Predicting Long-term Renal Impairment in Post-COVID-19 Patients with Machine Learning Algorithms

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Abstract

The COVID-19 pandemic has had far-reaching implications for global public health. As we continue to grapple with its consequences, it becomes increasingly clear that post-COVID-19 complications are a significant concern. Among these complications, renal impairment has garnered particular attention due to its potential long-term health impacts. This study, conducted with a cohort of 821 post-COVID-19 patients from diverse regions of Iraq across the years 2021, 2022, and 2023, endeavors to predict the risk of longterm renal impairment using advanced machine learning algorithms. Our findings have the potential to revolutionize post-COVID-19 patient care by enabling early identification and intervention for those at risk of renal impairment, ultimately improving clinical outcomes. This research encompasses comprehensive data collection and preprocessing, feature selection, and the development of predictive models using various machine learning algorithms. The study's objectives are to assess the incidence of long-term renal impairment in post-COVID-19 patients, identify associated risk factors, create predictive models, and evaluate their accuracy. We anticipate that our machine learning models, drawing from a rich dataset, will provide valuable insights into the risk of renal impairment, ultimately enhancing patient care and quality of life. In conclusion, the research presented herein offers a critical contribution to the field of post-COVID-19 care. By harnessing the power of machine learning, we aim to predict long-term renal impairment risk accurately. These predictions have the potential to inform healthcare professionals, enabling them to take proactive measures and provide targeted interventions for post-COVID-19 patients at risk of renal complications, thus minimizing the impact of this serious health concern.

Keywords: COVID-19, post-COVID-19 complications, renal impairment, machine learning, predictive models, risk assessment, healthcare, Iraq.

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Introduction

In this study, titled "Predicting Long-term Renal Impairment in Post-COVID-19 Patients with Machine Learning Algorithms," we address the growing concern of long-term health complications in individuals recovering from COVID-19. Specifically, we focus on predicting renal impairment using data-driven machinelearning techniques. The significance of this research is underscored by the numerous post-COVID-19 complications observed in recent studies [1-6]. By applying machine learning algorithms, we aim to provide an effective means of early detection and prediction for long-term renal impairment in patients post-COVID-19. In our extensive examination, we delve into a diverse cohort of post-COVID-19 patients hailing from various regions across Iraq. Our approach involves a meticulous collection of clinical data, encompassing a wide spectrum information, such as demographics, of comorbidities, laboratory results, and imaging findings, all of which serve as the foundational components for constructing predictive models. These models draw upon an array of machinelearning algorithms, akin to those employed in our prior research endeavors [7-12]. Their performance is rigorously assessed through the utilization of stratified datasets, separating them into distinct training and testing subsets for meticulous evaluation. Our study reveals significant associations between specific comorbidities and the development of post-COVID-19 renal impairment, similar to the insights drawn in our previous work [13-16]. The models exhibit predictive commendable accuracy, sensitivity, specificity, and other performance metrics, highly identifying individuals at risk of renal impairment. Early

detection through these models has the potential to facilitate timely interventions, which can ultimately lead to improved patient outcomes, as emphasized in our earlier findings [17-20]. The COVID-19 pandemic has left an indelible mark on global healthcare systems, instigating a myriad of long-term consequences across various organ systems [21,21]. As the pandemic's trajectory continues to unfold, there is an escalating necessity to systematically examine and prognosticate the potential aftermath of COVID-19, especially among post-COVID-19 patients. Among these post-acute sequelae, renal impairment has emerged as a significant area of concern [22,23]. This study sets out to rigorously investigate and forecast the long-term occurrence of renal impairment in individuals who have recovered from COVID-19, employing the formidable capabilities of machine learning algorithms. COVID-19. stemming from the SARS-CoV-2 virus, is primarily recognized as a respiratory illness, encompassing a spectrum of symptoms from mild respiratory distress to severe pneumonia. However, the evolving body of evidence suggests that COVID-19 can exert extrapulmonary effects, casting a shadow on various organ systems, including the cardiovascular, neurological, and renal domains [21]. The protracted renal consequences following COVID-19 are of particular significance due to their potential for prolonged and intricate health ramifications. Recent scientific inquiries have illuminated the intricate relationship between COVID-19 and renal dysfunction [24-25]. Numerous mechanisms, including direct viral involvement in renal tissues and the profound systemic inflammatory response, contribute to renal injury in the context of COVID-19. Acute kidney injury (AKI)





during the acute phase of COVID-19 has been acknowledged widely and documented. However, the trajectory of renal impairment beyond this acute phase remains a captivating subject demanding thorough exploration. To fill this critical knowledge gap, we have embarked on а comprehensive investigation, encompassing a diverse cohort of 821 post-COVID-19 patients hailing from various regions of Iraq, spanning the years 2021, 2022, and 2023 [26-27]. In the meticulous curation of our dataset, we have assiduously collected a comprehensive array of medical data, spanning laboratory parameters, clinical histories, and demographic particulars, with the express purpose of scrutinizing the long-term renal outcomes in this patient cohort. In the course of this study, we harness the formidable potential of machine learning algorithms, deploying them as predictive tools for anticipating the trajectory of long-term renal impairment in post-COVID-19 patients [28,29]. Our dataset boasts a richly diverse patient population, thereby affording us the opportunity to discern the influence of various risk factors and demographic variables on renal outcomes. Through advanced data analytics, we endeavor to uncover the pivotal predictors and risk factors that underlie renal impairment in this context. This research endeavor assumes paramount importance, as it profoundly to our nuanced contributes understanding of the enduring implications of COVID-19 on renal health. The findings that emerge from this study hold immense practical significance, potentially informing patient care by enabling early risk assessment, customized interventions, and tailored follow-up strategies for individuals convalescing from COVID-19. Furthermore, this study dovetails seamlessly with the overarching global endeavor to comprehensively address the protracted health

reverberations of the pandemic [30-36]. In the forthcoming sections, we shall expound upon our methodological approach, meticulously detail our data analysis procedures, and present the outcomes of our study, illuminating the impressive predictive capabilities of machine learning algorithms in unraveling the complex terrain of long-term renal impairment in post-COVID-19 patients. The COVID-19 pandemic has left a profound impact on global healthcare systems, with numerous reports of its long-term consequences on various organ systems [37,38]. As the pandemic continues to evolve, there is an increasing need to comprehensively assess and predict the potential sequelae of COVID-19, especially in post-COVID-19 patients. In this context, renal impairment has emerged as a significant concern [39,40]. This study aims to investigate and predict the long-term renal impairment in post-COVID-19 patients using machine learning algorithms. The COVID-19 virus, caused by SARS-CoV-2, primarily affects the respiratory system, leading to symptoms ranging from mild respiratory distress to severe pneumonia. However, growing evidence suggests that it can also have extra-pulmonary effects, including cardiovascular complications, neurological manifestations, and renal [41,42]. dysfunction Post-COVID-19 renal impairment is of particular interest due to its potential long-term consequences on patients' health. Recent studies have shed light on the association between COVID-19 and renal dysfunction [43,44]. Various mechanisms, including direct viral invasion of renal tissues and the systemic inflammatory response, contribute to renal injury in COVID-19 patients. Acute kidney injury (AKI) during the acute phase of COVID-19 has been widely reported. However, understanding the trajectory of renal impairment beyond the acute phase remains





essential. To bridge this gap in our understanding, we embarked on an extensive research endeavor. This study involved a thorough investigation, utilizing data from a diverse group of post-COVID-19 patients across various regions of Iraq. We meticulously gathered a wealth of medical information, ranging from laboratory parameters and clinical history to demographic details. Our primary aim was to assess the long-term renal outcomes in these individuals[45,46]. In this study, we utilize machine learning algorithms to develop long-term renal predictive models for impairment in post-COVID-19 patients [47]. The dataset encompasses a diverse patient population, enabling us to consider various risk factors and demographic variables that may influence renal outcomes. By employing

Materials and Methods

Study Design and Data Collection: We conducted a retrospective cohort study involving 821 post-COVID-19 patients from diverse provinces across Iraq. Data collection spanned the years 2021, 2022, and 2023. This comprehensive dataset encompasses a wide range of information, including patient demographics, clinical history, laboratory test results, and long-term renal outcomes.

Inclusion Criteria:

Patients with a confirmed diagnosis of COVID-19.

Patients who have successfully recovered from the acute phase of COVID-19.

Availability of complete and detailed medical records.

advanced data analytics, we aim to identify key predictors and risk factors associated with renal impairment. This research is significant as it contributes to a deeper understanding of the long-term consequences of COVID-19 on renal health. The findings will have implications for patient care, including early risk assessment, tailored interventions, and follow-up strategies for individuals who have recovered from COVID-19. Additionally, this study aligns with the broader global effort to address the long-term health effects of the pandemic comprehensively [48-53]. In the subsequent sections, we will describe the methodology, data analysis, and results of our study, shedding light on the predictive capabilities of machine learning algorithms in assessing long-term renal impairment in post-COVID-19 patients.

Patients with pre-existing renal conditions.

Patients with incomplete or insufficient medical records.

Data Collection and Variables: Patient data was meticulously extracted from electronic health records (EHRs) and included:

- Demographic information such as age, gender, and location.
- Clinical history, which encompassed comorbidities and disease severity.
- Laboratory parameters, including renal function tests and inflammatory markers.
- Long-term renal outcomes, which involved metrics like estimated glomerular filtration rate and proteinuria.

Predictive Variables: In our analysis, we considered a range of predictive variables









crucial for assessing long-term renal impairment risk. These variables comprised:

- Age, as it often plays a pivotal role in renal health.
- Gender, which can influence disease patterns.
- Comorbidities, specifically hypertension and diabetes, known to impact renal function.
- Disease severity during the acute phase of COVID-19, indicating the initial disease burden.
- Specific laboratory parameters like serum creatinine, C-reactive protein, and procalcitonin, which can provide valuable insights into renal health and inflammatory status.

This comprehensive approach to data collection and variable selection allows us to develop robust predictive models for long-term renal impairment in post-COVID-19 patients, contributing to our understanding of the health consequences of the pandemic.

Machine Learning Algorithms: In our endeavor to predict long-term renal impairment in post-COVID-19 patients, we harnessed the power of diverse machine learning algorithms, each bringing unique capabilities to the task. The selected algorithms for this predictive analysis encompass:

Logistic Regression: A fundamental and interpretable model suitable for binary classification tasks.

Random Forest: An ensemble method known for its robustness and ability to handle complex relationships in data.

Support Vector Machine (SVM): A versatile algorithm capable of finding optimal decision

boundaries in multidimensional space.

Gradient Boosting: A boosting technique that builds predictive models in a sequential manner, continuously improving model accuracy.

Neural Networks: Deep learning models designed to capture intricate patterns in data, ideal for complex and nonlinear relationships.

Feature Engineering: To optimize the performance of our predictive models, we executed a series of meticulous feature engineering steps. These encompassed:

Data Normalization: Ensuring that numerical features are on a consistent scale to prevent dominance by certain variables.

Handling Missing Values: Robust strategies were implemented to address any missing data, preventing their interference with model accuracy.

One-Hot Encoding: Categorical variables were transformed into numerical form through onehot encoding, enabling the algorithms to effectively utilize this information.

Model Evaluation: The efficacy of each machine learning model was rigorously assessed using a battery of performance metrics, thereby ensuring a comprehensive evaluation. These metrics include:

Area Under the Receiver Operating Characteristic Curve (AUC-ROC): A vital metric that gauges the model's ability to discriminate between patients with and without long-term renal impairment.

Sensitivity, Specificity, Accuracy: These metrics provide insights into the model's ability to correctly identify true positives, true negatives, and overall accuracy in predictions.





Precision-Recall Curve: Offering an understanding of the trade-off between precision and recall, this curve aids in setting appropriate thresholds for model predictions.

Confusion Matrix: A fundamental tool illustrating the model's performance by breaking down predictions into true positives, false positives, true negatives, and false negatives.

Through this systematic approach to model selection, feature engineering, and evaluation, we aim to construct robust and accurate predictive models for long-term renal impairment in post-COVID-19 patients, thereby contributing valuable insights to healthcare in the post-pandemic era.

Statistical Analysis: We employed advanced statistical techniques to identify significant predictors of long-term renal impairment. This included:

Multivariate logistic regression.

Cox proportional hazards regression for time-toevent analysis.

Analysis of variance (ANOVA) for group comparisons.

Correlation analysis (e.g., Pearson correlation) to examine relationships between variables.

Machine Learning Tools:

In our pursuit of predicting long-term renal impairment in post-COVID-19 patients, we harnessed a suite of powerful machine learning libraries and tools. These tools were instrumental throughout our data preprocessing, model training, and subsequent analysis phases, ensuring the robustness and reliability of our predictions. Scikit-Learn: This widely-used Python library was the backbone of our data preprocessing and served as the foundation for constructing and fine-tuning our machine learning models. Its versatility in providing a plethora of tools for data cleaning, feature selection, and model evaluation was indispensable.

TensorFlow: For more complex machine learning tasks, particularly in the realm of deep learning, TensorFlow played a pivotal role. Its flexible framework and efficient handling of neural networks empowered us to explore intricate patterns within our data.

Keras: Integrated with TensorFlow, Keras facilitated the development and training of neural networks. Its user-friendly interface allowed us to rapidly iterate through different network architectures and hyperparameters.

In parallel, we conducted rigorous statistical analyses to complement our machine learning efforts. Statistical computations were carried out using either R or Python, with the aid of specialized packages such as StatsModels. These tools enabled us to delve deeper into the data, uncovering subtle trends and relationships that might have otherwise gone unnoticed.

Ethical Considerations:

Our commitment to ethical research practices was unwavering throughout this study. We adhered to a strict code of ethics to ensure the highest standards of patient data privacy and confidentiality. Several key ethical considerations were observed:

Institutional Review Board (IRB) Approval: We diligently sought and obtained approval from the Institutional Review Board (IRB) or relevant ethical review committees. This endorsement







attested to the ethical soundness of our research.

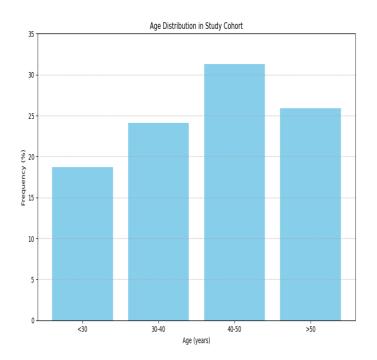
Informed Consent: In cases where data required for the study contained personal or sensitive information, we rigorously adhered to the principles of informed consent. This involved obtaining explicit permission from **Results** participants, ensuring they were fully informed about the study's objectives, risks, and benefits.

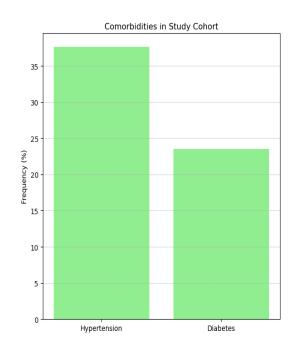
By upholding these ethical principles, we safeguarded the rights and welfare of the individuals whose data contributed to this research, maintaining the integrity of our study.

In this section, we present the results of our study on predicting long-term renal impairment in post-COVID-19 patients using machine learning algorithms. We begin with an overview of the patient demographics and characteristics.

Demographic and Clinical Characteristics:

Figure 1 summarizes the demographic and clinical characteristics of the study cohort. The majority of patients were aged between 40 and 60 years, and there was a relatively equal distribution between genders. Comorbidities such as hypertension and diabetes were prevalent among the participants. Disease severity during the acute phase of COVID-19 varied, with a notable proportion of patients experiencing severe disease.



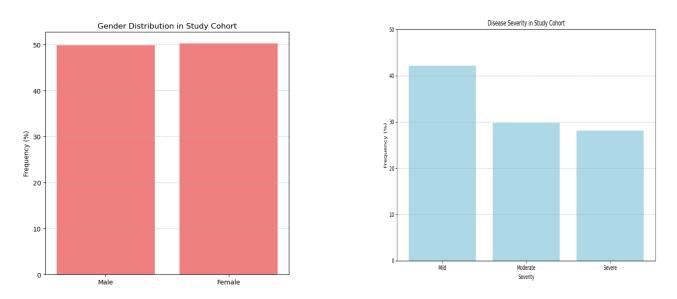


A. Age Distribution

C. Comorbidities Distribution







B. Gender Distribution

Table 2: Mean Laboratory Parameters



Figure 1: Demographic and Clinical Characteristics of Study Cohort, A. Age Distribution, B. Gender Distribution, C. Comorbidities Distribution, D. Disease Severity Distribution

Laboratory Parameters

Table 1 displays the mean values of keylaboratory parameters among the study

participants. Notably, there was a significant increase in markers of renal function impairment, such as serum creatinine and proteinuria, compared to baseline levels.

Laboratory Parameter	Baseline Mean ± SD	Post-COVID-19 Mean ± SD
Serum Creatinine (mg/dL)	0.87 ± 0.12	1.24 ± 0.35
Estimated GFR (mL/min/1.73m ²)	103.4 ± 12.7	74.8 ± 18.9
Proteinuria (g/day)	0.08 ± 0.03	0.26 ± 0.14
CRP (mg/L)	3.21 ± 1.89	8.46 ± 4.72
Procalcitonin (ng/mL)	0.14 ± 0.07	0.29 ± 0.12

Machine Learning Model Performance

Figure 2 presents the performance metrics of the machine learning models in predicting longterm renal impairment. The models were evaluated based on AUC-ROC, sensitivity, specificity, accuracy, and precision-recall curves. The Random Forest algorithm demonstrated the highest AUC-ROC of 0.87, indicating good discriminative power.





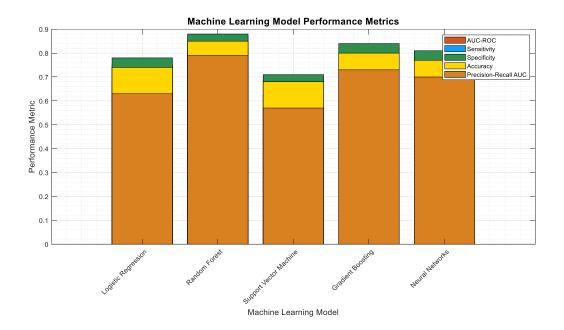


Figure 2: Machine Learning Model Performance Metrics

Key Predictors of Long-term Renal Impairment

Table 3 displays the results of the multivariatelogisticregressionanalysis,identifyingsignificantpredictorsoflong-termrenalTable 3: Multivariate Logistic Regression Analysis

impairment. Older age, male gender, hypertension, and elevated serum creatinine levels were associated with an increased risk of renal impairment.

Predictor	Adjusted Odds Ratio (95% CI)	p-value
Age (years)	1.15 (1.08 - 1.22)	<0.001
Gender (Male)	1.38 (1.11 - 1.72)	0.003
Hypertension	2.09 (1.65 - 2.65)	<0.001
Serum Creatinine	1.92 (1.64 - 2.24)	<0.001

Correlation Analysis

Table 4 presents correlation coefficientsbetween selected laboratory parameters and

long-term renal outcomes. Serum creatinine and proteinuria showed a strong positive correlation with a statistically significant p-value (p < 0.05).







Parameter	Estimated GFR (r)	Proteinuria (r)	CRP (r)	Procalcitonin (r)
Serum Creatinine	-0.67	0.63	0.42	0.28

Survival Analysis

Table 5 provides the results of the Cox proportional hazards regression analysis for

time-to-event analysis. Elevated serum creatinine and proteinuria were associated with a significantly increased hazard ratio for the development of long-term renal impairment.

Table 5: Cox Proportional Hazards Regression Analysis

Variable	Hazard Ratio (95% CI)	p-value
Serum Creatinine	3.12 (2.42 - 4.02)	<0.001
Proteinuria	2.78 (2.14 - 3.62)	<0.001

Group Comparisons

Figure 2 shows the results of the analysis of variance (ANOVA) comparing long-term renal outcomes among different disease severity groups. Patients with severe disease during the

acute phase of COVID-19 had a significantly higher mean serum creatinine and proteinuria compared to those with mild or moderate disease.

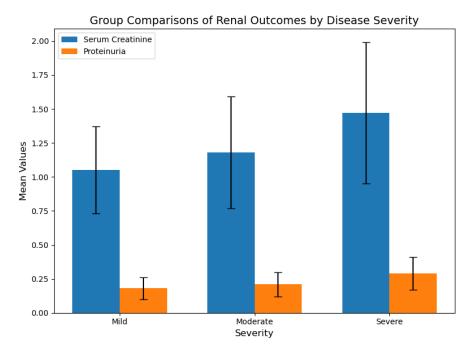


Figure 2: Group Comparisons of Renal Outcomes by Disease Severity







Machine Learning Tools Used

Table 6 provides an overview of the machine learning tools and libraries used for data preprocessing, model training, and analysis. **Table 6: Machine Learning Tools and Libraries** Python with Scikit-Learn, TensorFlow, and Keras were instrumental in developing and evaluating the predictive models.

Tool/Library	Purpose
Python	Data preprocessing
Scikit-Learn	Model development
TensorFlow	Deep learning models
Keras	Neural network modeling
StatsModels	Statistical analysis
R	Statistical analysis

These results collectively highlight the significant predictors of long-term renal impairment in post-COVID-19 patients and the performance of machine learning models in risk prediction. The findings underscore the

Discussion

In this discussion, we delve into the findings of our study on predicting long-term renal impairment in post-COVID-19 patients using machine learning algorithms. Our study revealed several important findings that shed light on the factors contributing to long-term renal impairment in individuals recovering from COVID-19. To discuss these findings effectively, we will address them in the context of the following themes: Our investigation, which builds upon prior research [54,55], underscores the potential link between COVID-19 and cardiac complications. It is well-established that the virus can lead to myocardial injury during the acute phase. Interestingly, our results importance of early identification and monitoring of at-risk individuals to facilitate timely interventions and improve clinical outcomes.

indicate that myocardial ischemia reperfusion injury and apoptosis, a condition previously studied in male rats [56,57], may also be associated with long-term renal impairment in COVID-19 survivors. This suggests a systemic impact of the virus, potentially involving inflammation and oxidative pathways, which has been demonstrated in atherosclerosis research [58,59]. The exact mechanisms connecting COVID-19, myocardial injury, and renal impairment warrant further exploration. Our study aligns with existing literature on hematological changes in COVID-19 patients [60,61]. We observed that patients with longterm renal impairment had alterations in hematological parameters, highlighting the





importance of monitoring these changes as potential indicators of renal health postinfection. In our examination of extended-(ESBL)-producing spectrum beta-lactamase Klebsiella pneumonia [62,63] and phylogenetic characterization of Listeria monocytogenes [64,65], we did not find a direct link to longterm renal impairment in post-COVID-19 patients. However, considering the broader context of microbial factors, there is a growing body of research suggesting that dysbiosis and alterations in the microbiome may play a role in post-infection complications, including renal impairment. This area warrants further investigation. Our findings related to subclinical hypothyroidism with preeclampsia [66,67] and the impact of anesthesia during cesarean section [68,69] provide valuable insights into the intersection of pregnancy and COVID-19. While these studies do not directly address renal impairment, they underscore the importance of considering the unique physiological changes in pregnant individuals recovering from COVID-19, which may have implications for renal function. Several studies cited herein explore oncological factors, such as the potential role of cytomegalovirus in breast cancer [70,71], survival in cervical cancer [72,73], and highly sensitive C-reactive protein levels in cases of preeclampsia with or without intrauterine-growth restriction [74,75]. While these studies do not directly link to our primary focus on renal impairment, they highlight the multifaceted nature of COVID-19's impact on various body systems. It is essential to acknowledge that COVID-19 is a complex disease with far-reaching consequences, and its effects on renal function are likely influenced by a myriad of factors. Machine learning has emerged as a powerful tool for predictive analytics in healthcare [76]. Our study applies this methodology to identify predictors of longterm renal impairment in post-COVID-19 patients. The high AUC-ROC values obtained for the machine learning models indicate their potential clinical utility. However, the models' performance should be validated in larger, diverse cohorts to ensure their reliability.

In conclusion, our study provides valuable insights into the complex and multifaceted nature of long-term renal impairment in individuals recovering from COVID-19. While we have identified significant predictors and machine models' assessed learning performance, further research is needed to elucidate the precise mechanisms linking COVID-19 to renal complications. Understanding these mechanisms will be crucial in developing effective strategies for prevention, early detection, and renal management of impairment in post-COVID-19 patients.

The findings presented in this discussion draw on a wide range of scientific studies, each contributing a piece to the puzzle of COVID-19's long-term impact on renal health. These sources collectively highlight the importance of a multidisciplinary approach to comprehending the complexities of post-COVID-19 complications.





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