



ORIGINAL RESEARCH

A Nomogram for Predicting the Risk of Death in Patients with Prolonged Hospital Stays in Internal Medicine Wards: A Retrospective Study

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Objective: Prolonged hospital length of stay (PLOS) is associated with adverse outcomes, including increased healthcare costs, higher risk of complications, and increased mortality. This study aimed to investigate the relationship between PLOS and mortality among patients hospitalized in internal medicine wards and to develop a nomogram to predict the risk of death in this patient population.

Methods: This retrospective study included patients hospitalized for more than 30 days in internal medicine wards between January 1, 2022, and December 31, 2022. Multivariate logistic regression analysis was used to identify independent risk factors for in-hospital mortality. The nomogram was constructed based on the independent factors. Calibration curves and receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of the nomogram, and decision curve analysis (DCA) was conducted to assess its clinical utility.

Results: A total of 1042 patients were included in this study, resulting in a mortality rate of 10.17%. Multivariate logistic regression analysis showed that age (OR=1.043, 95% CI: 1.026–1.061, P<0.001), tumor (OR=2.274, 95% CI: 1.441–3.589, P<0.001), blood transfusion (OR=4.667, 95% CI: 2.932–7.427, P<0.001), ADL score (OR=0.966, 95% CI: 0.952–0.981, P<0.001) and MNA-SF score (OR=0.825, 95% CI: 0.760–0.895, P<0.001) as independent risk factors for mortality among patients hospitalized in internal medicine wards. The nomogram constructed using these factors demonstrated well discriminatory ability, with an AUC of 0.803 (95% CI: 0.761–0.846). Decision curve analysis further validated the clinical utility of the nomogram, highlighting its potential to improve risk assessment and guide clinical decision-making.

Conclusion: This nomogram effectively evaluates the risk of death for prolonged hospitalization of patients in internal medicine wards and holds significant potential for promotion in clinical practice.

Keywords: prolonged hospital length of stay, internal medicine wards, ADL score, MNA-SF score, in-hospital mortality

Introduction

Hospital length of stay (LOS) is a measure used to assess the utilization and turnover rates of hospital beds, reflecting the efficiency of medical resource use, ^{1,2} and is defined as the number of days between admission and discharge.³ In recent years, the rapidly aging global population has contributed to the growing diversity and complexity of internal diseases.⁴ Patients in internal medicine wards with prolonged hospital stays are at risk for complications such as infections, pressure ulcers, thrombosis, and organ failure.⁵ Moreover, extended hospitalization can lead to negative emotions like anxiety and depression, inadvertently increasing both the economic and social burden on patients.⁶

Prolonged hospital length of stay (PLOS) is a critical healthcare issue associated with increased morbidity, healthcare costs, and resource utilization. The prevalence of PLOS varies significantly across countries and healthcare systems,

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influenced by factors such as healthcare policies, resource allocation, and patient demographics.⁷ In Asia, particularly in countries like China and Japan, aging populations and the growing burden of chronic diseases have contributed to a rising trend of PLOS, impacting hospital efficiency and patient outcomes.⁸ Although the incidence of PLOS varies across countries and regions due to differences in research methodologies and healthcare systems, studies have shown that PLOS is generally an important factor affecting the prognosis of hospitalized patients.

In clinical practice, identifying high-risk patients among those with prolonged hospital stays is crucial for guiding targeted interventions and improving clinical outcomes. The Activities of daily living (ADL) scale is a widely used tool for assessing a patient's self-care ability, with lower ADL scores consistently associated with higher risks of adverse outcomes, including mortality. Similarly, the Mini Nutritional Assessment-Short Form (MNA-SF) offers a quick and reliable evaluation of nutritional status, a key prognostic factor, especially in older adults. Existing studies have shown that factors such as marital status, hospital size, sociocultural background, discharge disposition, and illness severity can significantly influence prolonged length of stay. However, few studies have evaluated the risk factors for poor prognosis in PLOS patients in internal medicine wards. This study aimed to analyze the risk factors contributing to mortality in PLOS patients in internal medicine wards and provide scientific evidence for clinical prevention and treatment. By identifying these risk factors, physicians can develop more precise, individualized treatment plans, reduce the likelihood of complications, and ultimately improve treatment outcomes and the quality of life for patients.

Methods

Patients

This retrospective study included patients hospitalized in the internal medicine departments of the Second Affiliated Hospital of Wannan Medical College between January 1, 2022, and December 31, 2022. The number of hospitalizations across different departments and the confirmed diagnoses for each type of disease were recorded separately. Additionally, the patients' general and clinical data were analyzed and compared. The study was approved by the Institutional Review Board of the Second Affiliated Hospital of Wannan Medical College (IRB No. wyefyls202205) and conducted in accordance with the principles outlined in the Declaration of Helsinki. Due to the study's retrospective design and the use of anonymized patient data, the Institutional Review Board waived the requirement for informed consent. All patient data were de-identified to ensure confidentiality and used exclusively for research purposes.

The inclusion criteria for the study were as follows: (1) hospitalization duration of \geq 30 days; (2) age \geq 18 years; (3) diagnosis of internal medicine diseases with hospitalization in internal medicine departments. Exclusion criteria included: (1) hospitalization duration of \leq 30 days; (2) diagnosis of surgical diseases; (3) incomplete clinical data; (4) loss of follow-up information. The research flowchart was shown in Figure 1.

Clinical Data Collection

The baseline clinical characteristics were collected within 24 hours of admission from the health information system (HIS). Baseline clinical characteristics were collected within 24 hours of admission using the Health Information System (HIS). These characteristics included: (1) demographic data, such as age, gender, and length of stay; (2) underlying diseases or comorbidities, including hypertension, coronary heart disease, diabetes, chronic obstructive pulmonary disease, cerebrovascular accident, and history of neoplasm; (3) medical payment method, categorized as public medical insurance for urban residents, basic medical insurance for urban employees, or other types; (4) mode of admission, classified as emergency or outpatient admission; (5) details of diagnosis and treatment during hospitalization, such as nosocomial infections, use of transfusions and blood products, invasive procedures, and intensive care treatments; and (6) relevant rating scale scores, including ADL, MNA-SF, and Padua scores. The primary endpoint of the study was in-hospital mortality.

Definition

PLOS was defined as any hospitalization with a length of stay exceeding 30 days, ¹⁶ which was a widely recognized indicator for evaluating resource utilization and cost-efficiency in healthcare. ¹⁷ Activities of daily living, comprising

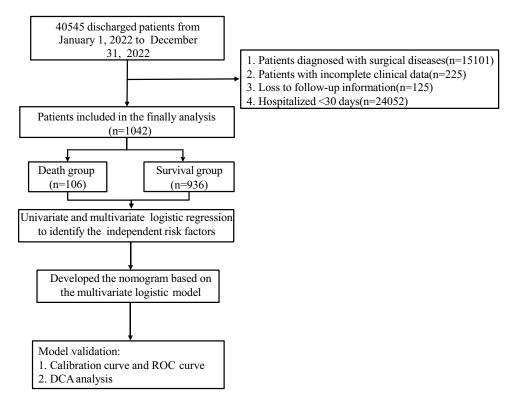


Figure 1 The flowchart of study.

Abbreviations: ROC, Receiver operating characteristic; DCA, Decision curve analysis.

basic actions such as personal care, mobility, and eating, were used to assess an individual's ability to care for themselves. Our study utilized the Katz ADL scale as the primary outcome measure to evaluate ADL function. He Katz ADL scale included six items: (1) bathing, (2) dressing, (3) transferring, (4) using the toilet, (5) continence, and (6) feeding. Higher ADL scores indicated a greater level of independence, while lower scores were associated with a poorer quality of life. The Mini Nutritional Assessment-Short Form comprised six questions that take approximately three minutes to complete. It was designed to quickly identify individuals at risk of malnutrition, ensuring that they received appropriate and targeted interventions. The MNA-SF had a total score of 14, with a score of 10 or less indicating potential undernutrition and a score of 11 or higher suggesting normal nutritional status. The Padua score was a validated tool for clinicians to identify patients at high risk for venous thromboembolism (VTE). This scale ranges from 0 to 20 points, with higher scores indicating a greater risk of VTE, necessitating drug therapy as preventive treatment.

Sample Size

In this study, the events per variable (EPV) method was used to determine the sample size, ensuring adequate statistical power for predictive model development.²³ Based on the guideline of at least 10–15 events per variable in multivariate logistic regression and considering that 5–6 predictive factors were expected to be included in the model, a minimum of 50–90 mortality events was required to maintain model stability.

Statistical Methods

Continuous variables were tested for normality using the Kolmogorov–Smirnov. Continuous variables with a normal distribution were expressed as the mean± standard deviation, while those without a normal distribution were presented as the interquartile range. Categorical variables were reported as frequencies and percentages (%). Univariate analysis was conducted to identify potential risk factors associated with mortality in patients hospitalized for more than 30 days in internal medicine departments. To identify independent risk factors for mortality in patients hospitalized in internal

medicine for more than 30 days, variables with P < 0.05 in the univariate analysis were included in a multivariate logistic regression model. A predictive nomogram was then developed based on the identified independent risk factors using the "rms" package in R software. The receiver operating characteristic (ROC) curve was generated, and the area under the ROC curve (AUC) was calculated to assess the nomogram's discrimination ability. The decision curve analysis (DCA) was performed to estimate the clinical value of the nomogram by illustrating its net benefit. The nomogram was internally validated using a 1,000-resample bootstrap method to assess its stability and predictive accuracy. The calibration curve was plotted to evaluate the agreement between the predicted and actual outcomes. Finally, Kaplan-Meier (K-M) survival analysis was employed to explore the differences in survival outcomes across the independent risk factors. The statistical significance for all variables was set at P < 0.05 (two-sided tests), and the regression coefficients were reported with 95% confidence intervals (CI). The statistical analysis was performed by using R software (version 3.6.2).

Results

Department Distribution and Average Length of Stay of Internal Medicine Patients Hospitalized for More Than 30 days

The rehabilitation medicine department had the highest proportion of patients with prolonged hospitalization (306, 29.40%), with an average LOS of 64.73±28.98 days. This was followed by the tumor radiotherapy department (19.80%) and neurology department (9.50%). Other departments with notable prolonged hospitalizations included respiratory and critical care medicine department (8.60%), cardiovascular medicine department (8.10%), and hematology department (6.60%), among others (Table 1).

Disease Diagnosis Distribution of Internal Medicine Patients Hospitalized for More Than 30 days

The most common conditions among patients hospitalized for more than 30 days were factors affecting health status and contact with health institutions (23.44%), followed by circulatory system diseases (19.40%) and tumors (15.37%). Respiratory (14.70%) and nervous system diseases (14.12%) were also prevalent. Other less frequent conditions included digestive system diseases (2.79%), injuries and poisoning (1.92%), and urogenital diseases (1.54%), unspecified symptoms (1.34%), and endocrine/metabolic diseases (1.25%) (Table 2).

Table I Department Distribution and Average LOS of Internal Medicine Patients Over 30 days

Department	Cases	Percent (%)	Cumulative Proportion (%)	Average Length of Stay (d)
Rehabilitation medicine department	306	29.40	29.40	64.73±28.98
Tumor radiotherapy department	206	19.80	49.20	46.67±15.89
Neurology department	99	9.50	58.70	60.02±28.81
Respiratory and critical care medicine department	90	8.60	67.30	56.08±28.41
Cardiovascular medicine department	84	8.10	75.40	58.33±33.17
Hematology department	69	6.60	82.00	48.06±23.06
Emergency department	68	6.50	88.50	59.31±25.09
Geriatric medicine department	57	5.50	94.00	43.40±8.58
Intensive care unit	33	3.20	97.20	78.18±37.93
Gastroenterology department	30	2.80	100.00	45.23±12.51
Total	1042	100	_	56.69±27.06

Abbreviation: LOS, Length of stay.

Table 2 Disease Diagnosis Distribution of Internal Medicine Patients Hospitalized for More Than 30 days (Top 10)

ICD Number	Disease		Percent (%)	No.
Z00-Z99	Factors affecting their health status and contact with health institutions	244	23.44	I
100-199	Circulatory diseases	202	19.40	2
C00-D48	Tumors	160	15.37	3
J00-J99	Respiratory diseases	153	14.70	4
G00-G99	Diseases of the nervous system	147	14.12	5
K00-K93	Diseases of digestive system	29	2.79	6
S00-T98	Diseases caused by injury, poisoning and other external causes	20	1.92	7
N00-N99	Diseases of the urogenital system	16	1.54	8
R00-R99	Symptoms, signs and clinical and laboratory abnormalities which not classified elsewhere	14	1.34	9
E00-E90	Endocrine, nutritional and metabolic diseases	13	1.25	10

Baseline Characteristics of Patients in the Survival and Non-Survival Groups

Descriptive analysis revealed significant differences between the two groups in terms of age (P<0.001), intensive care unit treatment (P=0.001), type of admission (P<0.001), nosocomial infection (P<0.001), transfusion of blood (P<0.001), tumor (P<0.001), ADL score (P<0.001), MNA-SF score (P<0.001) and Padua score (P=0.001) (Table 3).

Table 3 Comparison of General and Clinical Data Between the Survivors and Non-Survivors Groups

Clinical Features	Non-Survivors (n=106)	Survivors (n=936)	Test Statistic	P-value
Basic data				
Age (years), †	78.25±9.83	69.48±15.95	8.057	<0.001
Male (n, %), ‡	74(69.80)	579(61.90)	2.574	0.109
LOS (d), †	58.92±27.21	56.44±27.04	0.897	0.370
Intensive care unit treatment (n, %), ‡	12(11.30)	36(3.80)	12.106	0.001
Type of admission (n, %), ‡			31.075	<0.001
Outpatient admission	86(81.10)	833(89.00)		
Emergency admission	20(18.90)	103(11.00)		
Nosocomial infection (n, %), ‡			13.286	<0.001
Yes	79(74.50)	525(56.10)		
No	27(25.50)	411(43.90)		
Payment method (n, %), ‡			3.063	0.216
Public medical insurance for urban residents	29(27.40)	305(32.60)		
Basic medical insurance for urban employees	64(60.40)	482(51.50)		
Others	13(12.30)	149(15.90)		
Blood transfusion (n, %), ‡			55.546	<0.001
Yes	44(41.50)	125(13.40)		
No	62(58.50)	811(86.60)		
Invasive operation (n, %), ‡	25(23.60)	169(18.10)	1.921	0.166
Complication (n, %), ‡				
Tumor	43(40.60)	215(23.00)	15.825	<0.001
Hypertension	50(47.20)	450(48.10)	0.031	0.859
Diabetes	61(57.50)	460(49.10)	2.689	0.101
Coronary heart disease	37(34.90)	404(43.20)	2.659	0.103
Chronic obstructive pulmonary disease	39(36.80)	366(39.10)	0.214	0.644
Cerebrovascular accident	47(44.30)	342(36.50)	2.477	0.116
ADL score, §	35(30,50)	45(35,60)	-4.437	<0.001
MNA-SF score, §	6(5,8)	8(5,10)	-4.707	<0.001
Padua score, §	4(3,5)	3(3,4)	-3.246	0.001

Notes: §, Mann–Whitney *U*-test; †, Independent-samples *t*-Test; ‡, Pearson's χ^2 test.

Abbreviations: LOS, Length of stay; ADL, Activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form.

Table 4 The Independent Risk Factors for Death in Patients Hospitalized for More Than 30 days

Variables	Partial Regression Coefficient	Partial Regression Coefficient Standard Error	Wald χ²	P-value	OR (Odds Ratio)	95% CI	VIF
Age	0.042	0.008	24.878	<0.001	1.043	1.026-1.061	1.005
Tumor	0.822	0.233	12.463	<0.001	2.274	1.441-3.589	1.008
Blood transfusion	1.540	0.237	42.222	<0.001	4.667	2.932-7.427	1.009
ADL score	-0.034	0.008	19.247	<0.001	0.966	0.952-0.981	1.004
MNA-SF score	-0.193	0.042	21.358	<0.001	0.825	0.760-0.895	1.002

Notes: Hosmer-Lemeshow test: χ2=5.599, *P*=0.692; (Forward-wald).

Abbreviations: ADL, Activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form; VIF, Variance inflation factor.

Identification of Independent Risk Factors for in-Hospital Mortality

All potential risk factors (P<0.05) in the univariate regression analysis were included in the multifactor regression model. Multivariate logistic regression analysis showed that age (OR=1.043, 95% CI: 1.026–1.061, P<0.001), tumor (OR=2.274, 95% CI: 1.441–3.589, P<0.001), blood transfusion (OR=4.667, 95% CI: 2.932–7.427, P<0.001), ADL score (OR=0.966, 95% CI: 0.952–0.981, P<0.001) and MNA-SF score (OR=0.825, 95% CI: 0.760–0.895, P<0.001) were the independent factors for the mortality of patients in inpatient general internal medicine wards hospitalized for more than 30 days (Table 4).

The Predictive Nomogram Development

A nomogram was developed to predict the risk of death in patients hospitalized for more than 30 days, based on the results from the multivariate logistic regression model (Figure 2). The model included five variables: age, tumor, blood transfusion, ADL score, and MNA-SF score. By using the scale in the nomogram, the score for each risk factor can be determined. After summing the individual scores, a total score was obtained. The corresponding probability interval for the total score was then located on the risk probability scale, representing the probability of death for internal medicine patients hospitalized for more than 30 days. A higher total score indicated a greater risk of death.

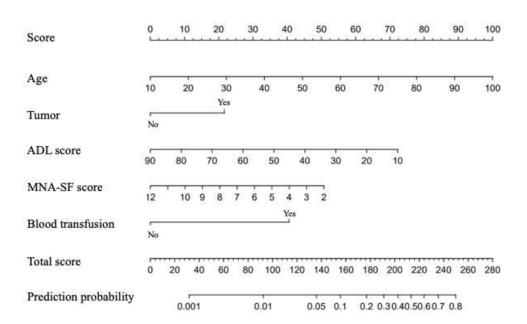


Figure 2 The nomogram for predicting mortality in patients hospitalized for more than 30 days. Abbreviations: ADL, Activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form.

Validation Of nomogram with ROC Curve

The AUC of the ROC curve was analyzed to assess the discrimination ability of the nomogram, which was found to be 0.803 (95% CI: 0.761–0.846) (Figure 3), indicating that the novel nomogram exhibited high predictive efficiency.

Evaluate the Accuracy and Clinical Practicability of Nomogram

The calibration curve was used to assess the goodness-of-fit of the nomogram using the Hosmer-Lemeshow test, demonstrating a good agreement between the predicted outcomes and the actual results (Figure 4A). A decision curve analysis was performed based on the nomogram model to evaluate its clinical effectiveness. The results confirmed that the nomogram has significant clinical value in identifying in-hospital mortality patients (Figure 4B).

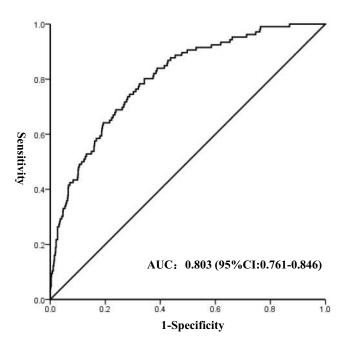


Figure 3 The receiver operating characteristic (ROC) curve of the nomogram. **Abbreviation**: AUC, Area under the ROC curve.

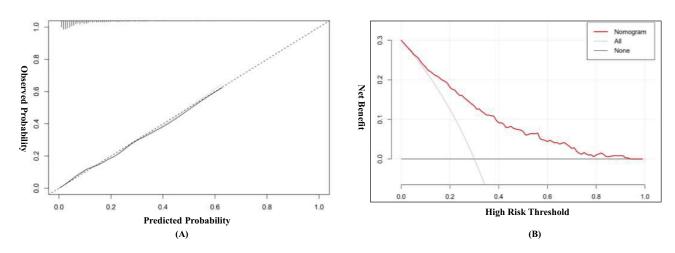


Figure 4 The calibration curve and decision curve analysis curve of nomogram. (A) Calibration curve. (B) Decision curve analysis.

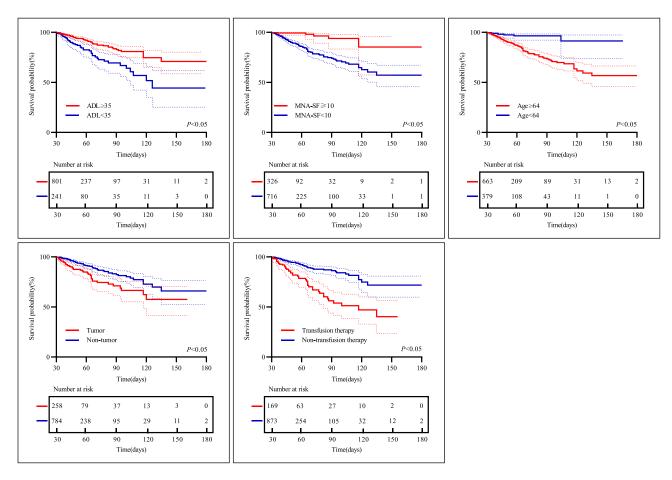


Figure 5 The Kaplan-Meier Curve of the independent risk factors.

The Kaplan-Meier Curve of the Independent Risk Factors

The Kaplan-Meier survival analysis demonstrated that patients hospitalized for more than 30 days exhibited significant differences in survival probabilities based on key risk factors. Older age, the presence of tumors, an ADL score<35, an MNA-SF score<10, and a history of blood transfusion were associated with a higher risk of in-hospital mortality (Figure 5). The survival curves for these subgroups indicated a greater probability of fatal outcomes as hospitalization length increased. Furthermore, a significant difference was observed between the survival and death groups, underscoring the strong predictive value of these risk factors in assessing the likelihood of in-hospital death.

Discussion

Prolonged length of hospital stay is a widely recognized indicator that reflects the utilization of medical resources.²⁴ With the increasing number of patients, hospitals are facing a shortage of medical resources and rising healthcare costs, which have become a significant concern for hospital administrators. Therefore, it is crucial to thoroughly evaluate the risk factors contributing to the mortality of prolonged hospitalization patients and to identify high-risk groups promptly.

Our study identified several traditional risk factors, including age, tumor presence, ADL score, MNA-SF score, and a history of blood transfusion, as independent contributors to patient mortality in internal medicine wards. Based on these findings, we developed a nomogram model incorporating these five factors to predict the risk of mortality among patients with prolonged hospital stays in internal medicine wards. The predictive accuracy of the nomogram was evaluated using the ROC curve, which yielded an AUC of 0.803 (95% CI: 0.761–0.846), indicating good predictive performance. Additionally, decision curve analysis demonstrated significant clinical utility for the model. By employing this

nomogram, clinicians can more effectively identify high-risk patients and deliver timely, comprehensive medical interventions, ultimately improving patient outcomes.

We found that age was a significant factor contributing to the mortality of patients with prolonged hospital stays. Our multivariate logistic regression analysis confirmed that the risk of death for elderly patients with PLOS increases with age. The underlying reasons for this trend are multifaceted. Younger patients typically have fewer underlying diseases and often present with acute conditions that can be treated effectively with short-term interventions. In contrast, elderly patients frequently suffer from multiple chronic conditions, such as cardiopulmonary diseases, diabetes, and cancer, which necessitate extended treatment durations.²⁵ Moreover, aging was associated with numerous physiological changes, including a decline in immune function, reduced organ reserve, and impaired regenerative capacity. Additionally, the physiological decline associated with aging further reduces their resistance to illness and impairs their recovery capacity. Together, these factors significantly increase the mortality risk for elderly patients with PLOS.

Malnutrition has been associated with cardiometabolic disease, respiratory disease, and a lower quality of life. ^{26–28} A prospective study involving 396 patients with type 2 diabetes demonstrated that malnutrition significantly increased the risk of mortality. ²⁹ Additionally, recent studies have confirmed malnutrition as an independent risk factor for increased mortality in patients with colorectal cancer and those undergoing hemodialysis. ^{27,30} The MNA-SF, a screening tool derived from the full MNA for assessing the nutritional status of the general elderly population, has been shown to possess high specificity, accuracy, and sensitivity. In our study, a lower MNA-SF score was associated with poorer nutritional status and a higher risk of mortality in patients. The mechanisms underlying this association are multifaceted. Malnutrition can impair the body's ability to recover from illness or surgery, leading to longer hospital stays and a higher likelihood of complications. Moreover, malnutrition weakens the body's ability to combat inflammation by increasing oxidative stress, reducing protein synthesis, and accelerating protein degradation. ³¹ It also promotes the development of atherosclerosis, thereby elevating the risk of cardiovascular events. ³²

Activities of daily living encompasses a range of fundamental self-care behaviors, including personal hygiene, eating, and mobility. These behaviors offer valuable insights into the condition of patients upon admission, reflecting their ability to perform essential tasks such as eating, bathing, and walking. Patients with low ADL scores often face significant challenges in carrying out daily activities and are at a higher risk of malnutrition. Research has established a correlation between patients' ADL scores at admission and their prognosis, a finding consistent with our study. We identified the ADL score as an independent predictor of mortality for patients hospitalized in internal medicine wards for over 30 days. A lower ADL score indicated a poorer state of health, often requiring extended treatment durations and elevating the risk of death.

Blood transfusions are frequently employed to treat conditions such as anemia, acute bleeding, and severe malnutrition. However, patients who receive blood transfusions often experience longer lengths of stay compared to those who do not. For instance, a study by Salma involving 271 patients undergoing orthognathic surgery found that blood transfusions were significantly associated with prolonged hospital stays. Similarly, research by Koch et al revealed that greater severity of anemia was linked to longer hospital stays and an increased risk of mortality. There are several reasons for these associations. Firstly, patients requiring blood transfusions are typically in more severe conditions, with poorer prognoses and a higher risk of death. Secondly, blood transfusions can increase circulatory pressure, placing additional strain on the heart and, in severe cases, lead to complications such as acute heart failure. Finally, transfusions can elevate the risk of infections, which may further contribute to mortality.

Our study also found that patients with tumors had significantly longer lengths of stay compared to other hospitalized patients. Cancer patients, particularly those with advanced-stage disease, are at higher risk of in-hospital mortality due to tumor-related complications such as metastasis, organ dysfunction, and immunosuppression. The extended LOS in cancer patients can be attributed to the severity and complexity of their illnesses, as well as the additional diagnostic and treatment procedures often required. Serious conditions and intricate treatment regimens increase the challenges of medical management, further elevating the risk of adverse outcomes, including mortality. With the growing strain on healthcare resources, achieving optimal patient treatment through rational planning and improving the efficiency of hospital resource utilization are critical priorities. Nomograms, as predictive tools, estimate the probability of specific clinical events and assist physicians in making more informed diagnostic and treatment decisions. Their establishment

and application enable clinicians to assess the risk of disease recurrence, personalize treatment plans, and allocate healthcare resources more effectively.

Limitations

However, this study has several limitations. First, the data and clinical information were derived from a single general hospital, making it a single-center retrospective study with a relatively small sample size. This limitation may introduce bias into the results, necessitating validation through large-scale, multicenter, and prospective studies. Second, the range of predictors included in this study was limited, and patients hospitalized in surgical wards were not surveyed. Expanding the scope of predictors and patient populations could improve the comprehensiveness and applicability of the predictive model. Finally, dynamic assessment of ADL and MNA-SF scores during hospitalization may further enhance the predictive performance and clinical relevance of the model. Therefore, dynamic assessment and the inclusion of more risk factors should be considered in future studies.

Conclusion

Age, presence of tumors, ADL score, MNA-SF score, and blood transfusion were identified as significant factors associated with in-hospital mortality among PLOS patients in internal medicine wards. The nomogram developed in this study demonstrated substantial clinical utility and predictive accuracy in assessing the risk of death for these patients.

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Disclosure

All authors have no conflicts of interest to declare in this work.

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