Voluven[®]) infusions, according to HUO or ITBVI. All patients were mechanically ventilated during the study period and survived the first week. Excision and grafting was started

within 72 h and enteral feeding was commenced on the first day after injury. Tracheostomy was performed before the first grafting in order to avoid complications due to coagulopathy (21).

Monitoring

ScvO_2 was measured continuously in both groups, serum lactate level was determined 8 hourly and HUO was averaged every 8 h. MODS (18) was calculated at admission and then every 24 h. Invasive hemodynamic measurements were performed 8 hourly in the HUO group, and 2 hourly in the ITBVI group. However, in the ITBVI group only the parameters recorded every 8 h were used for analysis and included confidence interval (CI), ITBVI, extravascular lung water index (EVLWI), stroke volume variability (SVV) and central venous pressure (CVP).

Statistics

Data from nine hemodynamic measurements (three time points daily for 3 days) on every patient were recorded (total 216 measurements). Statistical analysis was performed using Statistical Program for Social Sciences 11.5 software for Windows (SPSS[®], Chicago, IL). Correlations between variables were analyzed using the Spearman's test and variables were compared using the Mann-Whitney U -test, differences over time and differences between

groups at different time points were tested using repeated-measures ANOVA and distributions between groups were evaluated using the χ^2 test. All values are expressed as median and interquartile range (IQR). Statistical significance was ascribed to a P -value < 0.05 .

According to our power analysis for ScvO₂ performed with a pilot study on 10 patients, 22 cases were required for a 4.5% difference, SD 3.7, power 80% and α error 5%. For MODS 28 patients were required (three-point difference, SD 2.8, power 80%, α error 5%). Interim analysis was planned and performed after 24 patients, and the study was designed to stop after 30 patients. The study was terminated at this stage because the null hypothesis for MODS could be rejected after inclusion of 24 patients.

Results

The study population consisted of 24 patients (two females, 22 males), median age 46 years (IQR 39–63), and median BBS 43% (IQR 30–63). No significant differences were found regarding age, BBS, MODS and EVLWI at the time of inclusion between the HUO or the ITBVI groups (Table 1).

Significantly more fluid was administered in the ITBVI group than the HUO group on the first day after injury (5.7 ml/BBS/kg, IQR 4.5–6.5; 4.7 ml/BBS/kg, 4.4–5.2, respectively, $P = 0.019$). Moreover, 58% of the extra fluid was administered in the first 8 h, 28% in the second 8 h, and only 14% in the last 8 h.

ScvO₂ was significantly lower in the HUO group than in the ITBVI group for the first 24 h but no significant differences were detected on the second

and the third day. The MODS was significantly higher in the HUO group than the ITBVI group at 48 and 72 h after injury. However, no significant differences were present between groups in the first 24 h after injury. No significant differences were detected in lactate level, PaO₂, PaO₂/FiO₂ ratios and EVLWI between the HUO and the ITBVI groups, on the first, second and third day after injury (Table 2). Components of MODS concerning different organ systems are displayed in Table 3. Clinical outcome parameters are summarized in Table 4. No significant difference could be found between groups.

The two main outcome parameters, i.e., MODS calculated 48 and 72 h after injury, showed a significantly negative linear correlation with ScvO₂ measured on day 1 ($r = -0.684$, $P = 0.004$, $r = -0.677$, $P = 0.003$).

A significantly linear correlation was found between ITBVI and ScvO₂. A Strong correlation was found between ITBVI and CI. Similarly, there were correlations between ScvO₂ as the first outcome parameter and CI. There was a significantly negative correlation between SVV as a measure of pre-load and ScvO₂.

HUO and CVP did not correlate with ScvO₂, nor any other hemodynamic parameters. No correlation was found between serum lactate level and MODS measured on days 1–3, ScvO₂ measured on days 1–3, ITBVI, HUO and CVP values (Table 5).

Discussion

In this study, we found evidence that ITBVI may be a more superior target parameter for intravenous

Table 1
Demographic data and initial parameters of the patients.

	HUO Group (n = 12)	ITBVI Group (n = 12)	P-value
Females/Males	2/10	0/12	NS
Age (years)	45 (39–65)	46 (40–70)	NS
Smokers	9	10	NS
Documented ischemic heart disease	4	5	NS
Documented diabetes mellitus	1	2	NS
BBS (%)	38 (29–61)	45 (31–63)	NS
Presence of inhalation injury	5/12	6/12	NS
MODS on admission	2.0 (1.75–2.75)	2.0 (1.00–3.00)	NS
ITBVI on admission (ml/m ²)	780 (700–840)	790 (710–870)	NS
EVLWI on admission (ml/kg)	5.0 (4.8–6.0)	6.5 (5.0–8.0)	NS
ScvO ₂ on admission (%)	70 (68–73)	72 (66–73)	NS
Serum lactate level on admission (mmol/l)	1.8 (1.6–2.2)	2.0 (1.7–2.6)	NS

Data are expressed as median and interquartile range. BBS, burned body surface area; MODS, multiple organ dysfunction score; ITBVI, intrathoracic blood volume index; EVLWI, extravascular lung water index; ScvO₂, oxygen saturation of the central venous hemoglobin; NS, not significant.

Table 2

Summary of measured and calculated parameters of the patients during the study period (72 h).

Parameter	Group	Day 1	Day 2	Day 3
ScvO ₂ (%)	HUO	68 (64–71)	72 (61–77)*	76 (71–78) *,†
	ITBVI	74 (71–78)	74 (69–79)	77 (73–79)‡,†
		<i>P</i> = 0.024	NS	NS
MODS	HUO	4.0 (2.0–5.0)	5.0 (4.3–5.8)§	5.0 (4.3–6.0)§
	ITBVI	3.5 (3.0–5.0)	4.0 (3.0–4.3)	3.0 (3.3–3.8)¶
		NS	<i>P</i> = 0.024	<i>P</i> = 0.014
ITBVI (ml/m ²)	HUO	723 (590–844)	802 (701–959)*	860 (785–965) *,¶
	ITBVI	851 (753–970)	873 (817–920)	970 (903–1020)‡,†
		<i>P</i> = 0.009	<i>P</i> = 0.043	<i>P</i> = 0.003
CVP (cmH ₂ O)	HUO	6.0 (4.0–11.5)	8.0 (4.0–12.0)	11.5 (5.0–12.8)§
	ITBVI	8.0 (4.8–12.0)	10.0 (6.8–18.3)	12.0 (7.0–15.8)§
		NS	NS	NS
CI (l/m ²)	HUO	3.0 (2.4–3.5)	3.9 (3.0–5.0)‡	3.8 (2.9–4.7)‡
	ITBVI	3.5 (3.3–3.8)	4.2 (3.4–5.2)¶	4.3 (3.1–5.0)†
		<i>P</i> = 0.013	NS	NS
Serum lactate (mmol/l)	HUO	2.4 (1.7–3.6)	2.0 (1.6–3.1)§	1.7 (1.3–2.8)‡,¶
	ITBVI	2.3 (1.3–4.7)	2.2 (1.6–3.2)	2.0 (1.4–2.3)
		NS	NS	NS
PaO ₂ /FiO ₂ ratio (kPa)	HUO	43.7 (32.8–49.6)	34.5 (29.2–37.5)‡	32.6 (28.6–34.9)‡,¶
	ITBVI	44.5 (33.7–55.1)	29.7 (26.6–32.9)‡	30.5 (27.2–33.9)‡
		NS	NS	NS
EVLWI (ml/kg)	HUO	6.0 (5.0–7.0)	7.0 (6.0–9.0)	7.0 (6.5–7.0)
	ITBVI	6.0 (5.0–7.0)	6.0 (5.5–7.8)	6.5 (6.0–7.8)
		NS	NS	NS
EVLWI/ITBVI (m ² /kg)	HUO	0.0082 (0.0068–0.0098)	0.0085 (0.0078–0.0103)	0.0081 (0.0068–0.0098)
	ITBVI	0.0070 (0.0059–0.0088)	0.0072 (0.0055–0.0082)	0.0069 (0.0054–0.0086)
		<i>P</i> = 0.025	<i>P</i> = 0.008	<i>P</i> = 0.023
Urine output (ml/kg/h)	HUO	0.8 (0.6–1.0)	0.9 (0.8–1.0)§	0.8 (0.7–1.0)*
	ITBVI	1.1 (0.9–1.4)	1.0 (0.7–1.1)	1.0 (0.9–1.2)
		<i>P</i> = 0.0008	NS	<i>P</i> = 0.0012
Hemoglobin (g/l)	HUO	125.0 (110.0–138.8)	120.0 (102.5–130.0)	112.3 (101.3–120.3) *,†
	ITBVI	112.5 (100.3–120.5)	110.3 (100.3–115.5)	100.3 (90.5–110.3) *,†
		<i>P</i> = 0.002	<i>P</i> = 0.007	<i>P</i> = 0.009

Data are expressed as median and interquartile range. Median values were calculated taking all measurements of all patients of a group on the same day. ScvO₂, oxygen saturation of the central venous hemoglobin; MODS, multiple organ dysfunction score; ITBVI, intrathoracic blood volume index; CVP, central venous pressure; CI, cardiac index; EVLWI, extravascular lung water index. Symbols indicate within group differences.

**P* < 0.001 comparing to day 1; †*P* < 0.01; ‡*P* < 0.01; §*P* < 0.05; ¶*P* < 0.05; ||*P* < 0.001 comparing with day 2, *P*-values and NS indicate intergroup statistical differences.

fluid resuscitation than HUO in patients with severe burn injury.

MODS was investigated because it might correlate clinically with the ICU mortality risk in burned patients according to the paper of Fitzwater et al. (17).

According to our power analysis, more than 200 patients would be required for proving an association between fluid resuscitation and a mortality risk (2% reduction, power 80%, α error 5%). This sample size could only be reached in a multicenter study that may be considered in the future. The MODS was only analyzed up to the third day after admission because many factors may alter it thereafter (e.g., surgical interventions), after which the effect of different fluid resuscitation regimes cannot be closely correlated with the MODS. Holm et al. (7) did not find a mortality difference between the

ITBVI and the PF-based fluid resuscitation groups, but the differences in MODS were not studied. The main difference between the design of the two studies is the timing of the fluid resuscitation. In the present study, fluid replacement, according to the protocol, was commenced within 3 h after injury in contrast to the Holms study, where in-hospital fluid resuscitation started within 8 h, and any fluid administration commenced within 6 h after injury. Hemodynamic measurements were performed 2 hourly in our study and 8 hourly in the Holms study. Therefore, it is postulated that the present study was able to detect and treat hypovolemia earlier.

In our study, a significantly lower second- and third- day MODS was found in patients whose fluid resuscitation was guided by ITBVI. Similar to MODS, the ScvO₂ level was higher in the ITBVI

Q4

Table 3

Components of MODS concerning different organ systems.

Organ-system		Day1 (n = 12)	Day 2 (n = 12)	Day 3 (n = 12)
Respiratory	HUO	0.3 (0.0–0.5)	0.3 (0.3–0.5)	0.3 (0.3–0.8)
	ITBVI	0.3 (0.3–0.5)	0.3 (0.3–0.8)	0.3 (0.3–0.8)
		NS	NS	NS
Hematologic	HUO	0.8 (0.3–1.0)	1.0 (0.3–1.3)	1.0 (0.3–1.3)
	ITBVI	1.0 (0.3–1.3)	1.0 (0.3–1.3)	0.8 (0.3–1.0)
		NS	NS	NS
Hepatic	HUO	0.5 (0.3–0.8)	0.5 (0.3–1.0)	0.3 (0.5–0.8)
	ITBVI	0.5 (0.3–0.8)	0.8 (0.3–1.0)	0.5 (0.3–1.0)
		NS	NS	NS
Cardio-vascular	HUO	2.0 (1.3–2.8)	1.5 (1.0–2.0)	2.0 (1.0–2.3)
	ITBVI	1.0 (0.3–1.8)	1.0 (0.3–1.3)	1.0 (0.3–1.3)
		$P = 0.043$	$P = 0.032$	$P = 0.002$
GCS	HUO	0.7 (0.3–1.0)	0.7 (0.5–1.3)	0.7 (0.3–1.3)
	ITBVI	0.7 (0.5–0.1)	0.7 (0.3–1.0)	0.7 (0.3–1.0)
		NS	NS	NS
Renal	HUO	0.0 (0.0–0.0)	1.0 (0.3–1.3)*	1.0 (0.3–2.0)†
	ITBVI	0.0 (0.0–0.0)	0.3 (0.0–0.8)	0.3 (0.0–1.0)
		NS	$P = 0.026$	$P = 0.017$

Data are expressed as median and interquartile range. CNS, central nervous system, symbols indicate within group differences,

* $P = 0.024$ comparing day 1 with day 2.† $P = 0.007$ comparing day 1 with day 3, and NS indicate intergroup differences.

ITBVI, intrathoracic blood volume index; HUO, hourly urine output; MODS, multiple organ dysfunction score.

Table 4

Clinical outcome parameters.

	HUO Group (n = 12)	ITBVI Group (n = 12)	P-value
ICU mortality (n)	5	4	NS
Length of ICU stay (median day, IQR)	30 (19–36)	27 (18–32)	NS
Length of mechanical ventilation (median day, IQR)	17 (11–20)	15 (9–22)	NS
Renal insufficiency in the first 3 days (n)	0	0	NS
Renal insufficiencies during ICU stay (n)	3	1	NS
Patients on noradrenalin in the first 3 days (n)	6	2	NS

IQR, interquartile range; NS, not significant; Renal insufficiency, patient requiring haemodialysis; ICU, intensive care unit; ITBVI, intrathoracic blood volume index; HUO, hourly urine output.

Table 5

Correlation coefficients between parameters on the first day.

Parameters	Correlation factors	P value
ITBVI – ScvO ₂	0.855	0.0008
ITBVI – CI	0.491	0.0008
ScvO ₂ – CI	0.412	0.0009
SVV – ScvO ₂	–0.329	0.001
ScvO ₂ – HUO	0.114	NS
ScvO ₂ – CVP	0.087	NS
ScvO ₂ – lactate	–0.218	NS
Lactate – ITBVI	–0.241	NS
Lactate – HUO	–0.018	NS
Lactate – CVP	–0.248	NS

ITBVI, intrathoracic blood volume index; CI, cardiac index; ScvO₂, saturation of the central venous hemoglobin; SVV, stroke volume variability; HUO, hourly urine output; CVP, central venous pressure; NS, non-significant.

group on the first day. These data suggest that resuscitation guided by ITBVI may have been more appropriate as reflected by a higher mean ScvO₂ level on day 1, and in lower MODS on days 2 and 3, than the resuscitation based on HUO. The negative correlation between ScvO₂ levels measured on the first day and the MODS on days 2 and 3 may support this hypothesis. In the study by Holm et al., (22) survivors, compared with non-survivors, showed a significantly higher CI and oxygen delivery rate. These findings point to the importance of adequate circulation in burned patients during fluid resuscitation.

More fluid was administered in the ITBVI than in the HUO group. Not only the total amount of fluid,

but the timing of administration was different between groups. The ITBVI group received more volume in early resuscitation than the HUO group. This may be the underlying cause of the higher ITBVI in the ITBVI group. No patient showed any signs of intravenous volume overload as monitored by CVP or pulmonary edema formation reflected by the EVLW, characteristic auscultation sounds, decline in PaO₂ or chest radiography. Escharotomy on unaffected extremities was not necessary.

No differences were found in the EVLWI and PaO₂/FiO₂ ratio between both groups and the decline in PaO₂/FiO₂ ratio was similar. Our findings support the results of Holm et al. who also found no increase in EVLW or the pulmonary permeability index during fluid resuscitation of burned patients. Their study found no correlation between the resuscitation volume and EVLW and there was no significant difference between patients with or without inhalation injury (23). Holm et al measured EVLW by the transpulmonary double-indicator dilution technique, in contrast to our study. Sakka et al. (24) reported a significant correlation between single- and double-indicator techniques regarding EVLWI and ITBVI in critically ill patients. The good agreement between the two hemodynamic methods (24) supports the observations from both our study and that of Holm et al. (21) despite the different monitoring techniques.

Different goals of fluid resuscitation have been proposed in major burn injuries (1–9). Usually, the efficiency of fluid resuscitation is monitored by an HUO of between 0.5 and 1.0 ml/kg/h (5, 25). No report is available regarding the association between HUO and adequacy of tissue perfusion. But according to the paper by Choi et al. (6) in patients with adequate HUO, an increase in BD could also develop. Our data suggest that there is no significant correlation between HUO and ScvO₂ or other invasive hemodynamic parameters. We observed patients with ScvO₂ levels lower than 70%, despite adequate HUO in both groups. Base deficit may also increase, despite adequate urine output, due to insufficient tissue perfusion, as reflected by an ScvO₂ below 70%. Alternatively, an excessive lactate load by the LR solution may decrease the possible association between BD and HUO or ScvO₂.

Serum lactate levels and BD were basically the same in both groups and failed to correlate with ScvO₂. In burned patients, lactate acidosis is the most common underlying cause of increase in BD. Therefore, our findings support the result of Choi et al. (6).

SVV showed a significantly negative correlation with ScvO₂. In the literature, thus far, there have been no evidence of data regarding the use of this parameter in burned patients. However, the applicability of this parameter is restricted to patients who are fully ventilated and in sinus rhythm.

CVP did not show any significant correlation with the ScvO₂ level and CI. CVP during burn resuscitation is influenced more by intra-abdominal pressure than by the actual intravascular volume status of the burned patient (9). This parameter is therefore inadequate for guiding fluid resuscitation in burned patients.

In contrast to HUO and or CVP, ITBVI showed a significant positive correlation with ScvO₂ and CI. Our search of Medline database revealed no available data regarding the correlation between ITBVI and ScvO₂ in burn injury. Because ScvO₂ is a marker of the ratio between oxygen supply and demand, our findings support the results of Holm et al. (8) who showed that ITBV correlates with CI and DO₂ in burned patients. The measurement of ITBVI allowed earlier recognition and more adequate treatment of hypovolemia reflected by the higher ScvO₂. Our data may suggest that patients suffering from burn injury benefit from early goal directed therapy, with a key point being ITBVI-guided fluid resuscitation. The early normalization of ScvO₂ can decrease the mortality. This view should be investigated by a large prospective, multicenter, randomized study.

The main limitation of our study is the relatively small sample size. Although MODS showed a correlation with the mortality risk in burned patients (17), mortality rate would have been the most relevant endpoint.

Conclusion

Our data may suggest that ITBVI is a better target parameter than HUO in the fluid resuscitation of severely burned patients in the first 3 days post-injury. An ideal target range of ITBVI in combination with fluid resuscitation guided by ScvO₂ should be studied in the future.

References

1. Cartotto RC, Innes M, Musgrave MA et al. How well does the Parkland formula estimate actual fluid resuscitation volumes? *J Burn Care Rehabil* 2002; **23**: 258–65.
2. Engrav LH, Colescott PL, Kemalyan N et al. A biopsy of the use of the Baxter formula to resuscitate burns or

- do we do it like Charlie did it? *J Burn Care Rehabil* 2000; **21**: 91–5.
3. Cancio LC, Chávez S, Alvarado-Ortega M et al. Predicting increased fluid requirements during the resuscitation of thermally injured patients. *J Trauma* 2004; **56**: 404–14.
 4. Mitra B, Fitzgerald M, Cameron P et al. Fluid resuscitation in major burns. *ANZ J Surg* 2006; **76**: 35–8.
 5. American Burn Association Evidence-Based Guidelines Group. Practice guidelines for burn care. *J Burn Care Rehabil* 2001; **22** (Suppl. 2): 27–52.
 6. Choi J, Cooper A, Gomez M et al. The 2000 Moyer Award. The relevance of base deficits after burn injuries. *J Burn Care Rehabil* 2000; **21**: 499–505.
 7. Holm C, Mayr M, Tegeler J et al. A clinical randomized study on the effects of invasive monitoring on burn shock resuscitation. *Burns* 2004; **30**: 798–807.
 8. Holm C, Melcer B, Hörbrand F et al. Intrathoracic blood volume as an end point in resuscitation of the severely burned: an observational study of 24 patients. *J Trauma* 2000; **48**: 728–34.
 9. Küntscher MV, Germann G, Hartmann B. Correlations between cardiac output, stroke volume, central venous pressure, intra-abdominal pressure and total circulating blood volume in resuscitation of major burns. *Resuscitation* 2006; **70**: 37–43.
 10. Rivers E, Nguyen B, Early Goal-Directed Therapy Collaborative Group et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; **345**: 1368–77.
 11. Scalea TM, Holman M, Fuortes M et al. Central venous blood oxygen saturation: an early, accurate measurement of volume during hemorrhage. *J Trauma* 1988; **28**: 725–32.
 12. Reinhart K, Rudolph T, Bredle DL et al. Comparison of central-venous to mixed-venous oxygen saturation during changes in oxygen supply/demand. *Chest* 1989; **95**: 1216–21.
 13. Dueck MH, Klimek M, Appenrodt S et al. Trends but not individual values of central venous oxygen saturation agree with mixed venous oxygen saturation during varying hemodynamic conditions. *Anesthesiology* 2005; **103**: 249–57.
 14. Scalea TM, Hartnett RW, Duncan AO et al. Central venous oxygen saturation: a useful clinical tool in trauma patients. *J Trauma* 1990; **30**: 1539–43.
 15. Rady MY, Rivers EP, Martin GB et al. Continuous central venous oximetry and shock index in the emergency department: use in the evaluation of clinical shock. *Am J Emerg Med* 1992; **10**: 538–41.
 16. Hutter AM Jr, Moss AJ. Central venous oxygen saturations. Value of serial determinations in patients with acute myocardial infarction. *JAMA* 1970; **212**: 299–303.
 17. Fitzwater J, Purdue GF, Hunt JL et al. The risk factors and time course of sepsis and organ dysfunction after burn trauma. *J Trauma* 2003; **54**: 959–66.
 18. Marshall JC, Cook DJ, Christou NV et al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. *Crit Care Med* 1995; **23**: 1638–52.
 19. Reske A, Bak Z, Samuelsson A et al. Computed tomography – a possible aid in the diagnosis of smoke inhalation injury? *Acta Anaesthesiol Scand* 2005; **49**: 257–60.
 20. Baxter CR, Shires T. Physiological response to crystalloid resuscitation of severe burns. *Ann N Y Acad Sci* 1968; **150**: 874–94.
 21. Veelo DP, Donglemans DA, Phoa KN et al. Tracheostomy: current practice on timing, correction of coagulation disorders and peri-operative management – a postal survey in the Netherlands. *Acta Anaesthesiol Scand* 2007; **51**: 1231–6.
 22. Holm C, Melcer B, Hörbrand F et al. Haemodynamic and oxygen transport responses in survivors and non-survivors following thermal injury. *Burns* 2000; **26**: 25–33.
 23. Holm C, Tegeler J, Mayr M et al. Effect of crystalloid resuscitation and inhalation injury on extravascular lung water: clinical implications. *Chest* 2002; **121**: 1956–62.
 24. Sakka SG, Rühl CC, Pfeiffer UJ et al. Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. *Intensive Care Med* 2000; **26**: 180–7.
 25. Warden GD, Saunders WB. Fluid resuscitation and early management. In: Herndon DN, eds. (Hrsg) *Total Burn Care*, Aufl. 2, 2001.

Address:

Csaba Csontos
 Department of Anaesthesia and Intensive Care
 Faculty of Medicine
 University of Pécs
 Akác u. 1
 Pécs 7632
 Hungary
 e-mail: csaba.csontos@gmail.com

Author Query Form

Journal **AAS**
Article **1658**

Dear Author,

During the copy-editing of your paper, the following queries arose. Please respond to these by marking up your proofs with the necessary changes/additions. Please write your answers clearly on the query sheet if there is insufficient space on the page proofs. If returning the proof by fax do not write too close to the paper's edge. Please remember that illegible mark-ups may delay publication.

[illegible]

USING E-ANNOTATION TOOLS FOR ELECTRONIC PROOF CORRECTION

Required Software

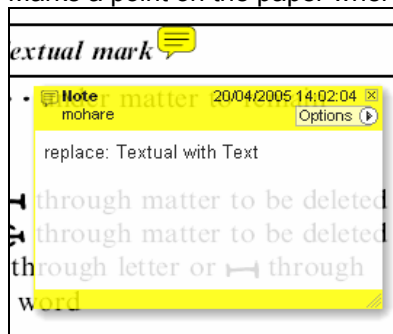
Adobe Acrobat Professional or Acrobat Reader (version 7.0 or above) is required to e-annotate PDFs. Acrobat 8 Reader is a free download: <http://www.adobe.com/products/acrobat/readstep2.html>

Once you have Acrobat Reader 8 on your PC and open the proof, you will see the Commenting Toolbar (if it does not appear automatically go to Tools>Commenting>Commenting Toolbar). The Commenting Toolbar looks like this:



Note Tool — For making notes at specific points in the text

Marks a point on the paper where a note or question needs to be addressed.

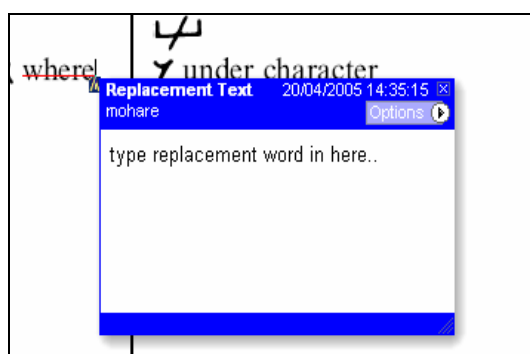


How to use it:

1. Right click into area of either inserted text or relevance to note
2. Select Add Note and a yellow speech bubble symbol and text box will appear
3. Type comment into the text box
4. Click the X in the top right hand corner of the note box to close.

Replacement text tool — For deleting one word/section of text and replacing it

Strikes red line through text and opens up a replacement text box.

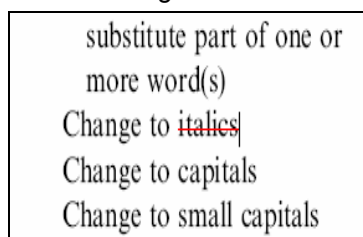


How to use it:

1. Select cursor from toolbar
2. Highlight word or sentence
3. Right click
4. Select Replace Text (Comment) option
5. Type replacement text in blue box
6. Click outside of the blue box to close

Cross out text tool — For deleting text when there is nothing to replace selection

Strikes through text in a red line.



How to use it:

1. Select cursor from toolbar
2. Highlight word or sentence
3. Right click
4. Select Cross Out Text

Approved tool — For approving a proof and that no corrections at all are required.

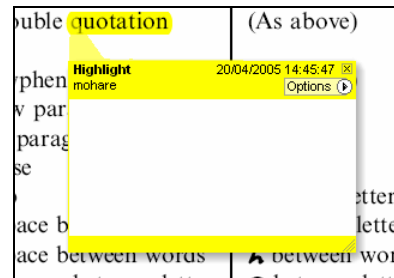


How to use it:

1. Click on the Stamp Tool in the toolbar
2. Select the Approved rubber stamp from the 'standard business' selection
3. Click on the text where you want to rubber stamp to appear (usually first page)

Highlight tool — For highlighting selection that should be changed to bold or italic.

Highlights text in yellow and opens up a text box.

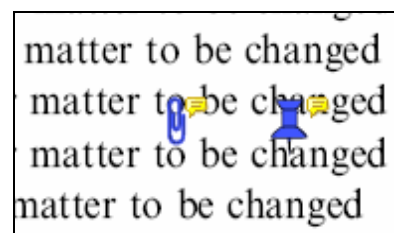


How to use it:

1. Select Highlighter Tool from the commenting toolbar
2. Highlight the desired text
3. Add a note detailing the required change

Attach File Tool — For inserting large amounts of text or replacement figures as a files.

Inserts symbol and speech bubble where a file has been inserted.

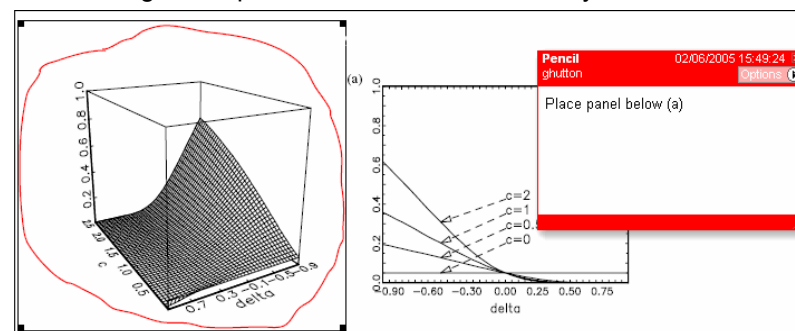


How to use it:

1. Click on paperclip icon in the commenting toolbar
2. Click where you want to insert the attachment
3. Select the saved file from your PC/network
4. Select appearance of icon (paperclip, graph, attachment or tag) and close

Pencil tool — For circling parts of figures or making freeform marks

Creates freeform shapes with a pencil tool. Particularly with graphics within the proof it may be useful to use the Drawing Markups toolbar. These tools allow you to draw circles, lines and comment on these marks.



How to use it:

1. Select Tools > Drawing Markups > Pencil Tool
2. Draw with the cursor
3. Multiple pieces of pencil annotation can be grouped together
4. Once finished, move the cursor over the shape until an arrowhead appears and right click
5. Select Open Pop-Up Note and type in a details of required change
6. Click the X in the top right hand corner of the note box to close.

Help

For further information on how to annotate proofs click on the Help button to activate a list of instructions:

