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ORIGINAL RESEARCH

Dementia, Systemic Biomarkers, and Risk of 30-Day Readmission After Pneumonia: A Multi-Center Cohort Study

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Background: Dementia is a significant risk factor for adverse health outcomes, including pneumonia-related hospitalizations and readmissions. While comorbidities have been shown as predictors of poor pneumonia outcomes, the interplay between chronic comorbidities and acute physiological conditions, reflected by systemic biomarkers, remains underexplored. This study investigates the independent and joint effects of dementia and acute biomarkers on 30-day readmission risk following pneumonia hospitalization.

Subjects and Methods: We conducted a multicenter cohort study using data from three hospitals within the Taipei Medical University Clinical Research Database. Patients aged ≥45 years hospitalized for pneumonia between 2014 and 2021 were included. Dementia status was identified via ICD-9/10 codes, and acute systemic biomarkers were measured at the time of emergency department presentation. The primary outcome was 30-day all-cause readmission. Multivariable logistic regression assessed independent associations, while joint-effects models examined the combined impact of dementia with biomarker abnormalities and comorbidities.

Results: Among 11,989 patients, 6.7% experienced 30-day readmission. Dementia was independently associated with readmission (adjusted OR: 1.31, 95% CI: 1.07–1.61). Other significant predictors included abnormal hemoglobin (OR: 1.55), creatinine (OR: 1.42), glucose (OR: 1.32), and comorbidities such as cancer, chronic kidney disease, and diabetes mellitus. Joint-effects models showed that dementia amplified the impact of abnormal biomarkers, eg, patients with low hemoglobin and dementia had an OR of 1.98 compared to those with normal hemoglobin and no dementia.

Conclusion: Dementia and acute biomarker abnormalities independently and synergistically increase 30-day readmission risk after pneumonia hospitalization, underscoring the need for integrated management strategies targeting both cognitive and systemic health.

Keywords: dementia, pneumonia, readmission, acute biomarkers, laboratory abnormalities, comorbidities, risk factors, multicenter cohort study, cognitive impairment, healthcare outcomes

Introduction

Dementia, a progressive neurodegenerative condition, poses an escalating public health challenge, with its global prevalence expected to triple by 2050.[1] This condition significantly burdens healthcare systems due to its associations with comorbidities,[2,3] hospitalizations, and high mortality rates.[1,4] Pneumonia is a common and severe condition among patients with dementia, with approximately 50% of hospitalized dementia patients succumbing to pneumonia.[5] Preventive strategies, such as adult vaccination against influenza and pneumococcus, are important in mitigating

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pneumonia risk in older adults, particularly those with dementia.[6] However, vaccination rates in this population remain suboptimal, and both community-acquired and nosocomial pneumonia frequently occur, as cognitive impairment increases susceptibility across healthcare and community settings.[5,7]

Dementia and pneumonia share a bidirectional and complex relationship. Patients with dementia are predisposed to pneumonia due to dysphagia, immune dysfunction, and impaired mobility, while pneumonia has been shown to accelerate cognitive decline and increase the risk of subsequent dementia diagnoses.[8] Laboratory abnormalities, such as anemia and hyperglycemia, have also been associated with poorer pneumonia outcomes, contributing to higher mortality, prolonged hospital stays, and increased readmission rates.[9,10]

However, the interplay between acute physiological responses and chronic conditions, such as dementia, remains poorly understood, particularly in the context of pneumonia, where acute systemic dysregulation may compound existing vulnerabilities. While prior studies have identified comorbidities as risk factors for adverse pneumonia outcomes,[11,12] acute systemic conditions at the time of infection—reflected by laboratory biomarkers such as glucose, hemoglobin, and creatinine—may provide additional insights into recovery capacity. These biomarkers may signal systemic stress or impaired physiological reserve,[13] which could independently or synergistically exacerbate poor outcomes. This effect may be particularly pronounced in older adults, who often have reduced physiological reserve and a diminished ability to compensate for acute illness.[14] Specifically, the inability to mount an adequate response, such as fever or leukocytosis, may indicate frailty or poor immune function, whereas exaggerated biomarker abnormalities may reflect severe systemic inflammation.[9] Understanding how dementia interacts with these acute physiological responses to shape pneumonia outcomes is critical for identifying high-risk patients and tailoring interventions.

Therefore, we aim to investigate the interplay between dementia and key laboratory biomarkers in relation to post-pneumonia readmission risks, drawing on a large multi-center database of patients with prior pneumonia diagnoses.

Methods

Study Design and Data Source

This current cohort study utilized data from the Taipei Medical University Clinical Research Database (TMUCRD), a comprehensive electronic medical records system encompassing three affiliated teaching hospitals: Taipei Medical University Hospital, Wan Fang Hospital, and Shuang Ho Hospital. These hospitals, located in the Greater Taipei area of Taiwan, serve populations of approximately 206,014, 259,735, and 406,183 residents, respectively. The TMUCRD database includes a wide array of information, including patient demographics, diagnoses, comorbidities, medical visits, laboratory reports, vital signs, treatments, and medications. All identifiable information was encrypted to ensure patient confidentiality. This study was approved by the Joint Institutional Review Board of Taipei Medical University (No.: N202308059).

Study Population

Patients aged 45 years or older who were admitted through the emergency department (ED) between January 1, 2014, and December 31, 2021, with a primary diagnosis of pneumonia were included in this study. Pneumonia diagnoses were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM: 480–486) and Tenth Revision, Clinical Modification (ICD-10-CM: J12-J18). Patients who died during their index hospitalization were excluded, resulting in a final study cohort of 11,989 patients.

Study Variables

Primary Outcome: 30-Day Readmission

The primary outcome was all-cause hospital readmission within 30 days following discharge from the index hospitalization for pneumonia.

Exposure: Dementia

Dementia status was determined using ICD-9-CM (290.x, 294.x, and 331.x) and ICD-10-CM (F01.x, F02.x, F03.x, and G30.x) diagnostic codes recorded during hospital visits prior to or during the index admission.

Covariates

Key covariates included patient demographics (age, sex), comorbidities (eg, diabetes mellitus [DM], chronic kidney disease [CKD], chronic heart failure [CHF], and cancer), and systemic biomarkers (hemoglobin, creatinine, and glucose levels) measured during the index admission. Comorbidities were identified using ICD-9-CM and ICD-10-CM codes, and biomarker abnormalities were categorized based on standardized reference ranges. To approximate pneumonia type (community- vs hospital-acquired), we used a proxy definition based on hospitalization history. Specifically, patients with a prior hospitalization within the preceding 14 days were classified as having probable hospital-acquired pneumonia. This approach is consistent with broader operational definitions used in retrospective studies when microbiological or timing-based data are unavailable.[15,16]

Statistical Analysis

The characteristics of patients readmitted and not readmitted within 30 days post-discharge were summarized using medians and interquartile ranges (IQR) for continuous variables, and counts with percentages for categorical variables. Comparisons between the two groups were performed using the Mann–Whitney test for continuous variables and Pearson's chi-squared test for categorical variables.

Time-to-readmission was evaluated using the Kaplan-Meier method to estimate the probability of remaining readmission-free within the 30-day follow-up period comparing patients with or without dementia. Differences in survival curves were assessed using the Log rank test. Multivariable logistic regression models were employed to evaluate the associations between independent variables and 30-day readmission. The analysis began with a model adjusted only for age and sex to establish the baseline association between dementia and readmission risk. Next, we included a variable for hospitalization history within the prior 14 days as a proxy for frequent hospitalizations, which may confound or predict readmission risk by reflecting a pattern of recent healthcare utilization or underlying instability. We then adjusted for chronic comorbidities, including conditions such as DM and CKD, to account for their impact on pneumonia outcomes. Finally, we incorporated laboratory biomarkers obtained at the time of the patient's presentation to the ED, such as hemoglobin, creatinine, and glucose levels. These biomarkers provide additional information beyond chronic comorbidities, as they reflect acute physiological stress, such as systemic inflammation.[9] Additionally, they may serve as indicators of an individual's response capacity, or physiological reserve,[17,18] which is particularly relevant in older adults facing acute illness. By including these markers, we aimed to assess their independent contributions to 30-day readmission risk beyond traditional comorbidities and evaluate their interaction with dementia in influencing outcomes. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported to quantify the strength of these associations.

To explore the combined effects of dementia and systemic biomarkers on 30-day readmission risk, joint-effects logistic regression models were constructed. Patients were categorized into three groups for each biomarker or comorbidity (eg, Normal glucose, No dementia; Abnormal glucose, No dementia; Abnormal glucose, Dementia).

Sensitivity analyses were performed to assess the robustness of our findings. These included addressing missing biomarker data using a missing indicator method, excluding extreme biomarker values to account for the influence of outliers, and incorporating interaction terms between dementia and key covariates to evaluate potential effect modification.

To evaluate potential collinearity between comorbidities and biomarker abnormalities, we calculated variance inflation factors (VIFs) for all variables in the multivariable logistic regression models, with VIF <5 indicating minimal multicollinearity. Additionally, to assess the strength of association between each comorbidity and its corresponding biomarker, we conducted Pearson's chi-squared tests and calculated Cramér's V statistics.

Exploratory Prediction Modeling

To evaluate the potential utility of our clinical and laboratory variables in predicting 30-day readmission, we developed three exploratory scoring models based on our fully adjusted logistic regression results. The first model used the natural logarithm of the adjusted odds ratios (ln[OR]) to assign weighted scores to each predictor. The second model applied a proportional point-based system, in which each variable's score was scaled relative to its OR. The third model was a standard logistic regression prediction model using the β coefficients to calculate the predicted probability of readmission for each individual. For all three models, we calculated the area under the receiver operating characteristic (ROC) curve (AUC) to assess their discriminative performance.

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA). A two-tailed P-value <0.05 was considered statistically significant for inferential analyses.

Results

Sample Characteristics

Table 1 presents the baseline characteristics of the study population, stratified by 30-day readmission status. Among the 12,989 patients included, 805 (6.2%) experienced 30-day readmission. Patients in the readmission group were older (median age: 84 years, IQR: 16, vs 78 years, IQR: 21, P < 0.001). The prevalence of dementia was significantly higher in the readmission group (19.3% vs 11.6%, P < 0.001), as were rates of comorbidities such as diabetes mellitus (DM, 29.3% vs 20.2%, P < 0.001), chronic kidney disease (CKD, 18.8% vs 11.7%, P < 0.001), chronic heart failure (CHF, 18.4% vs 12.6%, P < 0.001), and cancer (19.8% vs 9.6%, P < 0.001). Patients with readmission also had higher rates of abnormal

Table 1 Baseline Characteristics of the Study Population

Variables	No Readmission (n = 11184)	Readmission (n = 805)	*P*-value
Male sex, n (%)	6661 (59.56)	521 (64.72)	0.004
Age (years), median (IQR)	78 (21)	84 (16)	<0.001
Community pneumonia, n (%)	10,895 (97.42)	754 (93.66)	<0.001
Nosocomial pneumonia, n (%)	289 (2.58)	51 (6.34)	<0.001
Dementia, n (%)	1297 (11.60)	155 (19.25)	<0.001
DM, n (%)	2263 (20.23)	236 (29.32)	<0.001
CHF, n (%)	1412 (12.63)	148 (18.39)	<0.001
CKD, n (%)	1307 (11.69)	151 (18.76)	<0.001
Cancer, n (%)	1068 (9.55)	159 (19.75)	<0.001
Abnormal random glucose levels, n (%)	5387 (52.95)	439 (58.93)	0.002
Missing	1011 (9.04)	60 (7.45)	
Abnormal creatinine levels, n (%)	4181 (39.00)	377 (48.09)	<0.001
Missing	463 (4.14)	21 (2.61)	
Abnormal hemoglobin levels, n (%)	7082 (65.74)	621 (79.41)	<0.001
Missing	411 (3.67)	23 (2.86)	
Admission within preceding 14-day, n (%)	289 (2.58)	51 (6.34)	<0.001
Markers of Illness Severity During Index Hospitalization			
Transferred to ICU, n (%)	1380 (12.34)	112 (13.91)	0.191
Use of ventilator, n (%)	613 (5.48)	45 (5.59)	0.896
Use of BiPap, n (%)	482 (4.31)	41 (5.09)	0.293
Use of central venous catheters, n (%)	275 (2.46)	26 (3.23)	0.177
Transfusion, n (%)	194 (1.73)	16 (1.99)	0.597

Notes: Age was analyzed using Mann–Whitney test, while Pearson's chi-squared test was applied to examine associations between categorical variables.

Abbreviations: CHF, Chronic heart failure; CKD, Chronic kidney disease; DM, diabetes mellitus; BiPap, bilevel positive airway pressure; ICU, intensive care unit; IQR, interquartile range.

laboratory results, including random glucose (58.9% vs 53.0%, P = 0.002), creatinine (48.1% vs 39.0%, P < 0.001), and hemoglobin levels (79.4% vs 65.7%, P < 0.001). Based on the proxy classification using recent hospitalization history, 340 patients (2.8%) met criteria for probable hospital-acquired pneumonia, while 11,649 (97.2%) were considered to have community-onset pneumonia.

Time-to-Readmission by Dementia Status

Figure 1 depicts the Kaplan-Meier survival curve for time-to-readmission, stratified by dementia status. Dementia patients exhibited a significantly higher cumulative incidence of 30-day readmission compared to non-dementia patients (P < 0.001 by Log rank test).

Multivariable Analysis

Table 2 summarizes the results of multivariable logistic regression models evaluating the associations between dementia, comorbidities, laboratory biomarkers, and 30-day readmission. In the unadjusted model (Model 1), the OR for dementia was 1.82 (95% CI: 1.51–2.19, P < 0.001). After adjusting for age, sex, prior hospitalization, comorbidities, and laboratory biomarkers (Model 5), the OR for dementia was 1.31 (95% CI: 1.07–1.61, P = 0.009). Other significant predictors in the final model included age (OR: 1.02 per year, 95% CI: 1.02–1.03, P < 0.001), prior hospitalization (OR: 1.91, 95% CI: 1.38–2.63, P < 0.001), abnormal hemoglobin (OR: 1.55, 95% CI: 1.28–1.88, P < 0.001), and cancer (OR: 2.11, 95% CI: 1.72–2.57, P < 0.001). Using stepwise regression, dementia, age, abnormal hemoglobin, prior hospitalization, DM, CKD, and cancer were identified as significant predictors of 30-day readmission. Results remained similar in sensitivity analyses, including those accounting for missing biomarker data and excluding extreme biomarker values. Additionally, interaction terms between dementia and key covariates, including comorbidities and biomarkers, were tested but did not reach statistical significance.

Supplementary Table 1 shows the distribution of chronic disease diagnoses and their corresponding acute biomarker levels. Among patients with abnormal glucose levels upon ED presentation, 47.2% did not have a diagnosis of diabetes. Of those with abnormal creatinine levels, 33.5% did not have a diagnosis of CKD. Pearson's chi-squared tests and Cramér's V statistics revealed weak associations between comorbidities and their respective biomarkers. The association between diabetes and abnormal glucose yielded a Cramér's V of 0.24, cancer and low hemoglobin was 0.10, and CKD and abnormal creatinine was 0.34. All VIF values in the multivariable model were below 5, indicating no significant multicollinearity.

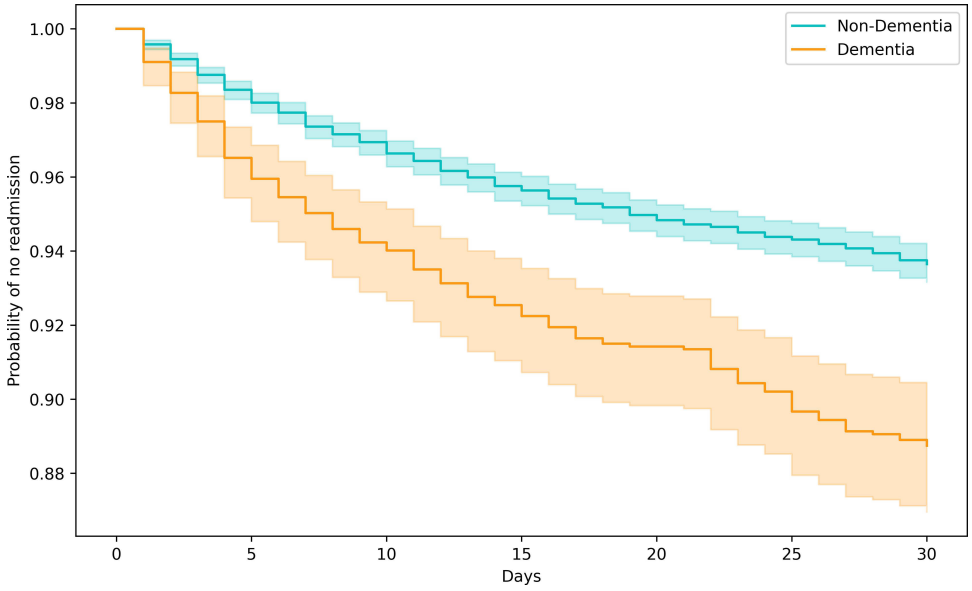

Figure 1 Kaplan-Meier Curve for Time-to-Readmission by Dementia Status.

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Table 2 Multivariable Analysis of Dementia and Post-Pneumonia Readmission Risks

	Model 1		Model 2		Model 3		Model 4		Model 5	
Variables	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Dementia	1.82 (1.51, 2.19)	<0.001	1.49 (1.23, 1.80)	<0.001	1.44 (1.19, 1.74)	<0.001	1.41 (1.16, 1.71)	0.001	1.31 (1.07, 1.61)	0.009
Male sex			1.30 (1.12, 1.51)	0.001	1.28 (1.10, 1.49)	0.001	1.24 (1.07, 1.44)	0.005	1.11 (0.94, 1.30)	0.209
Age (years)			1.03 (1.02, 1.03)	<0.001	1.03 (1.02, 1.03)	<0.001	1.03 (1.02, 1.03)	<0.001	1.02 (1.02, 1.03)	<0.001
Admission within preceding 14-day					2.15 (1.57, 2.93)	<0.001	1.92 (1.40, 2.63)	<0.001	1.91 (1.38, 2.63)	<0.001
DM							1.37 (1.15, 1.62)	<0.001	1.23 (1.02, 1.48)	0.027
CHF							1.17 (0.96, 1.43)	0.119	1.15 (0.94, 1.42)	0.182
CKD							1.45 (1.19, 1.76)	<0.001	1.30 (1.05, 1.61)	0.018
Cancer							2.30 (1.90, 2.77)	<0.001	2.11 (1.72, 2.57)	<0.001
Abnormal random glucose levels									1.17 (1.00, 1.37)	0.046
Abnormal creatinine levels									1.11 (0.95, 1.31)	0.200
Abnormal hemoglobin levels									1.55 (1.28, 1.88)	<0.001

Abbreviations: CHF, Chronic heart failure; CKD, Chronic kidney disease; DM, diabetes mellitus; OR, odds ratio; CI, confidence interval.

Table 3 Joint Effects of Dementia with Laboratory Biomarkers and Comorbidities on Post-Pneumonia Readmission Risks

Combined Variables	OR (95% CI)	*P*-value
Normal glucose, No dementia	Ref	
Abnormal glucose, No dementia	1.16 (0.97, 1.38)	0.104
Abnormal glucose, Dementia	1.40 (1.06, 1.84)	0.017
Normal Cr, No dementia	Ref	
Abnormal Cr, No dementia	1.10 (0.92, 1.31)	0.316
Abnormal Cr, Dementia	1.47 (1.09, 1.97)	0.011
Normal Hb, No dementia	Ref	
Low Hb, No dementia	1.53 (1.24, 1.89)	<0.001
Low Hb, Dementia	1.98 (1.50, 2.63)	<0.001
No DM, No dementia	Ref	
DM, No dementia	1.32 (1.07, 1.61)	0.008
DM, Dementia	1.37 (0.97, 1.94)	0.077
No CKD, No dementia	Ref	
CKD, No dementia	1.18 (0.92, 1.51)	0.186
CKD, Dementia	1.79 (1.22, 2.62)	0.003
No cancer, No dementia	Ref	
Cancer, No dementia	2.14 (1.72, 2.66)	<0.001
Cancer, Dementia	2.34 (1.43, 3.82)	0.001

Abbreviations: Cr, creatinine; Hb, hemoglobin; DM, diabetes mellitus; CKD, Chronic kidney disease; OR, odds ratio; CI, confidence interval.

Joint Effects of Dementia with Biomarkers and Comorbidities

Table 3 and Figure 2 present the joint effects of dementia with biomarkers and comorbidities on readmission risk. The combination of dementia with abnormal biomarkers was associated with a significantly higher risk of readmission compared to either factor alone. For example, the OR for dementia with low hemoglobin was 1.98 (95% CI: 1.50–2.63, P < 0.001), while the OR for dementia with abnormal creatinine was 1.55 (95% CI: 1.22–1.98, P < 0.001).

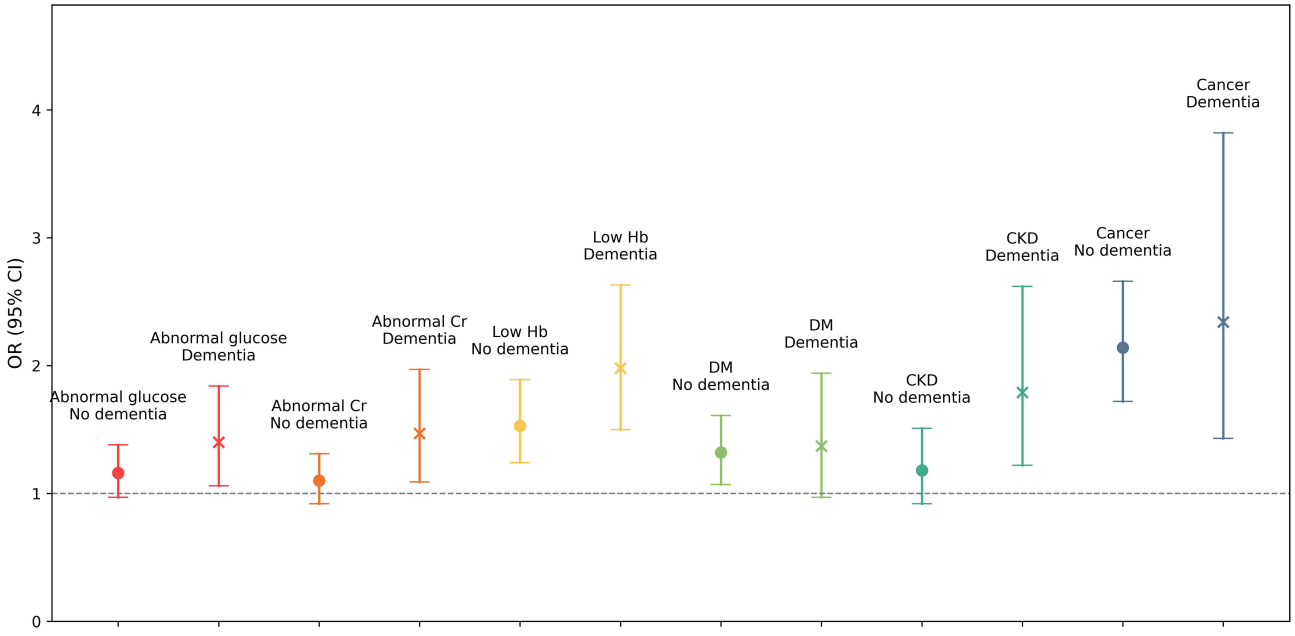

Figure 2 Forest Plot of Joint Effects of Dementia and Biomarkers/Comorbidities on Readmission Risks.
Abbreviations: Cr, creatinine; Hb, hemoglobin; DM, diabetes mellitus; CKD, Chronic kidney disease; OR, odds ratio; CI, confidence interval.

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Similarly, dementia patients with chronic conditions also had an elevated risk of readmission. The OR for dementia with chronic kidney disease was 1.69 (95% CI: 1.31–2.19, P < 0.001), and the OR for dementia with diabetes mellitus was 1.45 (95% CI: 1.14–1.84, P = 0.003).

Exploratory Prediction Modeling

Using the three exploratory models, we assessed the ability of dementia, comorbidities, and acute laboratory biomarkers to predict 30-day readmission. All three models—ln(OR)-weighted, proportional point-based, and logistic regression probability—demonstrated modest discrimination, with AUCs of approximately 0.664. A summary of the models and AUCs is presented in Supplementary Table 2.

Discussion

In this cohort of patients with a prior diagnosis of pneumonia, dementia was independently associated with higher odds of 30-day readmission after adjusting for systemic biomarkers and comorbidities. In addition, our findings indicated that acute laboratory abnormalities at the time of pneumonia diagnosis were independent predictors of readmission. Furthermore, we found that patients with both dementia and abnormal biomarkers had a higher risk of readmission compared to those with either factor alone. Notably, the Kaplan-Meier analysis revealed that patients with dementia experienced significantly earlier readmissions compared to those without dementia. These results underscore the critical interplay between cognitive impairment and systemic health in predicting pneumonia outcomes, emphasizing the need for targeted interventions in this high-risk population.

Our results align with previous studies highlighting the adverse impact of dementia on pneumonia outcomes. For example, Jo et al reported higher rates of adverse discharge outcomes, including mortality and prolonged stays, in dementia patients hospitalized for pneumonia.[11] Additionally, Janbek et al demonstrated that dementia is associated with a significantly higher risk of infection-related hospitalizations, particularly for respiratory infections such as pneumonia.[19] While previous studies have largely focused on chronic conditions as risk factors for poor pneumonia outcomes,[20,21] our findings expand this understanding by emphasizing the prognostic value of acute biomarkers measured at the time of ED presentation. Although chronic comorbidities such as diabetes, CKD, or cancer are often associated with long-standing abnormalities in glucose, creatinine, or hemoglobin levels, respectively, our findings highlight that these biomarkers frequently show discordance with comorbidity status. For instance, over 47% of patients with abnormal glucose did not have diagnosed diabetes, and over one-third of patients without CKD had abnormal creatinine levels at initial evaluation. Consistent with this, our statistical analyses showed only weak to moderate associations between biomarker abnormalities and their corresponding chronic diagnoses, reinforcing the idea that these acute markers may capture real-time physiological stress or decompensation beyond baseline chronic disease. Abnormal glucose in a patient without diabetes, for example, may reflect stress hyperglycemia, undiagnosed metabolic dysfunction, or systemic inflammation.[22] Additionally, elevated creatinine in a patient without known CKD could indicate acute kidney injury rather than stable chronic disease.[23] Such deviations may be especially clinically meaningful, signaling a decline in physiological reserve or the onset of complications in patients previously considered stable The association between abnormal biomarker levels and increased readmission risk suggests that patients with greater metabolic or hemodynamic disturbances during pneumonia hospitalization may be more vulnerable to complications and prolonged recovery. This vulnerability may be particularly relevant in dementia patients, who already face higher baseline health instability, functional limitations, and difficulty managing medical conditions post-discharge.[24] Moreover, pneumonia has been recognized as one of the leading causes of mortality in dementia patients, accounting for nearly 50% of in-hospital deaths in this population.[5] This underscores the urgent need for improved risk stratification and post-hospitalization care strategies to mitigate the impact of pneumonia in this high-risk group.

The observed joint effects of dementia and systemic biomarkers highlight the compounding impact of cognitive, physiological, and functional vulnerabilities on pneumonia outcomes. For instance, patients with both dementia and anemia faced nearly twice the risk of readmission compared to those with anemia alone, indicating that dementia exacerbates the detrimental effects of systemic abnormalities. A similar trend was observed for renal dysfunction (elevated creatinine) and metabolic dysregulation (abnormal glucose), suggesting that dementia amplifies the burden

of these conditions. This may be due to impaired physiological reserve, increased frailty, and difficulties in post-discharge disease management,[25] all of which can heighten the likelihood of hospital readmission.

While the joint effects analysis demonstrated an additive risk between dementia and systemic abnormalities, our interaction analyses did not show significant effect modification. This suggests that the impact of dementia on readmission risk is relatively consistent across different patient subgroups. Clinically, this underscores the importance of considering dementia as a universal risk factor for readmission, regardless of underlying health conditions. Our findings highlight the importance of addressing both physiological and cognitive factors in pneumonia management. Tailored interventions, such as correcting anemia, managing comorbidities like renal dysfunction, and implementing robust discharge planning that accounts for cognitive challenges—including cognitive-adapted interventions, addressing dysphagia, providing enhanced caregiver support, and ensuring regular follow-up and cognitive assessments[26]—could help reduce readmission risks and improve outcomes in this high-risk population.

We also conducted an exploratory analysis to evaluate the predictive utility of our findings. Although the primary aim of our study was not to develop a predictive tool, our model offers insight into important predictors of readmission following pneumonia. The AUCs observed in our models were consistent with those reported in previous studies, including a systematic review by Reynolds et al, which found that most 30-day pneumonia readmission models had C-statistics ranging between 0.63 and 0.69.[27] Many of these earlier models relied primarily on administrative or demographic data and lacked detailed clinical indicators. Our study contributes to addressing this gap by incorporating acute biomarkers measured at the time of ED presentation, which may more sensitively reflect real-time physiological stress than chronic comorbidity data alone. While the predictive performance remained modest, these findings reinforce that readmission risk is likely multifactorial. Future models may benefit from integrating acute clinical indicators with broader contextual data, such as post-discharge functional status, access to care, medication adherence, and social or caregiver support, and from being developed within a more balanced dataset.

This study benefits from a large, multi-center cohort with detailed data on systemic biomarkers, such as hemoglobin, creatinine, and glucose, as well as on comorbidities and diseases identified through ICD-9 and ICD-10 codes, enabling robust multivariable and joint effects analyses. However, several limitations should be noted. First, the observational design precludes causal inferences about the relationships between dementia, biomarkers, and readmission. Second, the cohort consisted of patients with a prior diagnosis of pneumonia, which may limit generalizability to first-time pneumonia cases. Third, residual confounding by unmeasured variables, such as nutritional and functional status, cannot be excluded. Future research should explore these factors and consider longitudinal designs to validate these findings. Lastly, while our findings highlight key predictors of readmission following pneumonia hospitalization, several external factors that may influence readmission outcomes were not captured in this study. For example, pneumonia vaccination status—which can reduce disease severity and potentially lower readmission risk—was not available in our dataset. Additionally, although we used recent hospitalization history to approximate nosocomial versus community-acquired pneumonia, a more precise classification based on microbiologic and clinical timing criteria would be valuable, as these subtypes may differ in pathogen profile, treatment response, prognosis, and risk of readmission.

In conclusion, this study highlights the significant interplay between dementia and systemic biomarkers in their association with 30-day readmission among patients with prior pneumonia diagnoses. Dementia not only independently increases the risk of readmission but also amplifies the adverse effects of systemic vulnerabilities, such as anemia, renal dysfunction, and glucose dysregulation. In addition, our results suggests that dementia's impact on readmission is relatively consistent across different patient subgroups. These findings underscore the importance of addressing both cognitive and physiological factors in pneumonia management to mitigate the heightened risks faced by this vulnerable population. In parallel, preventive strategies such as pneumonia vaccination may also play an important role in reducing disease severity and complications in at-risk populations. Future research could explore how combining preventive measures—such as vaccination—with tailored interventions targeting both cognitive and systemic vulnerabilities may help improve patient outcomes.

Data Sharing Statement

The data has not been previously presented orally or by poster at scientific meetings. The data used or generated in this study are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

The study received approval from the Joint Institutional Review Board of Taipei Medical University (No.: N202308059), with a waiver of informed consent due to a de-identified database. This study was conducted in accordance with the principles of the Declaration of Helsinki.

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Author Contributions

Specifically, TSY acts as the guarantor of the study, accepting full responsibility for the work and/or the conduct of the study, having access to the data, and controlling the decision to publish. TSY and CL designed the study and analysis, interpreted the data, wrote the manuscript, and revised and edited the manuscript. HCC, JT, and EFO contributed to the interpretation of the data, and revised and edited the manuscript. CCW performed the statistical analyses. TSY and EFO supervised the project. The final version of the manuscript was read and approved by all contributing authors. All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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