

ORIGINAL ARTICLE

Acute colchicine poisoning: prediction of in-hospital mortality at hospital admission using a nomogram. A bicenter retrospective cohort study

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Objective. Acute colchicine poisoning is associated with high mortality. Early identification of high-risk patients is crucial for timely intervention. The prognostic value of plasma colchicine concentration (ColC) has not been previously studied. The objective was to develop a nomogram for predicting in-hospital mortality in acute colchicine poisoning using admission ColC and time elapsed since ingestion.

Methods. We conducted a bicenter retrospective cohort study (2000–2020). Patients with colchicine poisoning from a French toxicology critical care service and an Italian poison control center were included. Validation datasets included data from the registry itself and previously published cases. Logistic regression models were developed using admission ColC (ng/mL), time from ingestion to ColC measurement (h), and in-hospital mortality as the outcome variable.

Results. A nomogram was developed using data from 52 patients (training cohort) and validated in 3 independent testing cohorts (n = 25, 13, and 16, respectively). In this retrospective study, the nomogram demonstrated potential for discriminating patients at greater risk.

Conclusions. An exploratory nomogram for early risk stratification of mortality after colchicine poisoning is presented. Clinical implementation requires prospective multicenter validation with adequate statistical power.

Keywords: Acute poisoning. Colchicine. Mortality.

Intoxicación aguda por colchicina: predicción de la mortalidad al ingreso hospitalario mediante un nomograma en una cohorte retrospectiva bicéntrica

Objetivo. La intoxicación aguda por colchicina se asocia con una elevada mortalidad. La identificación precoz de los pacientes de alto riesgo es crucial para una intervención oportuna. El valor pronóstico de la concentración plasmática de colchicina (ColC) no ha sido estudiado. El objetivo fue desarrollar un nomograma para predecir la mortalidad intrahospitalaria en la intoxicación aguda por colchicina utilizando la ColC al ingreso y el tiempo transcurrido desde la ingesta.

Métodos. Se realizó un estudio de cohorte retrospectivo, en dos centros (2000–2020). Se incluyeron pacientes con intoxicación por colchicina procedentes de un servicio francés de cuidados críticos toxicológicos y de un centro italiano de control de intoxicaciones. Para la validación se incluyeron datos del propio registro y de casos publicados en trabajos previos. Se desarrollaron modelos de regresión logística utilizando como variables la ColC al ingreso (ng/mL), el tiempo desde la ingesta hasta la determinación de la ColC (h) y la mortalidad intrahospitalaria como variable de resultado.

Resultados. Se desarrolló un nomograma a partir de datos de 52 pacientes (conjunto de entrenamiento), que fue validado en tres conjuntos de prueba independientes (n = 25, 13 y 16, respectivamente). En este estudio retrospectivo, el nomograma mostró potencial para discriminar a los pacientes con mayor riesgo.

Conclusiones. Se presenta un nomograma exploratorio para la estratificación precoz del riesgo de muerte tras intoxicación por colchicina. Su implementación clínica requiere una validación prospectiva multicéntrica con una potencia estadística adecuada.

Palabras clave: Intoxicación aguda. Colchicina. Mortalidad.

Introduction

Acute colchicine poisoning is uncommon but is associated with significant mortality.¹ This poisoning may result from drug overdose or ingestion of plants containing colchicine (eg, *Colchicum autumnale* and *Gloriosa*

superba). The clinical course typically progresses through 3 phases: an initial gastrointestinal phase (within the first 24 hours), a systemic cytotoxic phase (1–7 days) characterized by multiorgan failure and myelosuppression, and a recovery phase (7–21 days).^{1,2} Death usually results from cardiovascular collapse, secondary infec-

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tions, or coagulopathy. Current management is mainly supportive. The use of extracorporeal membrane oxygenation (ECMO) remains controversial, although favorable outcomes have been reported in isolated cases.^{3,4} No specific antidote is currently available for this poisoning.^{5,6}

Early prediction of the risk of death in acute colchicine poisoning is essential to guide timely intensive interventions and optimize resource allocation in the emergency department (ED). Although the risk of death has been related to the estimated ingested dose (≥ 0.8 mg/kg is associated with mortality approaching 90%),⁷ deaths have been reported with lower doses (< 0.4 mg/kg),^{8,9} and dose estimation is often unreliable because of vomiting, variability in the amount ingested in plant-related cases, and drug interactions.⁸⁻¹⁰ Prognostic factors such as leukocyte count and prothrombin index have been identified.⁷ Although plasma colchicine concentration (CoLC) is used for monitoring chronic colchicine treatment, its prognostic value in acute poisoning is unknown,¹¹ and some authors have suggested a poor correlation between ingested dose and poisoning severity.¹² Nevertheless, the similarities between colchicine-induced cellular injury and that caused by other toxic agents, such as acetaminophen or paraquat, in which plasma concentration is highly predictive of prognosis and nomograms are widely used, suggest that CoLC could represent a valuable prognostic tool.^{13,14} The absence of a reliable and accessible method for predicting mortality in acute colchicine poisoning represents an important limitation in the emergency management of these patients.

To address this unmet need, a clinical study was designed with the following endpoints: 1) to evaluate the prognostic value of CoLC measured at hospital admission according to the time elapsed since ingestion; and 2) to develop a nomogram to predict the probability of death.

Methods

Study design and setting

We conducted a retrospective, 2-center cohort study including patients with colchicine poisoning treated over a 20-year period (2000-2020) at the Department of Medical and Toxicological Critical Care of Hôpital Lariboisière (Paris, France) and the Clinical Toxicology Center of Istituti Clinici Scientifici Maugeri (Pavia, Italy). Hôpital Lariboisière is located in Paris (France) and specializes in the management of patients with severe poisoning from the city and metropolitan area. The Pavia center is a hospital-based 24/7 service in which clinical toxicologists advise and support, mainly through telephone consultation, the diagnosis and treatment of poisoned patients admitted to EDs and critical care units throughout Italy. The study was approved by the Ethics Committee of Istituti Clinici Scientifici Maugeri in Pavia (2599CE). Written informed consent was waived

because of the retrospective design of the study and the absence of research-related interventions.

Participant selection

Patients with colchicine poisoning were included if: 1) the time of ingestion was known; and 2) CoLC at hospital admission was available. Cases involving staggered overdose and those with incomplete data were excluded. Patients exposed to plants were included if they were symptomatic, CoLC at admission was available, and the ingested plant had been identified by a botanist. In patients poisoned by pharmaceutical colchicine, the following variables were collected: age, sex, estimated ingested dose and co-ingestants (including those with potential pharmacological interactions with colchicine), clinical manifestations, laboratory findings at admission and during hospitalization, treatment, and outcome.

Interventions and measurements

In all patients, CoLC (ng/mL) was measured, the time from ingestion to CoLC measurement (h) was recorded, and the outcome (death/survival) was documented to assess the prognostic value of CoLC and construct the nomogram. In the Paris cases, CoLC was measured between 2000 and 2010 by radioimmunoassay using a goat antibody minimally affected by the presence of metabolites, as described by Scherrmann *et al.*,¹⁵ and between 2010 and 2020 by liquid chromatography-mass spectrometry (LC-MS). In the Pavia cases, CoLC was measured in the same laboratory using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS).

Patients from Paris poisoned by pharmaceutical colchicine were considered the training group for fitting and comparing predictive models, whereas patients from Pavia with pharmaceutical colchicine poisoning were used as the first validation group to assess discriminative performance in an independent cohort. Patients from Pavia poisoned by colchicine-containing plants constituted a second independent validation group. In addition, published cases were used as a 3rd validation set to assess the robustness of the results. A systematic PubMed search (1959-2022) was therefore conducted using the terms “colchicine” and “poisoning.” Original studies, case reports or series, and reviews in English providing information on CoLC, time from ingestion to measurement, and outcome in patients with acute pharmaceutical colchicine poisoning were included. Cases involving plant ingestion, intravenous administration, staggered ingestion, and *post mortem* studies were excluded.

The primary endpoint was in-hospital mortality. This endpoint was selected because of its direct relevance to the study endpoint, which was to develop a nomogram for predicting the risk of death in acute colchicine poisoning. In the context of emergency medicine, estimating the probability of death during hospitalization is

essential for clinical decision-making and resource allocation.

Statistical analysis

Quantitative variables were expressed as median (25th-75th percentiles), and qualitative variables as absolute and relative frequencies (%). The Wilcoxon rank-sum test was used to compare distributions of quantitative variables between dichotomous categories. Pearson chi-square testing with 10,000 Monte Carlo simulations was used to assess independence between categorical variables. Correlations between quantitative variables were estimated using Spearman coefficient and its 95% CI, calculated with 10,000 bootstrap resamples.

Uni- and multivariable logistic regression models were used to estimate the probability of death according to the independent variables. ColC was natural log-transformed to approximate a Gaussian distribution because of its right skew, and the time from ingestion to measurement was rounded to the nearest whole hour.

Models were trained and evaluated using resampling of the training set (Paris patients): 10,000 bootstrap samples of the same size as the original set were generated. In each iteration, models were fitted, outcomes were predicted in the out-of-bag observations, and the area under the receiver operating characteristic curve (AUROC) was calculated. The median AUROC and its 95% CI were then estimated. Variable selection was performed using backward stepwise elimination based on the Akaike information criterion (AIC).

Two strategies were evaluated to determine the optimal probability decision threshold: the Youden J statistic¹⁶ and the point closest to the upper-left corner of the ROC curve. Balanced accuracy was calculated in the out-of-bag samples and its median was estimated. The final decision threshold was determined by applying the selected strategy to the final model fitted to the entire training set.

P values < .05 were considered statistically significant. Analyses were performed using R statistical software version 4.0.5. The Spearman coefficient and its 95%CI were calculated with the *spearman.ci* function (RVAideMemoire package); AUROC and ROC curves with the *roc* function (pROC package); the optimal decision threshold with *coords* (pROC); diagnostic performance with *epi.tests* (epiR package); and contour plots with *contour* (graphics package).

Results

Characteristics of the study participants

A total of 77 patients with acute pharmaceutical colchicine poisoning were included (52 in the Paris group and 25 in the Pavia group). Clinical signs at admission, complications, management, and outcomes are described in Table 1. The proportion of patients

who died was 25% in the Paris group and 36% in the Pavia group. ColC at admission was 6.0 ng/mL (3.6-12.3) in Paris and 8.3 ng/mL (6.0-14.0) in Pavia. Time from ingestion to ColC measurement was 18 h (8-30) in Paris and 11 h (4-14) in Pavia.

Data were also included from 30 Pavia patients poisoned by colchicine-containing plants (ColC at admission, 4.0 ng/mL [2.2-7.5]; time from ingestion, 16 h [10-28]) and from 16 published cases of colchicine poisoning from 11 studies,^{8-10,17-24} with ColC at admission of 8.1 ng/mL (5.2-16.9) and time from ingestion of 16 h (6-36), considered for exploratory external evaluation.

Multivariable model for predicting the probability of death

Four logistic regression models were evaluated in the training set (Paris) based on the following independent variables (Table 2): 1) log-transformed ColC; 2) time from ingestion; 3) log-transformed ColC and time from ingestion; and 4) log-transformed ColC, time from ingestion, and their interaction.

The inclusion of log-transformed ColC and time from ingestion (model 3) yielded the highest AUROC (0.78; 95% CI, 0.56-0.94) across 10,000 resamples. Furthermore, this model was selected as the most discriminative using backward elimination based on the AIC. Repeated analyses using untransformed ColC showed lower discriminative ability (AUROC < 0.75; Table 3) and were therefore not considered. Data from 1 Pavia patient and 2 published cases were excluded because they fell outside the range observed in the Paris training set.

When the model was applied to the Pavia set (*n* = 24; 8 deaths), the AUROC was 0.95 (95% CI, 0.86-1.00). In the published cases (*n* = 14; 7 deaths), the AUROC was 0.76 (95% CI, 0.46-1.00). In the independent plant-poisoning set (*n* = 30; 2 deaths), the model showed poorer performance (AUROC, 0.73; 95% CI, 0.26-1.00) (Figure 1).

Model performance using the identified optimal decision threshold (≥ 0.184 for high risk) is shown in Table 4.

Characterization of the variables in the multivariable model

The correlation between time from ingestion and log-transformed ColC in the Paris set was weak and negative (*r* = -0.19; 95% CI, -0.46 to 0.09; *P* = .18). Both variables were significantly associated with mortality in the multivariable analysis, with an increase in the probability of death according to both variables (Table 5). In the univariable analysis, only log-transformed ColC showed a significant association.

The pooled analysis (Paris, Pavia, and literature; *n* = 90; 28 deaths) confirmed these associations. No significant associations were observed in patients with plant poisoning.

Table 1. Characteristics, complications, and management of patients with colchicine poisoning in Paris and Pavia

	Total N = 77 n (%)	Paris N = 52 n (%)	Pavia N = 25 n (%)	P value
Demographic characteristics and past medical history				
Age (years)* [median (25 th -75 th percentile)]	42 (26-57)	40 (26-56)	45 (35-60)	.41
Sex (female)	46 (60)	28 (54)	18 (72)	.14
Estimated ingested dose (mg/kg) [median (25 th -75 th percentile)]	0.42 (0.25-0.70)	0.41 (0.24-0.66)	0.43 (0.29-0.81)	.40
Co-ingestants with potential drug interactions	56 (73)	47 (90)	9 (36)	.001
Clinical course				
Myelosuppression [§]	30 (42)	22 (43)	8 (38)	.80
Secondary sepsis [§]	28 (39)	22 (44)	6 (29)	.28
Liver failure [§]	27 (38)	19 (37)	8 (38)	> .99
Cardiogenic shock [§]	23 (31)	14 (27)	9 (38)	.42
Renal failure [§]	25 (35)	18 (35)	7 (33)	> .99
Acute respiratory distress syndrome [§]	15 (20)	9 (18)	6 (25)	.54
Disseminated intravascular coagulation [§]	24 (32)	14 (27)	10 (43)	> .99
Treatment				
GI decontamination	54 (70)	30 (58)	24 (96)	.001
Antibiotics	28 (36)	22 (42)	6 (24)	.13
Mechanical ventilation	25 (32)	17 (33)	8 (32)	> .99
Hemodialysis	22 (29)	16 (31)	6 (24)	.60
Vasopressors	25 (32)	16 (31)	9 (36)	.80
Extracorporeal membrane oxygenation	4 (5)	4 (8)	0 (0)	.30
Variables analyzed				
Plasma colchicine concentration (ng/mL) [median (25 th -75 th percentile)]	7.3 (4.0-12.5)	6.0 (3.6-12.3)	8.3 (6.0-14.0)	.26
Time from ingestion to concentration measurement (h) [median (25 th -75 th percentile)]	14 (6-26)	18 (8-30)	11 (4-14)	.01
Outcome				
Length of stay (days) [median (25 th -75 th percentile)]	4 (2-6)	4 (2-6)	6 (3-6)	.70
Death	22 (29)	13 (25)	9 (36)	.41

[§]Definitions of clinical events:

- Myelosuppression: ≥ 1 cytopenia attributable to poisoning (neutrophils $< 1.5 \times 10^9/L$, hemoglobin < 10 g/dL, and/or platelets $< 100 \times 10^9/L$).
 - Secondary sepsis: suspected or confirmed infection with organ dysfunction after admission (Sepsis-3: increase in SOFA score ≥ 2).
 - Liver failure: acute hepatic dysfunction with international normalized ratio (INR) ≥ 1.5 and/or marked transaminase elevation (AST/ALT > 10 times the upper limit of normal) with clinical deterioration.
 - Cardiogenic shock: systolic blood pressure < 90 mmHg or requirement for vasopressors or inotropic drugs with evidence of primary cardiac pump failure.
 - Renal failure: according to KDIGO criteria (increase in serum creatinine ≥ 0.3 mg/dL within 48 hours or ≥ 1.5 times baseline, or urine output < 0.5 mL/kg/h for 6 hours).
 - Acute respiratory distress syndrome (ARDS): according to the Berlin definition—acute hypoxemia ($PaO_2/FiO_2 \leq 300$ mmHg with PEEP ≥ 5 cmH₂O) with bilateral opacities not fully explained by heart failure.
 - Disseminated intravascular coagulation: consumptive coagulopathy with prolonged prothrombin time/INR, elevated D-dimer, low fibrinogen, and thrombocytopenia (eg, compatible with ISTH scoring).
- Bold values denote statistical significance ($P < .05$).

Nomogram for predicting the probability of death

A nomogram was developed to predict the probability of death according to ColC at admission and time from ingestion in patients poisoned by pharmaceutical colchicine (Figure 2). The diagonal dashed lines represent probability levels corresponding to ColC and time values. The solid line indicates the optimal decision threshold discriminating between high and low risk. Figure 3 provides a detailed view of the nomogram around this decision threshold, facilitating estimation of individual risk.

Discussion

Acute colchicine poisoning is characterized by high mortality. This study shows that ColC measured at hos-

pital admission, considered in relation to the time elapsed since ingestion, is significantly associated with outcome in patients with colchicine poisoning. These data made it possible to develop a nomogram for predicting the probability of death.

Patients included in the Paris and Pavia cohorts had broadly homogeneous characteristics, except for co-ingestion, which was more frequent in Paris. Clinical manifestations at admission, complications, and outcomes were consistent with those described in the literature.^{1,2,25} Despite advances in critical care management, colchicine poisoning continues to be associated with high mortality, as observed in both cohorts (25% in Paris and 36% in Pavia), in line with recent series (25.6%).²⁵ The absence of a specific antidote and the limited benefits of early ECMO initiation, given that colchicine toxicity involves not only functional abnormalities but also cellular injury, help explain the persistently high mortality due to multiorgan failure or refractory cardiac arrest.²⁶

Table 2. Area under the receiver operating characteristic curve for 4 different models evaluated using log-transformed plasma colchicine concentration values to predict the probability of death in colchicine poisoning

Model	Variables	AUROC (95% CI)*
1	log ColC	0.76 (0.52-0.94)
2	Time from ingestion to ColC measurement	0.61 (0.14-0.86)
3	log ColC + time from ingestion to ColC measurement	0.78 (0.56-0.94)
4	log ColC + time from ingestion to ColC measurement + log ColC × time from ingestion to ColC measurement	0.74 (0.46-0.93)

*Derived from 10,000 resamples of the Paris training set.

CI: confidence interval; ColC: plasma colchicine concentration; AUROC: area under the receiver operating characteristic curve.

The prognostic value of ColC has been poorly evaluated. High ColC levels associated with fatal outcomes are more frequently observed in older patients poisoned by *Gloriosa superba*, a finding consistent with kinetic data reported in pharmaceutical colchicine poisoning.²⁷ In that study, both unadjusted ColC at admission and ColC corrected using 2 methods to account for temporal variation showed high predictive ability for mortality (AUROC, 0.98; 95% CI, 0.94-1.00). More recently, a Chinese series of 23 patients with colchicine poisoning suggested that the product of the initial plasma concentration (range, 0.42-53.61 ng/mL) and the time since poisoning was associated with prognosis (mortality rate, 35%).²⁸

In the present study, cases with uncertain ingestion time were excluded and only patients with reliable timing were analyzed. Nevertheless, we recognize that in routine clinical practice, particularly in unconscious or critically ill patients, this information is often unavailable. Even so, as occurs with other toxic agents such as paracetamol or acetaminophen, the availability of a nomogram may facilitate interpretation of ColC, which has traditionally been considered difficult to interpret in acute poisoning. The results suggest that considering ColC together with time from ingestion improves predictive ability compared with either variable alone. Consistent with this finding, the multivariable association observed in the Paris training set was reproduced in terms of direction of effect in the Pavia and literature sets.

The absence of a significant association in the plant-poisoning sets could be explained by the small sample size and possible toxicokinetic differences related to the plant matrix. In addition, nomogram performance in plant poisoning differed from that reported by Wijerathna *et al.*,²⁷ probably because of differences in the ingested species (mainly *Colchicum autumnale* in the present series vs *Gloriosa superba*) and the context of ingestion (accidental in this cohort compared with intentional in other studies), which could influence the effective dose and therefore ColC.

In clinical practice, this easy-to-use nomogram could help identify patients at high risk of death early and support decisions such as intensification of supportive treatment or transfer to specialized centers with ECMO

Table 3. Estimates of the area under the receiver operating characteristic curve for 4 different models evaluated using untransformed values

Model	Variables	AUROC (95% CI)*
1	ColC	0.74 (0.13-0.94)
2	Time from ingestion to ColC measurement	0.61 (0.14-0.86)
3	ColC + time from ingestion to ColC measurement	0.73 (0.41-0.93)
4	ColC + time from ingestion to ColC measurement + ColC × time from ingestion to ColC measurement	0.72 (0.32-0.94)

*Derived from 10,000 resamples of the Paris dataset.

CI: confidence interval; ColC: plasma colchicine concentration; AUROC: area under the receiver operating characteristic curve.

capability. The time window during which the nomogram is applicable ranges from 2 to 96 hours after ingestion. From a practical standpoint, however, the most relevant period for estimating the risk of death from ColC is the first 48 hours, because other prognostic markers subsequently become more relevant⁷ and the clinical course itself better reflects disease severity. The clinical usefulness of the nomogram could become particularly important in the future if specific therapies, such as colchicine-specific Fab fragments, become available, by helping identify patients who are candidates for targeted treatment.

The results identify an informative decision threshold corresponding to a probability of death of 0.184, shown in Figures 2 and 3, which maximizes discrimination between high- and low-risk patients. This threshold showed good performance in the pharmaceutical-poi-

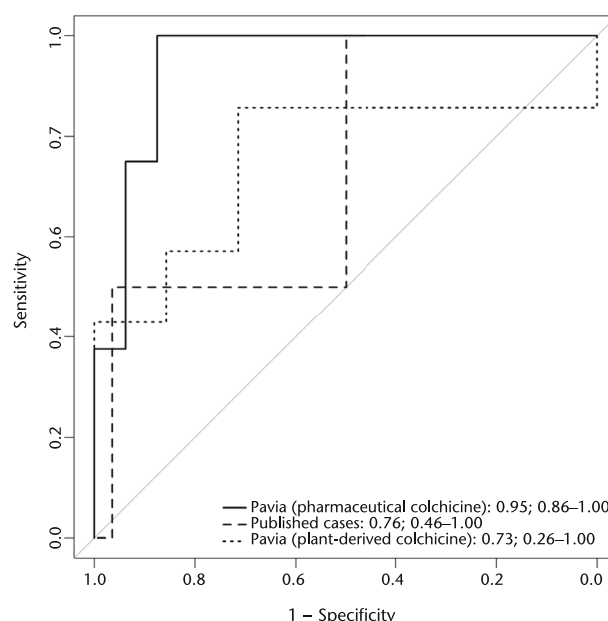


Figure 1. Receiver operating characteristic (ROC) curves for prediction of death in patients with colchicine poisoning across different datasets.

The values shown in the lower right-hand corner of the graph correspond to estimates of the area under the ROC curve and their respective 95% confidence intervals.

Table 4. Discriminative performance of the selected model for predicting mortality in colchicine poisoning, estimated in different datasets

Dataset	Sensitivity Median (95% CI)	Specificity Median (95% CI)	PPV Median (95% CI)	NPV Median (95% CI)
Pharmaceutical colchicine				
Pavia	0.88 (0.47-1.00)	0.88 (0.62-0.98)	0.78 (0.40-0.97)	0.93 (0.68-1.00)
Published cases	0.86 (0.42-1.00)	0.71 (0.29-0.96)	0.75 (0.35-0.97)	0.83 (0.36-1.00)
Plant-derived colchicine				
Pavia	0.50 (0.01-0.99)	0.86 (0.67-0.96)	0.20 (0.01-0.72)	0.96 (0.80-1.00)

CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

soning cohorts but not in the plant-poisoning cohort. Notably, only a small number of patients with an estimated probability < 0.184 died across the different sets, and in these cases death was not attributed directly to colchicine toxicity but to comorbidities or late infectious complications.

The study has several limitations. It was retrospective. Different analytical methods were used to measure ColC (radioimmunoassay, LC-MS, and LC-MS/MS) without direct comparison between them, which may introduce confounding. Inclusion of cases from the literature may have introduced selection and publication bias; therefore, these results should be considered exploratory. The model may be affected by overfitting because of the limited sample size and low number of events. In addition, the optimal decision threshold was estimated in the same training set and should therefore be interpreted cautiously.

Larger prospective multicenter studies will be needed to develop more robust and generalizable models. A sex-stratified analysis would also be of interest, although this was not feasible in the present study because of the limited sample size. Nevertheless, this study represents the largest available series with ColC

measurements. Once validated, this model could facilitate clinical decision-making by estimating the risk of death from readily available variables. In conclusion, we present a nomogram that estimates the probability of death after colchicine poisoning based on ColC at admission and time from ingestion. These findings are exploratory and hypothesis-generating because they derive from a retrospective study and therefore require independent prospective validation before clinical implementation. If confirmed, this tool could facilitate bedside risk stratification and guide decisions regarding intensification of supportive care or referral to higher-complexity centers. Wider availability of rapid ColC testing, together with the development of specific antidotes and a better understanding of the factors influencing colchicine kinetics, will strengthen its clinical applicability and may guide future use of specific therapies such as anti-colchicine Fab fragments.

Conflict of Interest Disclosures: None reported.

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Table 5. Uni- and multivariable logistic regression analyses including the selected variables for predicting the probability of death in colchicine poisoning across different datasets

Dataset	Univariable ^a OR (95% CI)	P value	Multivariable ^a OR (95% CI)	P value
Pharmaceutical colchicine				
Paris (n = 52; mortality, 25%)				
Time since ingestion	1.02 (0.99-1.05)	.19	1.03 (1-1.07)	.046
Log ColC	2.12 (1.17-4.42)	.03	2.92 (1.4-7.34)	.01
Pavia (n = 24; mortality, 33%)				
Time since ingestion	1.26 (1.05-1.71)	.06	1.74 (1.13-5.05)	.12
Log ColC	4.93 (1.26-35.6)	.05	55.3 (2.77-111511.89)	.10
Published cases (n = 14; mortality, 50%)				
Time since ingestion	1.09 (1.01-1.28)	.15	1.12 (1.02-1.41)	.17
Log ColC	0.71 (0.18-2.28)	.57	1.99 (0.38-16.24)	.44
Combined data (n = 90; mortality, 31%) [†]				
Time since ingestion	1.03 (1.01-1.06)	.004	1.05 (1.03-1.09)	< .001
Log ColC	1.93 (1.20-3.36)	.01	3.31 (1.76-6.95)	< .001
Plant-derived colchicine				
Pavia (n = 30; mortality, 7%)				
Time since ingestion	0.97 (0.79-1.06)	.63	0.99 (0.74-1.08)	.84
Log ColC	13.74 (1.03-140.08)	.12	12.37 (1.02-1438.18)	.15

^aUni- or multivariable logistic regression according to time since ingestion or natural log-transformed ColC.

[†]An indicator variable identifying whether each patient belonged to the Paris cohort, Pavia cohort, or published-case dataset was included in the logistic regression model to adjust the estimates.

CI: confidence interval; ColC: natural log-transformed plasma colchicine concentration; OR: odds ratio.

Bold values denote statistical significance ($P < .05$).

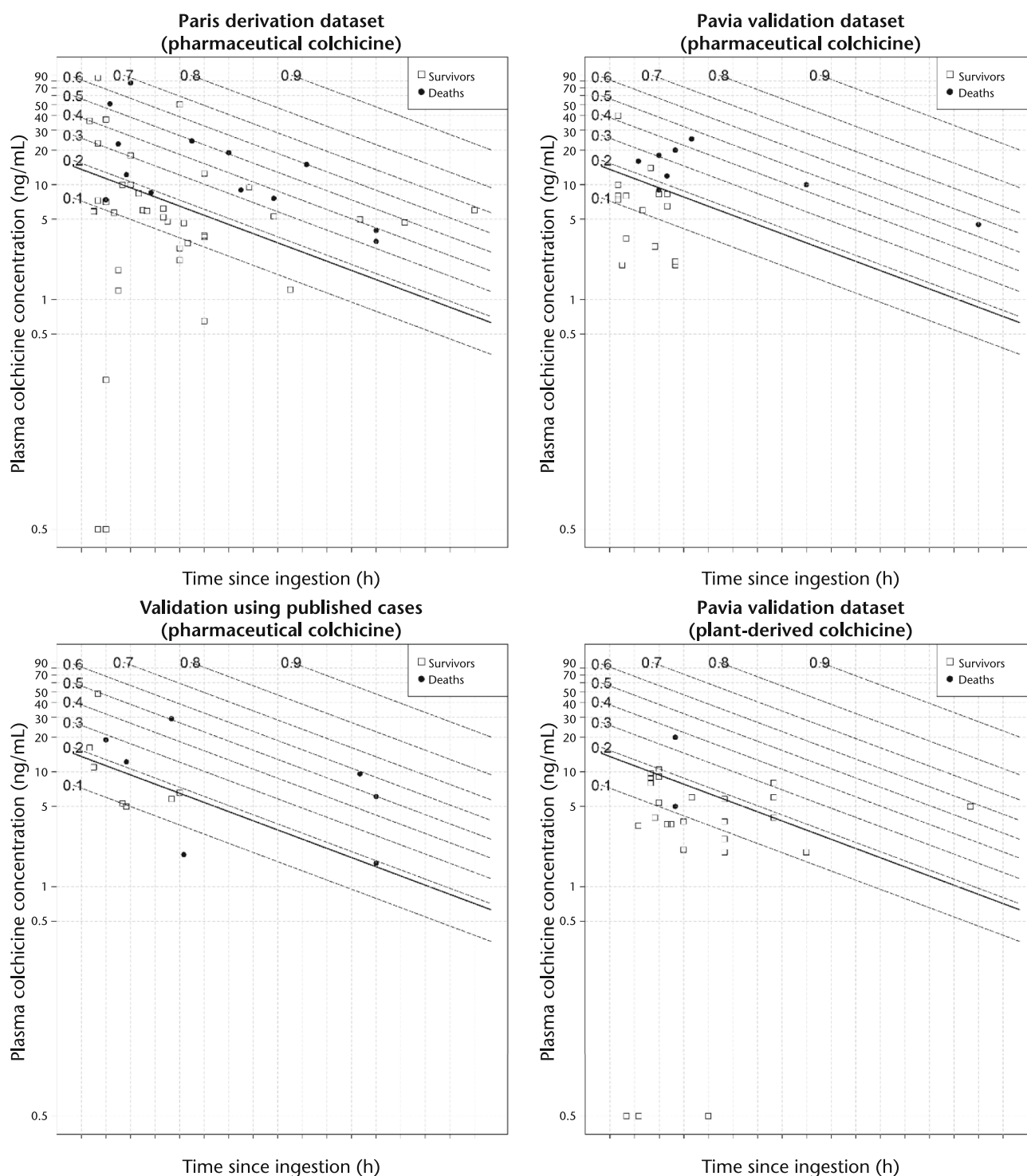


Figure 2. Contour plots (nomogram) describing the probability of death predicted by the multivariable logistic regression model developed in the training set.

The x-axis represents the time elapsed since ingestion (h), and the y-axis represents plasma colchicine concentration (ng/mL). The black diagonal dashed lines represent the predicted probability of death, which is also indicated on the graph. The solid black diagonal line represents the decision threshold corresponding to an approximate event probability of 0.184.

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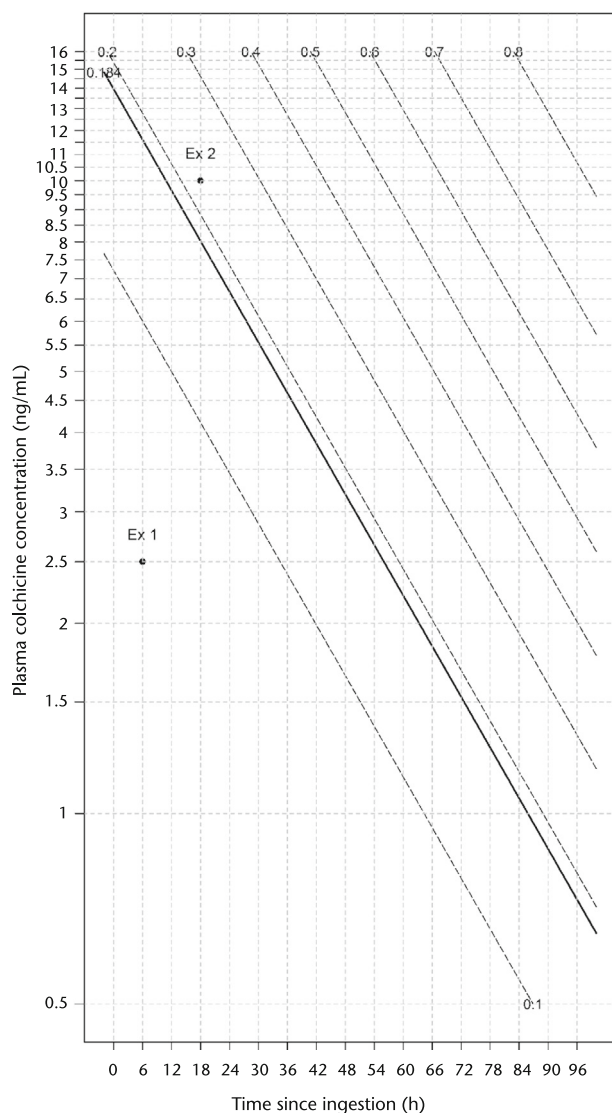


Figure 3. Detailed view of the nomogram around the decision threshold.

The x-axis represents the time elapsed since ingestion (h), and the y-axis represents plasma colchicine concentration (ng/mL). The black diagonal dashed lines represent the predicted probability of death, which is also indicated on the graph. The solid black diagonal line represents the decision threshold corresponding to a probability of death of 0.184.

As an example of a low-risk patient, simulated patient 1 (Ex1) has a ColC of 2.5 ng/mL measured 6 h after ingestion, resulting in a predicted probability of death < 0.1, below the decision threshold (ie, below the solid black line corresponding to a probability of death of 0.184).

As an example of a high-risk patient, simulated patient 2 (Ex2) has a ColC of 10 ng/mL measured 18 h after ingestion, resulting in a predicted probability of death between 0.2 and 0.3, above the decision threshold (ie, above the solid black line corresponding to a probability of death of 0.184).

The probability of death can only be estimated in patients with ColC values between 0.01 and 85.3 ng/mL and post-ingestion times between 2 and 96 hours, corresponding to the ranges observed in the training dataset.

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