Detecting Potentially Ineffective Care in Critically Ill Patients in a Community Hospital: Assessing Sustained Predictive Value after Two Decades

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Research

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Abstract

Background: Eighteen years ago, we derived a formula to predict 100-day post-discharge mortality, utilizing the Acute Physiology and Chronic Health Evaluation III (APACHE III) data. This study was designed to reassess this formula when applied to a new cohort of patients, utilizing the updated predictive hospital mortality equations derived from APACHE IV.

Methods: Compared with the 1995–1997 cohort in our original study, this study included a cohort of intensive care unit patients from 2012–2017, with similar demographics. Both cohorts included patients >18 years old admitted to and surviving at least five days of intensive care in the Sarasota Memorial Hospital in Sarasota, Florida, USA.

Results: In the recent cohort, the formula exhibited a specificity of 99.7%, sensitivity of 17.8%, false positive rate of 0.3%, and positive predictive value of 92.6%; applied to the original cohort, the formula exhibited values of 98.7%, 33.8%, 1.3%, and 93.3%, respectively. There was no statistical difference between the two databases, except in sensitivity.

Conclusions: Potentially ineffective care can be predicted with nearly the same specificity and predictive value using the formula developed in the 2002 study. If these results are reproducible at other institutions, they could assist in patient/family and palliative care discussions.

Background

Acute Physiology and Chronic Health Evaluation (APACHE) is a prognostic evaluation system developed in 1981 for assessment of disease severity in intensive care units (ICUs) [1]. Currently, this system is in its fourth iteration. A higher APACHE score indicates higher disease severity. In 1995, Esserman et al. utilized data from APACHE III to derive a formula to predict mortality and avoid potentially ineffective care (PIC). In this study, Esserman et al. developed the concept of PIC to refer to a combination of high resource utilization (top 25% of total hospital charges) and limited inpatient survivability within 100 days post-hospital discharge [2]. The main purpose of this concept was to generate a model to identify patients with poor prognoses (specifically, mortality) despite intensive treatment and high resource utilization.

In 2002, Fleegler et al., utilizing a community hospital database from 1995–1997, used a retrospectively derived formula implementing longitudinal and individual-specific APACHE III hospital mortality risk prediction (APHM) to predict 100-day post-discharge mortality [3]. The retrospectively derived model was validated during the second half of the two-year period. Fleegler et al. established a threshold of mortality between ICU day 5 and 100 days post-discharge as intermediate survival (based on Esserman et al.'s study). However, in contrast with Esserman et al., Fleegler et al. did not integrate resource utilization into the model, as this had the potential to interfere with its utilization in prognostic clinical discussions with family or health care surrogates.

Afessa et al. [4] observed that if an Acute Physiology Score (APS) on the third day of the patient's admission into the ICU (APS3) was greater than that on their first day in the ICU (APS1), and the APACHE III-predicted mortality was ≥ 80% on day 1, the patient would expire within 100 days post-discharge. Their study was limited to patients treated in the ICU for three days or more, who had an APACHE-predicted mortality of ≥ 80%. To the best of our knowledge, no other study has evaluated 100-day mortality using APACHE. More recently, some have suggested it is time for a re-evaluation of PIC and have proposed PIC as an outcome measure to evaluate quality of critical care delivery [5].

The fourth iteration of APACHE (APACHE IV), published in 2006, allows improved accuracy and inclusion of patients with a history of coronary artery reconstruction [6, 7]. APACHE IV exhibits excellent discrimination (area under receiver operating characteristic curve = 0.88) and hospital mortality prediction (13.51%) statistically identical to that observed in the validation data set (13.55%; p = 0.76). The difference between the observed and mean predicted hospital mortality across risk deciles is 0.1—0.4%, except for the 70—80% decile (1.1%) and the 90—100% decile (1.6%). For most subgroups, the ratio of observed to mean predicted hospital mortality is near 1.0, and 90% of the standardized mortality ratios (SMR) within disease groups are not significantly different from 1.0. APACHE and APACHE IV have been considered a useful tool for decision-making and to benchmark performance across ICUs in the United States [3, 7].

To the best of our knowledge, no studies have examined PIC prediction over 20 years utilizing the same predictive equation. This study was designed to examine reproducibility of the PIC model using APACHE IV, applying the same formula we derived in 2002, with a new cohort at the same medical institution almost two decades later [6].

Methods

This retrospective observational cohort study tested the hypothesis that the performance—sensitivity, specificity, false positive rate, and positive predicted value (PPV)—of a PIC model developed using a cohort of patients obtained from July 1995—June 1997 (using APACHE III) would be statistically equivalent when using APACHE IV-based APHM in a cohort of patients from July 2012—June 2017 [3].

A patient consent waiver was obtained from the Institutional Review Board as part of a continuing review amendment to include a validity replication cohort.
The sample included patients > 18 years old admitted to and surviving at least five days of intensive care in medical-surgical (32 beds) and cardiac-surgical (20 beds) units at the 832-bed publicly owned acute care Sarasota Memorial Hospital, Sarasota, FL (the same institution as in our 2002 study).

Data collection

Data collected included age; APS1 and APS5, as well as APHMs; ICU and hospital discharge status; and vital status for the 100 days post-discharge. Inpatient data were obtained from the APACHE IV Outcomes Database (Cerner Corporation Kansas City, MO). If patients had more than one ICU stay during their

admission, data from the first hospital stay was used for this study. Our 2002 study utilized the last ICU admission on a given hospitalization since it was closest to the 100-day endpoint [3]. However, unlike APACHE III, APACHE IV did not include an adjustment co-efficient for readmissions. Therefore, only the initial ICU admission was recorded and utilized for the current data set.

To establish vital status between ICU day 5 and 100 days post-discharge, multiple methods were employed.

Patients were followed up from hospital admission until discharge to ascertain mortality between ICU day 5 and hospital discharge.
Mortality between discharge and 100 days post-discharge was established in one of two ways. Demographic data, including medical record numbers, were used to identify subsequent hospital admissions after incident ICU admission. This permitted tracking outcomes for patients treated subsequently or who died within the institution. Patient mortality was confirmed using an Obituaries Database (http://www.legacy.com) or the National Death Index, a centralized database of death record information filed with the National Center for Health Statistics. Patients were excluded from analysis if vital status could not be established within 100 days post-hospital discharge.

Replication of PIC model

We applied the previously derived formula to evaluate the PIC model's performance using APACHE IV-based APHM [3]. Mortality within 100-days post-hospital discharge was predicted if the patient had either an APHM5 ≥ 0.92 or if the product of APHM1×APHM5 was ≥ 0.40 and there was an increase in APHM ≥ 0.10 between day 1 and day 5 after ICU admission.

Analytic strategy

The predictive performance of the PIC model was quantified according to several parameters, including sensitivity, specificity, false positive rate, and PPV. For the current dataset, data were pooled from 2012 to 2017 due to the small number of ICU patients that met the PIC criteria in a given year. The PIC model's performance was compared using the same formula, albeit adapted to APACHE III (1995–1997) and APACHE IV (2012–2017) hospital mortality predictions. Similarly, SMR tendencies were compared between APACHE III and APACHE IV. SMRs were computed as the actual mortality divided by estimated mortality, utilizing APACHE III and APACHE IV. Continuous variables, summarized as means (standard deviation), were compared through an analysis of variance. Categorical variables, summarized as counts/proportions (interquartile range), were compared using a chi-square test. Statistical analyses were performed using SAS 9.4 software (Cary, NC). A two-tailed $p < 0.05$ was considered significant.

Results

The updated cohort comprised 13,585 patients admitted to the ICU between July 1, 2012 and June 30, 2017. A total of 2,590 patients met the threshold requirement of a 5-day ICU stay for ICU day 1 and day 5 predictive criteria. Eighteen patients who were in the ICU for 5 days did not have a social security number

and were excluded from the analysis. Patients who met both the PIC criteria were only counted once. Due to the small number of patients who met the PIC criteria in the updated cohort, a five-year sample was chosen to enable sufficient evaluation.

Demographics for the 1995–1997 cohort, as shown in Table 1, are shown separately in the original publication [3]. There was no statistically significant difference between both cohorts regarding APS, APHM, or SMR.

Table 1
Demographics, APACHE scores, and SMR for the initial and replication PIC study populations.

	1995–1996 APACHE III	1996–1997 APACHE III	2012–2017 APACHE IV
Patients (n)	4,045	4,086	13,588
Age (mean, SD)	69.6	69.5	66.7 (± 16.7)
25th percentile	64	64	57
75th percentile	78	78	79
APACHE score (mean, SD)	52.2	53.2	56.4 (± 28.6)
25th percentile	35	36	37
75th percentile	61	64	69
APACHE-predicted hospital mortality % (mean, SD)	11.1	12.2	11.6 (±18.9)
25th percentile	2	3	1
75th percentile	12	13	12
SMR	0.91	0.87	0.88
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; SMR, standardized mortality ratio; PIC, potentially ineffective care			

Table 2 shows the 100-day survival figures for both cohorts. Of the 94 patients predicted to die in the 2012–2017 cohort, only 3 survived; of 2,496 patients predicted to survive, 942 did not. In the 1995–1997 cohort, of those predicted to die, 9 survived; of 898 patients predicted to survive, 242 did not. The number of patients who met the threshold criteria in the 1995–1997 and 2012–2017 cohorts was 1,031 and 2,590, respectively.

Table 2
Outcome predictions of the application of the PIC formula to APACHE III APACHE IV cohorts.

	Outcome		
	Died within 100 days post-discharge	**Survived 100 days post-discharge**	**Total**
1995–1997 (APACHE III) patients predicted to die within 100 days post-discharge	124	9	133
1995–1997 (APACHE III) patients predicted to survive within 100 days post-discharge	242	656	898
Total	366	665	1,031
2012–2017 (APACHE IV) patients predicted to die within 100 days post-discharge	91	3	94
2012–2017 (APACHE IV) patients predicted to survive 100 days post-discharge	942	1,554	2,496
Total	1,033	1,557	2,590
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation			

Table 3 shows the results of the statistical analysis of the formula for predicting PIC, indicating the specificity, sensitivity, false positive rate, and PPV for both cohorts. The only difference that was statistically significant was the sensitivity parameter: 33.8% for the 1995–1997 cohort and 17.8% for the 2012–2017 cohort.

Table 3
Statistical analyses of the application of the PIC formula to APACHE III and APACHE IV cohorts.

	1995–1997	1995–1997	2012–2017	2012–2017
	Point Estimate	95% Confidence Interval	Point Estimate	95% Confidence Interval
Specificity	98.7	97.9–99.6	99.7[a]	93.3–99.9
Sensitivity	33.8	29.0–38.6	17.8[b]	14.5–21.4
False positive rate	1.3	0.5–2.2	0.3[c]	0.1–0.7
Positive predictive value	93.3	89.1–97.5	92.6[d]	85.5–97.0
[a] p = .62 vs. 1995–1997				
[b] p < .0001 vs. 1995–1997				
[c] p = .62 vs. 1995–1997				
[d] p = .97 vs. 1995–1997.				
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation				

Discussion

Only three studies have previously predicted mortality 100-day post-discharge utilizing APACHE III [2, 4, 5]. To the best of our knowledge, this is the first study to evaluate the predictive value of PIC using the same formula after almost two decades utilizing updated APACHE predictions. It is noteworthy that the PPV of this PIC model utilizing APACHE III (93.3%) was sustained when applied to a more recent cohort utilizing APACHE IV (92.6%). These mortality predictions were in a replication population with a similar SMR (0.88) compared to the earlier cohort (0.91) [3].

For decisions regarding mortality prediction, a high specificity is required for use in family discussions regarding possible prognoses and outcomes. The high sensitivity of the predictive equation was maintained in the current study, in spite of the considerable time gap. Given the high specificity required for potential decision-making, a low sensitivity is expected. There was a significantly lower sensitivity in the updated database (from which we obtained the 2012–2017 cohort) compared to the original database (wherein we obtained the 1995–1997 cohort). The low sensitivity partially explains the smaller number of patients identified in any one-year period.

Since the PIC model was developed [3], many clinical features potentially influencing mortality risk and end-of-life management have undergone change, including (a) continued modifications in ICU design and process, with a focus on shared decision-making; (b) the progressive aging of the general population; (c)

the changing of the cultural milieu regarding the process of dying (7); and physicians' estimate of intensive care benefits [8–10].

In 2006, APACHE III was updated to APACHE IV. This update improved its accuracy and included patients with a history of coronary artery reconstruction [6, 7]. APACHE IV exhibited excellent discrimination and hospital mortality prediction that was statistically identical to that observed for the validation data set (13.55%). Although it is expected that the updated prediction equation would maintain sensitivity, it is possible that the difference in sensitivity between the original and updated PIC prediction equation is related to the use of APACHE IV. The sensitivity in the current cohort is consistent with an earlier study [4] that used APACHE III APS3 to predict PIC, which demonstrated a sensitivity of 0.15, similar to that in our study (0.11). The lack of a formal palliative care service 18 years ago might explain the reduced sensitivity in the current data set. Nevertheless, we have demonstrated that by utilizing both APACHE IV APM1 and APM5 data, 100-day mortality can be predicted with a high PPV over a prolonged period at a single institution utilizing the same formulas, which had been derived from APACHE III on a cohort two decades earlier.

Widely employed prognostic models for assessing overall severity of illness in critically ill adults include APACHE, the Simplified Acute Physiology Score (SAPS), and the Mortality Probability Model (MPMoIII). In a study with over 2,500 patients in three ICUs, Keegen et al. observed that APACHE III [0.868 (0.854–0.880)] and IV [0.861 (0.847–0.874)] exhibited statistically equivalent discrimination (area under the receiver operating characteristic curve with 95% confidence interval), which was significantly greater than that of the third iteration of SAPS [0.801 (0.785–0.816)], which itself was better than that of the MPMoIII [0.721 (0.704–0.738)] [11].

While our analysis represents mortality over a 100-day period, six-month morbidity and mortality have been analyzed for ICU patients receiving life-sustaining therapy. Factors that were associated with not returning to baseline included a higher APACHE III score and being non-white, elderly, recently hospitalized, with a history of transplantation, cancer, or neurologic or liver disease [12]. Some authors have also researched the frequency and cost of treatment perceived to be futile, but the point at which treatment is deemed futile has varied [13]. We utilized a 100-day mortality point, which could provide families with a concrete reference point.

Empirically based models estimating PIC in critically ill patients remain scarce. Furthermore, there has been a trend to embrace palliative care services. Clinical trends encouraging collaborative ICU provider-patient/surrogate decisions [14–16] motivated the present study to compare the reproducibility of our PIC model nearly 20 years after its original development. If these results can be duplicated at other institutions, they could have broad implications. Proactive identification of candidates for palliative care may be warranted when organ dysfunction does not respond to treatment and intensive care goals cannot be realized, or when life support becomes disproportional to the expected prognosis.

Integrating palliative with intensive care allows preferences of patients and families to be transparent, while also fostering dignity [15]. This integration of palliative care with ICU treatment also reduces the

length and costs of hospital stay [10]. Patients who receive palliative care consultations are more likely to have a code status change, be transferred to hospice, and be treated with comfort measures [17, 18]. Multiple studies have encouraged collaborative ICU provider-patient/surrogate decisions [13–16]. Since the PPV has statistical precision representing the “prospective” discriminant utility of PIC modeling, it could be used to complement the contextual, continuous, and evolving process of clinical decision-making [17]. This model may not have been pursued in the past due to the emphasis on autonomy. However, newer clinical approaches to the concept of autonomy suggest data from this model could be utilized in collaborative discussions [19, 20].

Limitations

In this study, our PIC model had a significantly lower sensitivity, compared with the original study. The current study also had the limitation of being a single institution study.

Conclusion

In this study, we reassessed a formula to predict 100-day mortality using APACHE IV in a community hospital in Sarasota, FL. Originally, we used this formula on a 1995–1997 cohort using APACHE III in the same hospital. Our findings showed that the formula has sustained predictive value, 18 years after we developed it. To the best of our knowledge, this is the first study to evaluate the predictive value for PIC using the same formula at an interval of almost two decades. If replicated in other institutions, these predictive equations could contribute to ICU management shared decision-making models of care.

Abbreviations

Acute Physiology and Chronic Health Evaluation (APACHE); intensive care units (ICUs); potentially ineffective care (PIC); APACHE hospital mortality (APHM); Acute Physiology Score (APS); standardized mortality ratios (SMR); positive predictive value (PPV); Simplified Acute Physiology Score (SAPS); Mortality Probability Model (MPMoIII)

Declarations

Ethics approval and consent to participate

A patient consent waiver was obtained from the Institutional Review Board as part of a continuing review amendment to include a validity replication cohort. The sample included patients > 18 years old admitted to and surviving at least five days of intensive care in medical-surgical (32 beds) and cardiac-surgical (20 beds) units at the 832-bed publicly owned acute care Sarasota Memorial Hospital, Sarasota, FL (the same institution as in our 2002 study).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

BF analyzed the data and contributed to the writing. CG extracted and summarized the data. CB contributed to the writing. All authors have approved the final manuscript.

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