ORIGINAL ARTICLE

Serial Evaluation of Sequential Organ Failure Assessment Score in Predicting 1-Year Mortality in Critically Ill Patients

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ABSTRACT

INTRODUCTION: The prediction of long-term prognosis or outcome of critically ill patients in the intensive care unit (ICU) is important for prognostication and administration purposes. The Sequential Organ Failure Assessment (SOFA) score was developed in order to estimate organ failure in patients with sepsis. Organ failures have been associated with mortality and hence SOFA score has been validated as an outcome measure. To the best of our knowledge, the association of SOFA, and serial SOFA score with 1-year mortality has not been well established. **MATERIALS AND METHOD**: This was a retrospective observational cross sectional study using the existing record of patients admitted to the general ICU at the Sultan Ahmad Shah Medical Centre from the 1st June 2017 to the 30th May 2018. Data was collected from daily clinical charts and medical records of patients. SOFA score on day-1, day-3, day-3, and on discharge were recorded and subsequently delta SOFA was calculated. **RESULTS**: Data from a total of 120 patients were collected. SOFA score within 3 days of admission predicted 1-year mortality, with the highest prediction for SOFA score on discharge from ICU. Serial SOFA score measured within 24 hours (day-1 to day-2) and 48 hours (day-1 to day-3) did not predict mortality; however, delta SOFA involving SOFA on discharge did. Cardiovascular and renal scores were the most significant individual component of SOFA score that contributed to 1-year mortality. **CONCLUSION**: SOFA score measured on discharge from ICU plays a key important factor in contributing for the prediction of 1-year mortality. Cardiovascular and renal scores were the most significant component that warrant risk stratification measures using the parameters.

Keywords
Sequential Organ Failure Assessment Score, Critically Ill, Risk Assessment

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Received: 4th October 2021; Accepted: 28th January 2022

Doi: https://doi.org/10.31436/imjm.v21i3

INTRODUCTION

The prediction of long-term prognosis or outcome of critically ill patient is very important for clinical and administrative purposes.[1] Clinically, such prediction of long-term outcome is beneficial to provide prognostication of patients for making appropriate decision or goal of therapy for patients. As for the administrative purposes, it serves as helpful tools in managing and allocating hospital resources appropriately. According to the Malaysian Registry of Intensive Care 2017 report, one third (36%) of patients admitted to the ICU had multiple organ failures, which was defined as two or more organ failure. Cardiovascular failure was the most common organ dysfunction followed by respiratory failure.[2]

There are two categories of outcome measures that are available which include severity scoring systems, and organ dysfunctions score to predict long-term prognosis in critically ill patients. Severity scoring system includes the Acute Physiology Chronic and Health Evaluation score (APACHE),[3] and Simplified Acute Physiology Score (SAPS),[4] and Mortality Prediction Model.[5] Limitations of these systems are that they are cumbersome for routine clinical use because of the burden of entering the data as the number of variables available is significant, and can only at their best predict the behaviour of a group of patients who exactly match the patients in the development population. The Sequential Organ Failure Assessment (SOFA) score was first introduced in 1994,

with an objective to estimate the severity of organ failure over time in sepsis patients.[6] Although it was originally developed to describe the sequence of complications in critical illness and not for the prediction of mortality, the relationship of organ failure with mortality were well described in several studies.[7–10]

Previous studies have shown the use of SOFA score and delta SOFA with 28-day and 90-day mortality in critically ill patients; however, studies that have investigated 1-year mortality of SOFA is limited.[11,12] Intensive care is a dynamic environment where the general condition of patients can change rapidly in either direction. Therefore, it is important for the clinicians to evaluate the changes by assessing the change of SOFA scores in the ICU.[13] Despite the advantages of the SOFA score, there are limited studies available that evaluated the validity of SOFA score in predicting long term mortality in critically ill patients, and fewer still studies that investigated the serial SOFA score. To the best of our knowledge, this is the first study in Malaysia that looked at the serial SOFA score of patients in ICU in predicting 1-year mortality. We evaluated the use of SOFA and serial SOFA score in predicting 1-year mortality in patients admitted to the ICU.

METHODS

This study was an observational cross-sectional study using existing records of admissions at ICU of the Sultan Ahmad Shah Medical Centre (SASMEC@IIUM), Kuantan, Pahang. This study has obtained the approval from the International Islamic University Malaysia Research and Ethics Committee (IREC) on 13th July 2020 – IREC ID No 2020-081. As this is a retrospective study the ethical committee waived the need for informed consent.

All patients admitted from the 1st July 2017 until 30th May 2018 were screened for eligibility to be included in the study. The inclusion criteria included patients 18 years old and above, and duration of ICU admission longer than 72 hours. The exclusion criteria were patients referred from other hospitals. SOFA scores at day-1, day-2 and day-3, and on discharge from ICU were recorded and subsequently delta SOFA was calculated. The positive total summation of each delta SOFA indicates the worsening of delta score while negative total summation indicates improving of delta SOFA. Delta SOFA was used to assess the correlation between the changes in SOFA and 1-year mortality. The study population was divided into either the survivor group and non-survivor group. Survivors are defined as patients who are still alive after 1 year, and non-survivor are those who died within 1 year. Patients were followed up by phone calls to assess the outcomes. Demographic data of the patients, namely age, gender, weight, height, and ethnicity were collected. The clinical data that was collected included APACHE II score, admission diagnosis, requirement of renal replacement therapy and the requirement and types of mechanical ventilation.

Statistical Analysis

Results are presented as mean ± SD for normally distributed variables or median (inter-quartile range) for non-normally distributed variables. Comparison of variables between the two groups was analyzed using the independent t test for normally distributed variables or the Mann-Whitney test for non-normally distributed variables. Categorical variables were compared with Chi-Square test. The diagnostic and predictive performances were assessed by the area under curve (AUC) of receiver operating characteristic (ROC) curve of the sensitivity verse 1-specificity. The optimal cut-off point was defined as the measured quantity, which maximised sensitivity and specificity.

RESULTS

Records of a total of 237 patients who were admitted to ICU from the 1st June 2017 till the 30th May 2018 (Figure 1) were assessed. After exclusions based on the exclusion criteria and missing contact numbers, eligible data of 120 patients was analysed. Of these 120 patients, 76 (63.3%) stayed longer than 3 days, and they were discharged on the 5.67 ± 5.26 days, with a maximum of 32.5 days. Of the recruited patients, 61 (50.8%) died within 1-year of ICU admission.

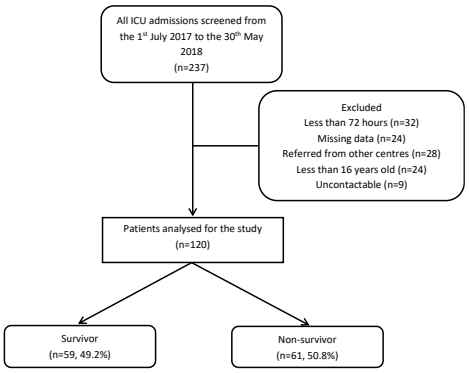

Figure 1: Patients' flow

Demographic and Clinical Characteristics

There were no differences in the age groups and gender between the survivor and non-survivor groups (Table 1).

Table 1: Demographic, and clinical characteristics

Variables	All Patients (n=120)	Non-survivors (n=61)	Survivors (n=59)	p-value
Age (years)	59.1 ± 13.9	60.7 ± 13.3	57.6 ± 14.5	0.22
Gender (male)	67 (55.8)	39 (63.9)	28 (47.4)	0.07
Category of Patients	80 (66.7)	48 (78.7)	32 (54.2)	0.01
Medical	40 (33.3)	13 (21.3)	27 (45.7)	
Surgical				
APACHE II score	16.1 ± 7.6	18.6 ± 7.1	13.6 ± 7.3	<0.0001
SOFA day-1	5.32 ± 3.73	6.92 ± 3.77	3.66 ± 2.90	<0.0001
SOFA day-2	4.96 ± 3.61	6.39 ± 3.64	3.47 ± 2.94	<0.0001
SOFA day-3	5.04 ± 4.29	6.90 ± 4.56	3.12 ± 2.98	<0.0001
SOFA on ICU Discharge	4.43 ± 5.05	7.13 ± 5.71	1.64 ± 1.74	<0.0001
Delta SOFA 24 hours (day-1 to day-2)	-0.36 ± 1.98	-0.53 ± 2.03	-0.19 ± 1.93	0.351
Delta SOFA 48 hours (day-1 to day-3)	-0.28 ± 2.78	-0.02 ± 2.66	-0.54 ± 2.91	0.303
Delta SOFA day-1 to Discharge	-0.88 ± 3.86	0.21 ± 4.49	-2.02 ± 2.68	<0.0001

Data expressed as mean ± SD, n (%), or median (lower quartile – upper quartile). APACHE II Score: Acute Physiological and Chronic Health Evaluation II Score. SOFA Score: Sequential Organ Failure Assessment.

Medical category patients were more frequently admitted to ICU compared to surgical patients. Surgical patients were more likely to survive than patients in the medical patients (p=0.01). APACHE II was higher in non-survivors compared to survivors. Day-1 to day-3 SOFA scores, and SOFA on ICU discharge were higher in the survivor group compared to the non-survivor. Correspondingly, delta SOFA within 24 hours (day-1 to day-2), and 48 hours (day-1 to day-3) were higher in the survivor groups compared to non-survivor groups. In addition, the differences of day-1 SOFA to SOFA on ICU discharge was also higher.

Predictive Utility of SOFA Score

SOFA scores within 3 days of admission predicted 1-year mortality, with the highest prediction for the SOFA score on discharge from ICU with AUC of 0.812 (0.734, 0.890) (Table 2 and Figure 2).

Table 2: SOFA scores in predicting 1-year mortality

	AUC	95% CI	p-value
Day-1 SOFA	0.750	(0.663, 0.836)	<0.0001
Day-2 SOFA	0.740	(0.651, 0.829)	<0.0001
Day-3 SOFA	0.753	(0.668, 0.839)	<0.0001
On discharge SOFA	0.812	(0.734, 0.890)	<0.0001

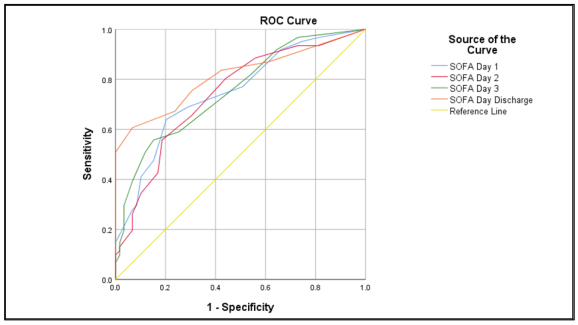

Figure 2: Receiver Operating Characteristics Curve for Sequential Organ Failure Assessment score in predicting 1-year mortality.

Predictive Utility of Serial SOFA Score

Serial SOFA score measured within 24 hours (day-1 to day-2) and 48 hours (day-1 to day-3) did not predict mortality, but delta SOFA involving SOFA on discharged did (Table 3 and Figure 3). Delta SOFA (day-1 to discharge) had an AUC of 0.648 (0.550, 0.747) in predicting 1-year mortality.

Components of SOFA Score that Most Contribute to 1-year Mortality

Throughout the 3 days SOFA and on discharged SOFA, cardiovascular and renal scores were consistently the most significant individual component of SOFA score that contributed to 1-year mortality (Table 4).

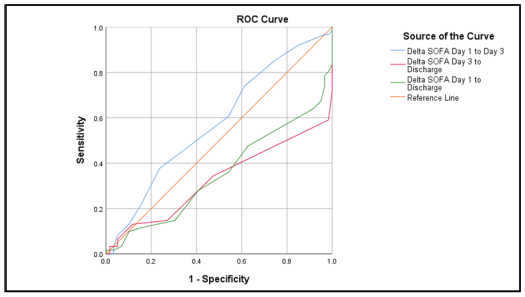

Figure 3: Receiver Operating Characteristics Curve for Sequential Organ Failure Assessment score in predicting 1-year mortality

Table 3: Delta SOFA in predicting 1-year mortality

	AUC	95% CI	p-value
Delta SOFA (day-1 to day-2)	0.466	(0.362, 0.569)	0.517
Delta SOFA (day-1 to day-3)	0.578	(0.476, 0.681)	0.139
Delta SOFA (day-1 to discharge)	0.648	(0.550, 0.747)	0.005

SOFA: Sequential Organ Dysfunction Syndrome

DISCUSSION

In this study we have shown that SOFA scores calculated within the three days of ICU admission, and on discharged predicted 1-year mortality. Of these, on discharged SOFA score had the best predicted 1-year mortality, with AUC of 0.812 (0.734, 0.890) Serial SOFA score of day-1 and day-3 to on discharged SOFA calculation predicted mortality. Among the individual components of SOFA score, cardiovascular and renal were the most significant component.

In our study, the average SOFA score on ICU admission was 5.32 ± 3.73, higher in patients who died, and this remained the same throughout the 3 days of ICU stay. The mean of duration in ICU stay in our study was 5.67 days; hence, the SOFA on discharged was measured on day-5, with 43 patients stayed longer than 5 days. The SOFA score on discharged was the highest in those who died compared to those who survived. In a study with a large cohort of 10,004 patients in Cardiac ICU over 8 years, the presence of organ failure independently increased the prediction of mortality by threefold (OR of 3.02 (9%CI 2.47 – 3.68)).[14] Increasing number of organ failure increased mortality rate, up to 70% in those with greater than four organ failures.

Table 4: Components of SOFA score in predicting 1-year mortality

		AUC (95%)	p – value
Day-1 SOFA	Respiration	0.579	0.137
	Coagulation	0.575	0.156
	Liver	0.599	0.060
	Cardiovascular	0.679	0.001
	Central Nervous System	0.538	0.474
	Renal	0.647	0.005
Day-2 SOFA	Respiration	0.608	0.042
	Coagulation	0.576	0.152
	Liver	0.596	0.069
	Cardiovascular	0.657	0.003
	Central Nervous System	0.542	0.425
	Renal	0.616	0.028
Day-3 SOFA	Respiration	0.598	0.065
	Coagulation	0.570	0.183
	Liver	0.575	0.155
	Cardiovascular	0.674	0.001
	Central Nervous System	0.619	0.025
	Renal	0.652	0.004
On discharge SOFA	Respiration	0.671	0.001
	Coagulation	0.589	0.091
	Liver	0.653	0.004
	Cardiovascular	0.705	<0.0001
	Central Nervous System	0.660	0.002
	Renal	0.670	0.001

SOFA: Sequential Organ Dysfunction Syndrome

The timing of the SOFA score measurement may also influence the result. Studies showed that early changes in organ function responses were observed within 1 day of admission in patients with severe sepsis.[15] An early change in the SOFA score was shown as a good and useful marker for mortality in critically ill patients as well as to evaluate the response of patients to the treatment given.[11] We showed that the SOFA score measured during the first 3 days of admission predicted 1-year mortality. However, the highest predictive value was for the SOFA score measured on ICU discharge. Measurement of the SOFA score for up to 5 days, but not beyond, improved the prediction of mortality in a study of 1290 sepsis patients in 11 ICUs.[16] Maximum score measured during ICU admission can signify the highest degree of organ failure, and this has been shown to be the best measures for mortality compared to the mean or initial score in 352 ICU patients,[9] and in a large study in the cardiothoracic

ICU.[14] A multicentre study involving 40 ICUs in 16 countries also showed maximum SOFA score was the best predictor of patient survival after ICU admission.[10]

Intensive care is a dynamic environment where the general condition of patients can change rapidly in either direction. Therefore, it is important for clinicians to evaluate the changes by assessing the serial change of SOFA scores. A change in the SOFA or delta SOFA is calculated as the change in total SOFA score (or that of an individual sub-score) between a defined time point and the baseline value. These can reflect response of patients to interventions, or development of complications in response to the disease processes or interventions. Thus, it is important for clinicians to monitor progress of patients, and for prognostication. Several studies have investigated the utility of serial SOFA score.[9–11,16,17] Incremental addition of SOFA of up to 5 days improves the prediction of ICU mortality in a multivariate analysis.[16] A change in the SOFA score was shown to be associated with ICU mortality, the prediction for the first 48 hours is better than the subsequent 48 hours.[9]

We have shown that there was no association between delta SOFA 24 hours (day-1 to day-2), and 48 hours (day-1 to day-3) with 1-year mortality. This may be due to as shorter time interval to allow capturing of the delta SOFA. A longer period of time interval may show positive results as shown by other investigators who showed that delta SOFA on day-1 to day-7 had strong relationship with 28-days mortality and 90-days mortality in sepsis patients.[11] In addition, in a large cohort study of 20,007 critically ill, change of SOFA between day-1 to day -7 was a better predictor of mortality compared to between day 8 to 14.[18] However, this differs from a study which showed lower mortality in patients who had improvement in organ function in the first 24 hours after admission to the ICU compared with those who had unchanged or increased SOFA scores in 2110 sepsis patients in the ICU.[12]

Of the six components of the SOFA score, we showed that the cardiovascular and renal components had the strongest prognostic capabilities for mortality across the first three days of ICU stay as well as on discharge. The finding was similar with a study done by Hewett *et al.* in 2012 on 1284 ICU patients which showed that cardiovascular component had significant relationship with mortality.[19] Similar with our findings, an earlier study in 1999 also reported that cardiovascular score had the highest relative contribution to ICU and hospital mortality.[10] The second most significant component that contributed to mortality was kidney related followed by neurology, haematology and respiratory dysfunctions. It is of interest that in our study we showed kidney plays an important factor in our setting. Acute Kidney Injury (AKI) is common occurrence in 65% of our patients, higher compared with other studies. [20] This is mainly due to high occurrence of sepsis, 52% of sepsis patients had AKI.[21] In a study in cardiac ICU, mortality risk was highest with cardiovascular, coagulation and liver failure.[14] Most of the other studies excluded the neurological score due to the lack of robustness, accuracy, and reliability of the Glasgow Coma Score (GCS).[22] In the initial validation of the SOFA score,[6] the assumed value for GCS in patients receiving sedation associated with significant variability in the recorded value. Other studies removed this component by using a five-component modified SOFA score, and some used the Richmond Agitation and Sedation Score.[13] Our study used a method where last GCS recorded prior to intubation and was carried forward in the daily assessment until the patient neurology function can be examined in the absence of sedation. We showed that central nervous system component did not help in predicting mortality.

Limitations of the Study

There are several limitations to this study. First, the study was done in a single centre. Therefore, the findings may be affected by the demographic and the medical practices of the centre. Second, as this was a retrospective study where all the clinical data were retrieved from records of data of patients who were admitted to the ICU. All scores were calculated *post hoc* and not applied in real time. We could only use the available recorded data and some of the data were not documented properly. Third, the sample size was smaller as compared to other previous studies, thus the population might be underrepresented and might have resulted in less precise estimation of the accuracy of

the SOFA score. Fourth, since SASMEC ICU population was mixed, and small sample size, prediction for a subset of specific diseases separately could not be done. However, despite these limitations, our study was the first in Malaysia that evaluated the association of SOFA score and 1-year mortality.

CONCLUSION

SOFA score is a simple, but effective prognostic indicator and assessment tool for patient progress in the intensive care setting. The analysis of our study has demonstrated that there is a significant correlation between the SOFA score and 1-year mortality in critically ill patient. The 1-year mortality increased with higher serial daily SOFA and delta SOFA. Among the individual components of SOFA score, cardiovascular and renal involvement were the most significant components that contributed to 1-year mortality. Future multicentre study should involve a larger sample size to accurately represent Malaysian population is warranted.

ACKNOWLEDGEMENTS

This study was funded by the Ministry of Higher Education Fundamental Research Grant Scheme (FRGS/1/2019/SKK02/UIAM/02/1, FRGS19-184-0793) of Malaysia. This paper was presented in Malaysian Society of Anaesthesiologists Annual Scientific Meeting 2021, and was awarded the First Prize for Best Poster Award.

REFERENCES

1. Friedrich JO, Wilson G, Chant C. Long-term outcomes and clinical predictors of hospital mortality in very long stay intensive care unit patients: A cohort study. *Critical Care*; 10. Epub ahead of print April 10, 2006. DOI: 10.1186/cc4888.
2. Li T, Tan LD, Cheng C. *Malaysian Registry of Intensive Care Report for 2015 Technical Committee of the Malaysian Registry of Intensive Care*, www.mric.org.my.
3. Wong DT, Knaus WA. Predicting outcome in critical care: the current status of the APACHE prognostic scoring system. *Canadian Journal of Anaesthesia* 1991; 38: 374–383.
4. le Gall J-R. A New Simplified Acute Physiology Score (SAPS II) Based on a European/North American Multicenter Study. *JAMA: The Journal of the American Medical Association* 1993; 270: 2957.
5. Teres D, Lemeshow S, Avrunin Js, et al. Validation of the mortality prediction model for ICU patients. *Critical Care Medicine* 1987; 15: 208–213.
6. Vincent J-L, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Medicine* 1996; 22: 707–710.
7. Nfor TK, Walsh TS, Prescott RJ. The impact of organ failures and their relationship with outcome in intensive care: Analysis of a prospective multicentre database of adult admissions. *Anaesthesia* 2006; 61: 731–738.
8. de Rooij SE, Govers A, Korevaar JC, et al. Short-term and long-term mortality in very elderly patients admitted to an intensive care unit. *Intensive Care Medicine* 2006; 32: 1039–1044.
9. Ferreira FL. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. *JAMA* 2001; 286: 1754.
10. Moreno R, Vincent J-L, Matos R, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. *Intensive Care Medicine* 1999; 25: 686–696.
11. Karakike E, Kyriazopoulou E, Tsangaris I, et al. The early change of SOFA score as a prognostic marker of 28-day sepsis mortality: Analysis through a derivation and a validation cohort. *Critical Care*; 23. Epub ahead of print November 29, 2019. DOI: 10.1186/s13054-019-2665-5.
12. Sakr Y, Lobo SM, Moreno RP, et al. Patterns and early evolution of organ failure in the intensive care unit and their relation to outcome. *Critical Care* 2012; 16: R222.
13. Lambden S, Laterre PF, Levy MM, et al. The SOFA score - Development, utility and challenges of accurate assessment in clinical trials. *Critical Care*; 23. Epub ahead of print November 27, 2019. DOI: 10.1186/s13054-019-2663-7.

14. Jentzer JC, Wiley B, Bennett C, et al. Early noncardiovascular organ failure and mortality in the cardiac intensive care unit. *Clinical Cardiology* 2020; 43: 516–523.
15. Levy MM, Macias WL, Vincent J-L, et al. Early changes in organ function predict eventual survival in severe sepsis*. *Critical Care Medicine* 2005; 33: 2194–2201.
16. Holder AL, Overton E, Lyu P, et al. Serial Daily Organ Failure Assessment Beyond ICU Day 5 Does Not Independently Add Precision to ICU Risk-of-Death Prediction. *Critical Care Medicine* 2017; 45: 2014–2022.
17. de Grooth HJ, Geenen IL, Girbes AR, et al. SOFA and mortality endpoints in randomized controlled trials: A systematic review and meta-regression analysis. *Critical Care*; 21. Epub ahead of print February 24, 2017. DOI: 10.1186/s13054-017-1609-1.
18. Soo A, Zuege DJ, Fick GH, et al. Describing organ dysfunction in the intensive care unit: A cohort study of 20,000 patients. *Critical Care*; 23. Epub ahead of print May 23, 2019. DOI: 10.1186/s13054-019-2459-9.
19. Hewett JN, Rodgers GW, Chase JG, et al. Assessment of SOFA score as a diagnostic indicator in intensive care medicine. In: *IFAC Proceedings Volumes (IFAC-PapersOnline)*. IFAC Secretariat, 2012, pp. 467–472.
20. Md Ralib A, Mat Nor MB. Acute kidney injury in a Malaysian intensive care unit: Assessment of incidence, risk factors, and outcome. *Journal of Critical Care* 2015; 30: 636–642.
21. Md Ralib A, Mat Nor MB, Pickering JW. Plasma Neutrophil Gelatinase-Associated Lipocalin diagnosed acute kidney injury in patients with systemic inflammatory disease and sepsis. *Nephrology* 2017; 22: 412–419.
22. Tallgren M, Bäcklund M, Hynninen M. Accuracy of Sequential Organ Failure Assessment (SOFA) scoring in clinical practice. *Acta Anaesthesiologica Scandinavica* 2009; 53: 39–45.