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ORIGINAL ARTICLE

Validation of SAPS3 admission score and its customization for use in Korean intensive care unit patients: A prospective multicentre study

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SUMMARY AT A GLANCE

We investigated to validate the simplified acute physiology score 3 (SAPS3) and to customize it in Korean ICUs. General and Australasia SAPS3 showed poor calibration, but the prognostic power was improved by customization. Prediction models should be customized before being used to predict mortality in different regions.

ABSTRACT

Background and objective: **To externally validate the simplified acute physiology score 3 (SAPS3) and to customize it for use in Korean intensive care unit (ICU) patients.**

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Methods: **This is a prospective multicentre cohort study involving 22 ICUs from 15 centres throughout Korea. The study population comprised patients who were consecutively admitted to participating ICUs from 1 July 2010 to 31 January 2011.**
Results: **A total of 4617 patients were enrolled. ICU mortality was 14.3%, and hospital mortality was 20.6%. The patients were randomly assigned into one of two cohorts: a development ($n = 2309$) or validation ($n = 2308$) cohort. In the development cohort, the general SAPS3 had good discrimination (area under the receiver operating characteristics curve = 0.829), but poor calibration (Hosmer–Lemeshow goodness-of-fit test $H = 123.06$, $P < 0.001$, $C = 118.45$, $P < 0.001$). The Australasia SAPS3 did not improve calibration ($H = 73.53$, $P < 0.001$, $C = 70.52$, $P < 0.001$). Customization was achieved by altering the logit of the original SAPS3 equation. The new equation for Korean ICU patients was validated in the validation cohort, and demonstrated both good discrimination (area under the receiver operating characteristics curve = 0.835) and good calibration ($H = 4.61$, $P = 0.799$, $C = 5.67$, $P = 0.684$).**
Conclusions: **General and regional Australasia SAPS3 admission scores showed poor calibration for use in Korean ICU patients, but the prognostic power of the SAPS3 was significantly improved by customization. Prediction models should be customized before being used to predict mortality in different regions of the world.**

Key words: calibration, discrimination, intensive care unit, severity of illness.

Abbreviations: AUS-SAPS3, Australasia SAPS3; GOF, goodness of fit; ICU, intensive care unit; SAPS3, simplified acute physiology score 3; SMR, standardized mortality ratio.

INTRODUCTION

Severity scoring systems are used to predict and compare outcomes to help guide the allocation of limited resources and to evaluate the process of care.[1] However, there is large variability in the performance of general severity scoring systems,[2,3] which is mostly attributable to differences in patient case-mix or changing medical practice over time.

Recently, the simplified acute physiology score 3 (SAPS3) was developed through a worldwide prospective study to predict hospital mortality in critically ill patients.[4] The SAPS3 admission score was designed to be used on multiple levels; thus, the system encompassed not only a general equation but also regional equations customized for use in specific geographical areas.[4] However, external validation studies of the SAPS3 have reported mixed results.[5–10] Although there are some reports of validation of the SAPS3 in Asian cohorts,[5,6] the general and Australasia SAPS3 (AUS-SAPS3) equations have never been validated in a large, prospective multicentre cohort in Asia.

Therefore, the aim of this study was to evaluate the prognostic performance of the SAPS3 in a large prospective cohort in Korea, and to assess the need for region-specific or country-specific customization of the SAPS3.

METHODS

This is a prospective multicentre cohort study. The validation of the SAPS3 in Korean intensive care units (ICUs) (VSKI) was conducted by the Korean Study Group on Respiratory Failure between 1 July 2010 and 31 January 2011. The study included patients from 22 participating ICUs (medical = 14, surgical = 6, multidisciplinary = 2) in 15 tertiary or university-affiliated hospitals. The study was approved by each hospital's institutional review board, and the requirement for informed consent was waived due to the non-interventional nature of the study.

Patients

All patients admitted to the 22 ICUs during the study period were eligible for this study. We excluded patients if they were younger than 17 years old or if the primary outcome of hospital mortality was uncertain. Patients who were transferred from other participating ICUs were also excluded. For patients with two or more admissions to the ICU during the same hospital stay, only the data from the first admission were used.

Data collection

Patient data were collected using a web-based database. The definitions of variables used in the original SAPS3 model were used for this study.[4] We used the most abnormal set of data from the period 1 h prior to or after ICU admission to calculate the SAPS3. Predicted hospital mortalities were calculated using the general SAPS3 and the customized AUS-SAPS3 equations as follows: $\text{Logit} = -32.6659 + \ln(\text{SAPS3} + 20.5958) \times 7.3068$ for general SAPS3, $\text{Logit} = -22.5717 + \ln(\text{SAPS3} + 1) \times 5.3163$ for AUS-SAPS3 and the probability of death $= e^{\text{logit}}/(1 + e^{\text{logit}})$.[4]

The study population was randomly divided into development or validation cohort. The performances of the general SAPS3 and the Asian-specific SAPS3 (AUS-SAPS3) were validated externally in the development cohort. After confirming poor performances of two scores, a new equation customized for use in Korean ICU patients was derived. Subsequently, the newly customized SAPS3 for Korea (K-SAPS3) was validated in the validation cohort using the AUS-SAPS3 for comparison.

Data quality

For data quality, 5% of the study participants were randomly selected and had their data recollected. Their original SAPS3 data and recalculated SAPS3 data were compared to assess the reliability of data collection process. The kappa value was 0.83 ($P < 0.001$).

Method of model customization

First-level customization was performed using logistic regression analysis by computing new logistic coefficient while maintaining the same variables with

the same weights as in the original model. Hospital mortality was the dependent outcome variable.

Statistical analysis

For statistical analysis, PASW 17.0 (SPSS Inc., Chicago, IL, USA) and STATA 11.0 (StataCorp LP, Texas, USA) were used. Data are shown as medians and interquartile ranges, or numbers with percentages. A two-tailed *P*-value of <0.05 was considered statistically significant.

Generally, evaluation of performance of scoring system usually includes assessment of calibration and discrimination. Calibration is defined as the agreement between individual probabilities and actual outcomes.[11] Hosmer–Lemeshow goodness-of-fit (GOF) *H* statistic and GOF *C* statistics were used to evaluate calibration.[11] To assess GOF, patients were divided into 10 groups either by expected mortality intervals (*H* statistic) or 10 equal number groups (*C* statistic), and the expected number of death as predicted by SAPS3 was compared with the observed number of death in each group. The number of expected outcomes was calculated by multiplying the mean of predicted probabilities and the number of patients in each group. A $P > 0.05$ was accepted as indicating good fit of the model.

The standardized mortality ratio (SMR) was calculated by dividing the number of observed deaths by the number of expected deaths in each cohort. To test for statistical significance, we calculated 95% confidence intervals according to the method described by Hosmer and Lemeshow.[11] In a perfect model, they should not be different from one.

Discrimination is the power to distinguish between survivors and non-survivors, and was assessed by calculating the area under the receiver operating characteristic curve, as described by Hanley and McNeil.[12] Generally, an area under the receiver operating characteristics curve greater than 0.9 is defined as indicating excellent discrimination, $0.8 \leq$ area under the receiver operating characteristics curve < 0.9 good discrimination and $0.7 \leq$ area under the receiver operating characteristics curve < 0.8 modest discrimination.[12,13]

RESULTS

Baseline characteristics of patients

A total of 4617 patients were enrolled during the study period. To customize and validate the K-SAPS3, the study population was randomly split into a development cohort ($n = 2309$) or a validation cohort ($n = 2308$).

The clinical characteristics and outcomes of the patients are described in Table 1. Males accounted for 64.7% (1493/2309) of the development cohort, and the median age overall in the group was 62 (interquartile range 49–72). Males accounted for 59.5% (1373/2308) of the validation cohort, and the median age was 62 (interquartile range 49–72). Patients were most frequently transferred to the ICU from the general medicine ward, and the second most common location prior to ICU transfer was the emergency room. Hypertension, solid cancer and diabetes mellitus were the most frequent comorbidities. The need for clinical observation was the most frequent reason for ICU admission. Respiratory and cardiovascular diseases were the most frequent organ-specific indications for ICU admission. The prevalence of nosocomial infection at the time of ICU admission was 8.1% in the development cohort and 6.4% in the validation cohort ($P < 0.001$). The prevalence of community-acquired infection was 21.4% in the development cohort and 14% in the validation cohort ($P < 0.001$). The median sequential organ failure assessment score was 5 (interquartile range 2–9) in the development cohort and 6 (interquartile range 3–10) in the validation cohort ($P < 0.001$). ICU mortality was 12.9% in the development cohort and 15.6% in the validation cohort ($P = 0.01$), with hospital mortalities of 20.1% and 21.1%, respectively ($P = 0.40$).

Performance assessment of general SAPS3 and AUS-SAPS3 in the development cohort

The calibration and discrimination of the general SAPS3 and the AUS-SAPS3 are reported in Table 2. Overall, a significant discrepancy was observed between the observed and expected mortalities across all strata when the general SAPS3 was used (Hosmer–Lemeshow GOF *H* of 123.06 ($P < 0.001$) and a Hosmer–Lemeshow GOF *C* of 118.45 ($P < 0.001$)) (Fig. 1). The general SAPS3 generated an SMR of 0.72 (95% confidence interval: 0.65–0.78). The overall discriminatory power of the general SAPS3, as measured by the area under the receiver operating characteristics curve, was 0.829. The AUS-SAPS3 also showed poor calibration ($H = 73.53$, $P < 0.0001$, $C = 70.52$, $P < 0.001$) (Fig. 2). The AUS-SAPS3 generated an SMR of 0.78 (95% confidence interval: 0.71–0.85). The discriminatory power of the AUS-SAPS3 was 0.829.

Derivation of new SAPS3 equation for Korean intensive care unit patients

The customized equation for Korea was derived as:

$$\text{Logit} = -35.1752 + \ln(\text{SAPS3} + 20.5958) \times 7.7379$$

Performance assessment of AUS-SAPS3 and K-SAPS3 in the validation cohort

The calibration and discrimination of the AUS-SAPS3 and K-SAPS3 in the validation cohort are reported in Table 3. The AUS-SAPS3 showed poor calibration, with a Hosmer–Lemeshow GOF *H* of 72.71 ($P < 0.001$) and a Hosmer–Lemeshow GOF *C* of 68.06 ($P < 0.001$). The SMR predicted by the AUS-SAPS3 model was 0.77 (95% confidence interval: 0.70–0.84). By comparison, the K-SAPS3 showed good calibration ($H = 4.61$, $P = 0.799$, $C = 5.67$, $P = 0.684$) (Fig 3). The SMR predicted by the K-SAPS3 was 0.99 (95% confidence interval: 0.90–1.08). The discriminatory power of the K-SAPS3 was 0.835.

Table 1 Baseline characteristics and outcome data of the two cohorts

	Development cohort		Validation cohort		
	N or Median	% or IQR	*N* or Median	% or IQR	*P*
Number of patients	2309		2308		—
Male	1493	64.7	1373	59.5	0.25
Age (years)	62	49–72	62	49–72	0.94
SOFA	5	2–9	6	3–10	<0.001
Intra-hospital location before ICU admission					<0.001
Emergency room	1066	46.2	989	42.9	
General ward	1163	50.4	1256	54.4	
Other ICU	53	2.3	20	0.9	
Others	27	1.2	43	1.9	
Comorbidity (overlapped)					—
Hypertension	842	36.5	714	30.9	
CHF	146	6.3	34	1.5	
Stroke	178	7.8	79	3.4	
COPD	79	3.4	56	2.4	
DM	526	22.8	450	19.5	
CRF	208	9.0	131	5.7	
Haematological cancer	103	4.5	71	3.1	
Solid cancer	848	36.7	669	29.0	
Unplanned ICU admission	1134	49.1	1001	43.4	<0.001
Reason for ICU admission					—
Observational†	1076	46.6	1064	46.1	
Cardiovascular	339	14.7	251	10.9	
Digestive	86	3.7	142	6.2	
Haematological cancer	8	0.4	10	0.4	
Hepatic failure	46	2.0	115	5.0	
Metabolic	57	2.5	33	1.4	
Neurological	140	6.1	101	4.4	
Renal	54	2.3	24	1.0	
Respiratory	370	16.0	374	16.2	
Others	133	5.8	194	8.4	
Surgical status					<0.001
No surgery	1390	60.2	1163	50.4	
Scheduled surgery	760	32.9	936	40.6	
Emergent surgery	159	6.9	209	9.1	
Acute infection at ICU admission	683	29.6	470	20.4	<0.001
Hospital-acquired	188	8.1	147	6.4	
Community-acquired	495	21.4	323	14.0	
ICU length of stay	3	2–7	4	2–10	<0.001
Hospital length of stay	23	21–25	21	12–40	<0.001
ICU mortality	299	12.9	359	15.6	0.01
Hospital mortality	463	20.1	486	21.1	0.40

† Preparation for routine post-surgery care including simple weaning from ventilator after surgery.

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; DM, diabetes mellitus; ICU, intensive care unit; IQR, interquartile range; SOFA, sequential organ failure assessment.

Table 2 Discrimination and calibration of general SAPS3 and AUS-SAPS3 in the development cohort

Prediction model	Score	Predicted mortality	GOF *H*-test	*P*	GOF *C*-test	*P*	SMR	95% CI	aROC
SAPS3	52 (41–64)	20.5 (7.2–44)	123.06	<0.001	118.45	<0.001	0.72	0.65–0.78	0.829
AUS-SAP 3	—	18.8 (6.3–40.6)	73.53	<0.001	70.52	<0.001	0.78	0.71–0.85	0.829

aROC, area under the receiving operator characteristics curve; AUS-SAPS, Australasia simplified acute physiology score; CI, confidence intervals; GOF, goodness of fit; SAPS3, simplified acute physiology score 3; SMR, standardized mortality ratio.

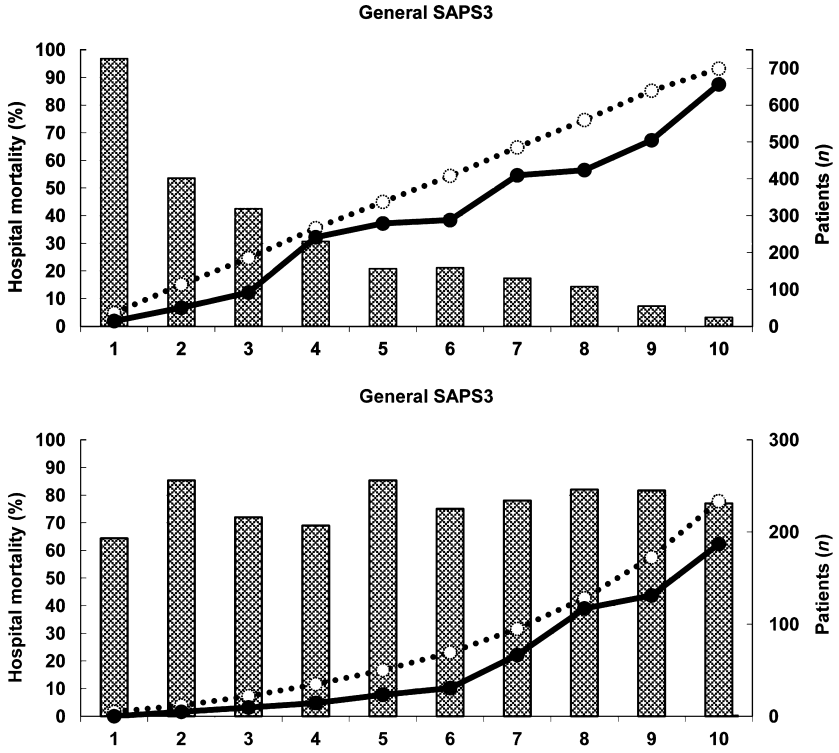

Figure 1 Calibration curves of the general simplified acute physiology score 3 (SAPS3) in development cohort. ▨, patients (right); ••○••, expected (left); ●—●, observed (left). Predicted risk of hospital mortality, observed hospital mortality and the corresponding number of patients are shown. In the upper panel, *x*-axis represents patients divided into 10 groups according to predicted mortality based on general SAPS3 model. In the lower panel, *x*-axis represents predicted rate of mortality by approximate decile of patients. In both curves, significant differences between curves representing predicted and observed mortalities are observed ($P < 0.001$). *Columns*: number of patients; *line with open circles*: mean predicted mortality; *line with closed circles*: mean observed mortality.

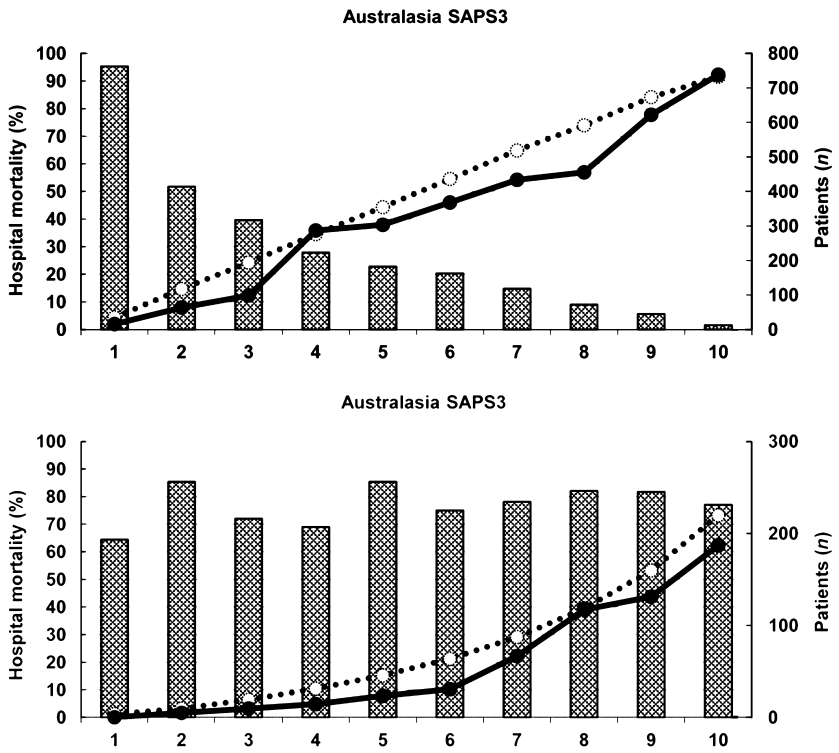

Figure 2 Calibration curves of the Australasia simplified acute physiology score 3 (SAPS3) in development cohort. ▨, patients (right); ••○••, expected (left); ●—●, observed (left). Predicted risk of hospital mortality, observed hospital mortality and the corresponding number of patients are shown. In the upper panel, *x*-axis represents patients divided into 10 groups according to predicted mortality based on Australasia SAPS3 model. In the lower panel, *x*-axis represents predicted rate of mortality by approximate decile of patients. In both curves, significant differences between curves representing predicted and observed mortalities are observed ($P < 0.001$). *Columns*: number of patients; *line with open circles*: mean predicted mortality; *line with closed circles*: mean observed mortality.

DISCUSSION

This study demonstrates that the general and regional AUS-SAPS3 had good discrimination but poor calibration in a region-specific cohort from an Asian country. Calibration was improved after customization of the SAPS3 equation with data from the development cohort, and this newly derived equation for Korea showed good discrimination and good calibration in a separate validation cohort.

Table 3 Discrimination and calibration of the AUS-SAPS3 and K-SAPS3 in the validation cohort

Prediction model	Predicted mortality	GOF *H*-test	*P*	GOF *C*-test	*P*	SMR	95% CI	aROC
AUS-SAPS3	20.3 (7.9–42.6)	72.71	<0.001	68.06	<0.001	0.77	0.70–0.84	0.835
K-SAPS3	12.9 (4.6–32.2)	4.61	0.799	5.67	0.684	0.99	0.90–1.08	0.835

aROC, area under the receiver operating characteristics curve; AUS-SAPS, Australasia simplified acute physiology score; CI, confidence intervals; GOF, goodness of fit; K-SAPS3, Korean simplified acute physiology score 3; SMR, standardized mortality ratio.

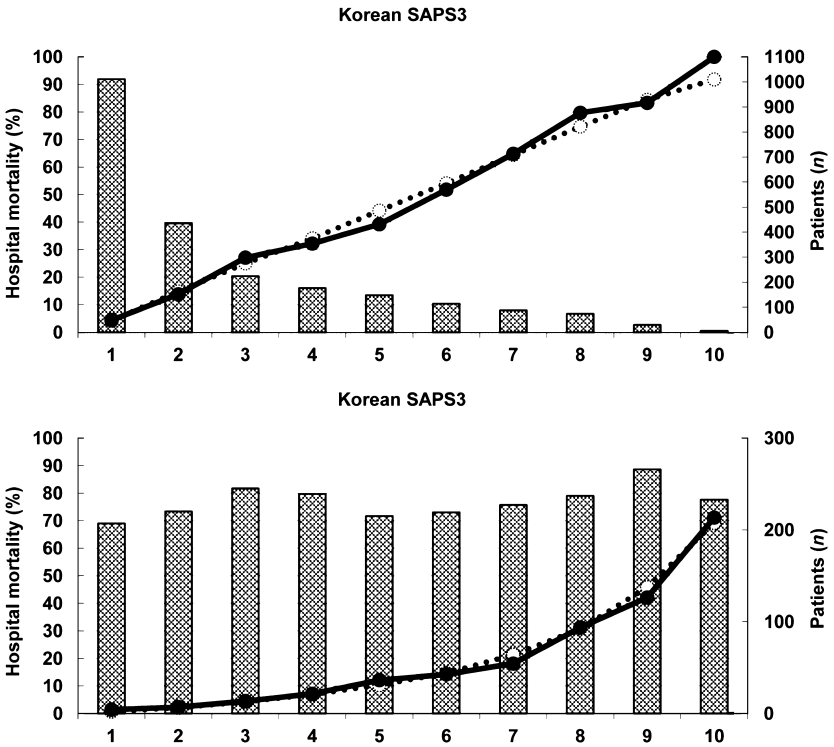

Figure 3 Calibration curves of the Korean simplified acute physiology score 3 (SAPS3) in validation cohort. ▨, patients (right); ••◌••, expected (left); ●—●, observed (left). Predicted risk of hospital mortality, observed hospital mortality and the corresponding number of patients are shown. In the upper panel, *x*-axis represents patients divided into 10 groups according to predicted mortality based on Korean SAPS3 model. In the lower panel, *x*-axis represents predicted rate of mortality by approximate decile of patients. In both curves, curves representing predicted and observed mortalities are almost overlap showing good calibration ($P > 0.05$). *Columns*: number of patients; *line with open circles*: mean predicted mortality; *line with closed circles*: mean observed mortality.

To our knowledge, this current study is the first study that aimed to validate the general SAPS3 and the AUS-SAPS3 equations by using a multicentre design in critically ill Asian patients. The only other prospective validation study of SAPS3 in Asian population was a smaller single-centre study performed in Thailand.[5] In that study, both general SAPS3 and AUS-SAPS3 had excellent discrimination but poor calibration in the medical ICU. After customization of the SAPS3, the calibration of SAPS3 was improved. There are important differences between this current study and the Thai study. This study was multicentre (15 vs 1), had more patients (4617 vs 1873) and included more diverse patients (both medical and surgical vs just medical). In the current study, the general and AUS-SAPS3 demonstrated good discrimination but poor calibration. Although the regional equations of SAPS3 were developed for use in specific geographical area, the AUS-SAPS3 did not perform well in this cohort of Korean patients. This is not surprising when we consider how AUS-SAPS3 equation was developed. The AUS-SAPS3 equation was derived from data collected from 1756 patients from Australia ($n = 651$), India ($n = 532$) and Hong Kong ($n = 573$).[4,14] There are likely to be vast differences in the characteristics of patients from these three areas stemming from significant variability in the genetic make-up, cultural and social structures, the availability of resources, and the delivery of critical care, as reflected in the wide range of reported SMR in the original SAPS3 study (0.7–1.4).[4,14] There is no clear advantage to grouping the data from these three countries simply because they are roughly within the same geographical area. It is interesting that Hong Kong, which is the most geographically and genetically similar to Korea, had an SMR of 0.7, which is similar to the value found in this study.[4,14] We believe that country-specific customization of the general or regional SAPS3 equation is needed to obtain accurate prediction.

Both the general SAPS3 and AUS-SAPS3 equations showed poor calibration, overestimating mortality rates (low SMR) across all strata. A low SMR has also been reported in other developed countries, such as Belgium,[8] Italy,[10] and Thailand.[5] Although variations in case-mix, genetic predispositions[15,16] and cultural differences[17] may explain some of this differences, another reason may be the change in practice of critical care since the completion of the SAPS3 project.

Effective treatment strategies, such as low tidal volume ventilation in acute respiratory distress syndrome[18] and early goal-directed therapy in severe sepsis and septic shock[19] which were just beginning to become popular in 2002 when SAPS3 was developed, have become standard of care. These and other interventions that have been implemented since 2002 surely would improve the outcome of patients, thus decreasing the SMR.

There are statistically significant differences in many of the baseline characteristics between development and validation cohort. Since we used a robust method in randomly allocating patients into two groups, these differences are not due to bias but due to randomness of the selection process. However, these differences do not compromise the validation process because, if anything, the differences in the two groups would have adversely affected calibration.

One limitation of this study is that first-level customization was used to customize SAPS3 to Korean population.[20] Although some suggest that customizing individual coefficients is more effective than customizing the logit of the original equation, first-level customization is a simple and practical method to improve the calibration of severity scores. Another is that all the participating centres were large university-affiliated tertiary hospitals. Thus, our model may not be accurate in patients admitted to smaller hospitals with different models of delivery of critical care.

In conclusion, general and regional AUS-SAPS3 admission scores showed poor calibration in Korean ICU patients, but the prognostic power of the SAPS3 model was significantly improved after country-specific customization. Prediction models should be customized before routine application to more accurately predict mortality rates in different regions of the world.

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