International Journal of Medical Toxicology & Forensic Medicine
2026, Volume 16, E51119

Review Article

Evaluation of the use of Lung transplantation in acute paraquat poisoning: A Review Study

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Citation Samsam-Shariat Sh, Jalali MH, Meamar R, Ebrahimi F, Nouri R, Maasoumi Gh, et al. Evaluation of the use of Lung transplantation in acute paraquat poisoning: A Review Study. International Journal of Medical Toxicology and Forensic Medicine. 2026; 16:E51119.

https://doi.org/10.22037/ijmtfm.v16.51119

Article info:

Received: 09 December, 2025

Accepted: 06 January, 2026

Published: 22 August, 2026

Keywords:

Lung transplantation, Lung fibrosis, Intoxications, Paraquat

BSTRACT

Background: Acute paraquat poisoning remains a critical therapeutic challenge with high mortality, primarily due to irreversible pulmonary fibrosis. Lung transplantation (LT) maybe is the only definitive life-saving option for these patients. This systematic review aimed to investigate the factors associated with survival outcomes in patients who underwent LT following paraquat poisoning.

Methods: This was a retrospective analysis of 12 reported cases from 1968 to 2025, identified through a comprehensive search of major international databases. The collected demographic, clinical, and outcome data were analyzed using statistical tests such as chi-square for categorical variables and t-test or Mann-Whitney U for continuous variables.

Results: Among the analyzed patients, 9 (75%) survived, and 3 died. The analysis revealed a significant association between preoperative liver function (p=0.03) and the type of lung transplantation (p=0.025) with survival. A 100% survival rate was observed in patients with recovered liver function and in all patients, who received a bilateral LT. Furthermore, a significantly shorter time from poisoning to both ECMO initiation and LT was associated with higher mortality (p=0.025 and p=0.009, respectively).

Conclusion: Lung transplantation is an effective treatment for paraquat poisoning with irreversible pulmonary fibrosis. Success depends on careful patient selection based on organ function recovery and optimal surgical timing, with ECMO serving as a crucial bridge. These findings underscore the need for standardized treatment protocols to maximize survival in this challenging patient population.

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Introduction

Paraquat, or 1,1′-dimethyl-4,4′-bipyridinium dichloride, is a highly toxic contact herbicide that is widely utilized but has been prohibited in numerous nations. Given the absence of antidotes, paraquat poisoning is severe and can be fatal [1] The mortality rate for paraquat poisoning ranges from approximately 40% to 80%. It's understood that ingesting as little as 30 mg/kg or 50 mL of a 21% (w/w) solution can lead to organ failure or death. Even doses as low as 1 mL could prove fatal [2, 3]. The metabolism of ingested paraquat is limited, with only 1% to 5% being processed. The bulk of gastrointestinal absorption happens within the small intestine, and unabsorbed paraquat exits the body through feces [4, 5]. Paraquat concentration in the plasma peaks between 30 minutes and 4 hours after absorption, leading to its broad distribution across the body, infiltrating numerous tissues and organs [6]. Paraquat, when present in tissue, can generate a superoxide radical, a potent reactive oxygen species. This radical is capable of directly inducing cellular damage or undergoing subsequent reactions to generate other reactive oxygen species and nitrite radicals [7]. lungs, heart, kidneys, and liver are most affected organs because of high blood flow and oxygen tension and energy requirement but because due to existence of blood-brain barrier, brain is not affected commonly [8, 9]. The lungs have been identified as the primary target organs injured by the active accumulation of paraquat, resulting in irreversible pulmonary fibrosis. Pulmonary edema, intra-alveolar hemorrhage, and inflammatory cell infiltration occur in the early stage of paraquat-induced lung injury. After several weeks, alveolar changes like myofibroblast infiltration, collagen deposition, and fibroblast differentiation can be observed. These changes are very dangerous and harmful so that studies show that acute respiratory distress syndrome and pulmonary fibrosis are the most common causes of death in paraquat poisoning cases [10]. Hemoperfusion, early gastric lavage, emesis induction, laxatives, immunosuppressive drugs, and mesenchymal stem cell infusions are among the current clinical treatments for paraquat poisoning. However, these therapeutic approaches merely help to postpone the progression of the disease, which is usually incurable. But these therapies don't guarantee patients' long-term survival because of the lung injury [11]. For critically ill patients unable to maintain adequate ventilation and oxygenation, ECMO (Extracorporeal Membrane Oxygenation) should be considered as a temporary measure until a lung transplant can be performed [12]. ECMO is being increasingly applied to treat patients exposed to paraquat substances at a toxic dose resulting in cardiorespiratory failure and metabolic dysfunction. Although ECMO does not neutralize or remove any substances, it provides hemodynamic assistance and oxygenation [12, 13]. Lung transplantation may be the only viable treatment for patients with progressive pulmonary fibrosis in the late stage of paraquat poisoning [13]. But lung transplantation is not that simple and comes with many problems and challenges. Some studies show that lung transplantation can only be successful when the body is completely depleted of paraquat, and when the waiting time for LT is too short, the transplanted lung can exhibit fibrosis again [14, 15]. Therefore, the time of transplantation is critical. Another point is finding a donor with the same blood type in this short time [14, 16]. LT can also cause serious complications such as severe infection, fistula, and pneumothorax, which can be life-threatening in themselves [17]. Here we want to review previous articles about lung transplantation in paraquat poisoning to discover and summarize the indication, benefit, timing, complications, and other things about LT in patients with paraquat poisoning.

Materials and Methods

This study was a systematic review. The Institutional Ethics Committee of Isfahan University of Medical Sciences approved the project with ethic code"IR.MUI.MEO.REC.1403.264".

Search strategy and study selection

Two experts from the research team conducted a comprehensive search of international reference databases, including Web of Science, PubMed, Google Scholar, Scopus, Cochrane, and Embase, for publications dated before April 1, 2025. Our search utilized specific keywords: Lung Transplantation, LT, Pulmonary Transplant, Paraquat, Methyl Viologen, Gramoxone, Paragreen A, Pathclear, Weedol, Poisoning, Intoxication, overdose, toxicity. In PubMed, our search strategy was as follows:

((("Paraquat"[Mesh]) OR ("Methyl Viologen"[Title/Abstract] OR Gramoxone[Title/Abstract] OR "Paragreen A"[Title/Abstract] OR grammoxone[Title/Abstract] OR gramoxone[Title/Abstract] OR methylviologen[Title/Abstract] OR pathclear[Title/Abstract] OR "methyl viologen"[Title/Abstract] OR weedol[Title/Abstract])) AND (("Lung Transplantation"[Mesh]) OR ("Lung Graft*"[Title/Abstract] OR "Lung Transplantation*"[Title/Abstract] OR "pulmonary transplantation*"[Title/Abstract])).

A similar search strategy was employed for other databases, and no limitations were set regarding article types. We included interventional (randomized clinical trial), noninterventional, and observational studies encompassing historical cohorts, cross-sectional studies, case-control studies, case reports, and case series.

Two researchers independently assessed articles and performed screening using PICO search tools, defined as follows: P (population) - Patients with Paraquat poisoning, either accidental or intentional as a suicide attempt; I (intervention) – Lung transplantation; C (comparison) - Conservative Medical Management and supportive care without lung transplantation.; O (outcome) - Survival or mortality of the patients.

These two researchers individually reviewed full articles and marked those meeting our inclusion/exclusion criteria. Our inclusion criteria consisted of articles written in English or Persian languages, articles examining patients with paraquat toxicity and Lung transplantation, and articles with full-text availability. For articles lacking full text, we obtained necessary data from article summaries when possible. Alternatively, we reached out to corresponding authors to access the full text, and articles without a response were excluded. We also excluded animal studies and narrative reviews.

Data extraction

Two researchers extracted the following information from the articles and recorded them in an Excel table. This data encompassed various aspects, including bibliographic details (such as the first author's name, publication year, country), participant characteristics (including gender and age), Volume and concentration of paraquat used, Primary treatment, Indication for lung transplantation, Time to LT after paraquat poisoning, other Specific Treatment, Total Hospitalization Time, and the Outcome of patients, indicating whether the patient survived or experienced mortality.

Statistical Analysis

The available data were entered into Stata (version 17) for descriptive analysis. Continuous variables are presented as mean ± standard deviation, and categorical variables as frequencies and percentages. Comparisons between survivors and non-survivors were performed using the independent t-test for continuous variables and Fisher's exact test for categorical variables. A two-sided p-value < 0.05 was considered statistically significant.

A priori, we extracted several clinical variables as potential prognostic factors and confounders, including age, sex, estimated amount of paraquat ingested, time from ingestion to hospital arrival, time from ingestion to LT initiation, LT configuration (single or bilateral), and concomitant extracorporeal therapies (e.g., ECMO, hemoperfusion, continuous renal replacement therapy). However, because the available evidence consisted of individual case reports and a single small case series, with substantial heterogeneity and incomplete reporting across studies, no formal pooled meta-analysis or multivariable regression modelling could be performed. Instead, these covariates were summarized descriptively and explored only in univariable comparisons between survivors and non-survivors, and the findings should be interpreted as hypothesis-generating.

Results

By the search in databases initially, we found 47 articles. We found this number of articles in each database; Cochrane: 0 articles Embase: 20 articles, PubMed: 17 articles, Scopus: 0 articles, and Web of Science: 10 articles. 25 articles were similar and deleted in the first step. Two researchers independently read the title and abstract of the articles. 5 articles were not relative to the context or were animal studies, excluded. In the next step, we used inclusion criteria to assess 20 remaining articles. All articles written in languages except English and Persian were excluded. In the cases where two researchers had different ideas, the third researcher read and assessed the article. In this step we had 12 articles for research. Figure 1. Shows our PRISMA flowchart for study selection.

Studies characteristics

In the end, we had 12 eligible studies in which there were case reports. The full number of patients from all studies (except cohort studies) is reported in Table 1. In this table each patient is only in one row and sorted based on the articles' findings. there were also 2 case report studies in our final articles which we explain.

Based on the analysis, there was no statistically significant association between gender and survival outcomes ($\chi^2 = 2$, $p = 0.157$), with all females surviving (100.0%) and 37.5% of males dying. Preoperative liver function showed a significant relationship with outcome ($\chi^2 = 7$, $p = 0.03$), as all patients with liver dysfunction died (100.0%), whereas those with recovery or stabilized function all survived. Preoperative renal function did not show a significant association with mortality ($\chi^2 = 4.5$, $p = 0.105$). ECMO mode was not significantly related to outcome ($\chi^2 = 2.593$, $p = 0.762$). Lung transplantation (LT) type demonstrated a significant association ($\chi^2 = 9.333$, $p = 0.025$), with all bilateral LT recipients surviving, while mortality was highest among right-then-left LT, single LT, and some left LT cases. The presence of bronchial stenosis/fistula was not significantly related to survival

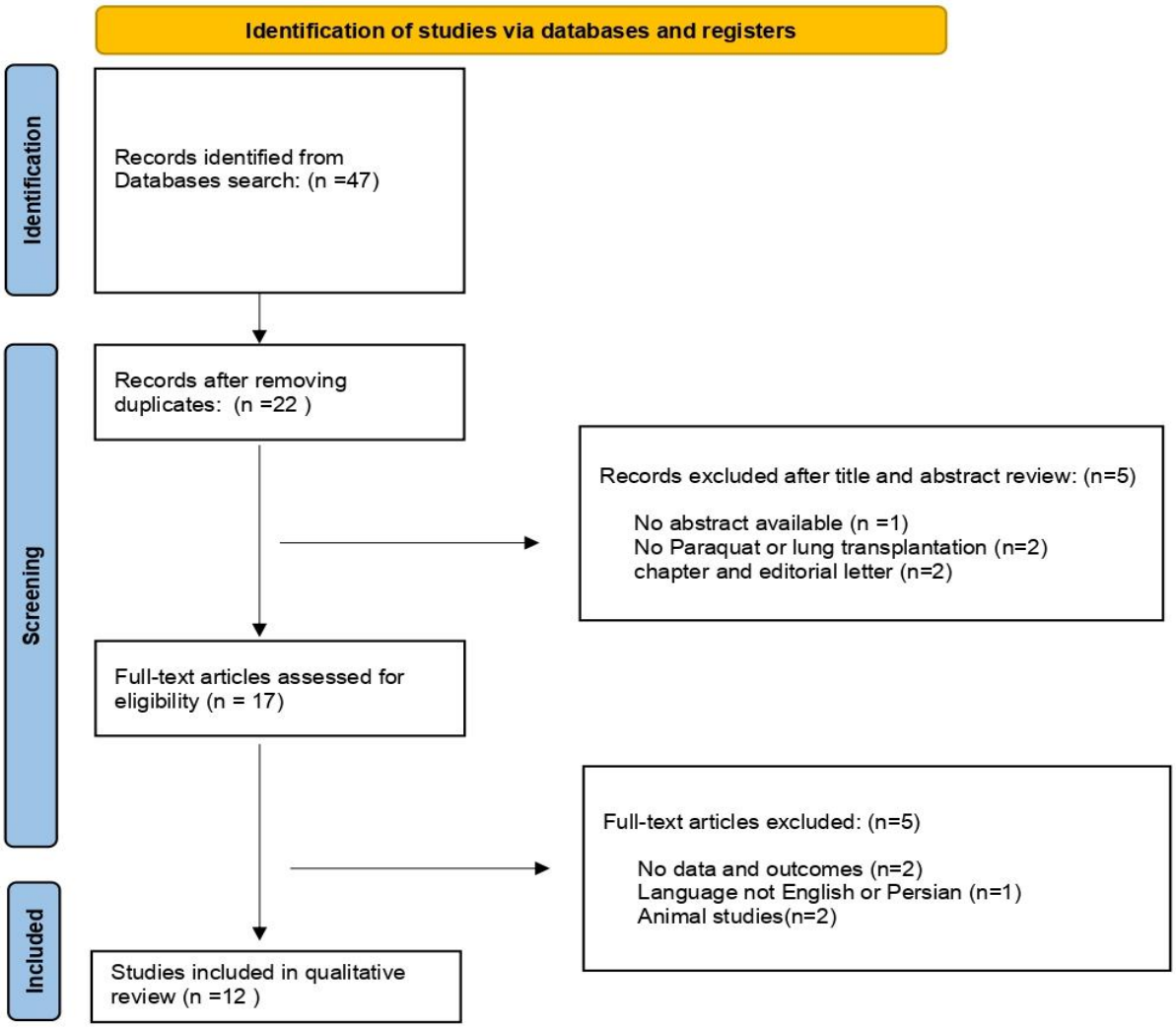

Figure 1. PRISMA 2020 flow diagram for vew systematic reviews which included searches of databases and registers only.

(χ^2 = 0.032, p = 0.858). However, respiratory stress/failure was significantly associated with higher mortality (χ^2 = 5.143, p = 0.023), as 66.7% of affected patients died. Other complications showed no statistically significant association with survival (χ^2 = 8, p = 0.092), though anuria with myopathy and pneumothorax were present only in deceased patients.

Regarding continuous variables, there was no significant difference in mean age between deceased (21.33 ± 8.51 years) and surviving patients (26.22 ± 9.85 years; t = –0.764, p = 0.462). The time from poisoning to ECMO initiation was significantly shorter among deceased patients (14 days) compared with survivors (35.56 ± 7.45 days; t = –2.744, p = 0.025). The poison volume was lower in deceased patients (20.00 ± 0.00) than in survivors (48.57 ± 13.45), but this difference was not statistically significant (U = 1.000, p = 0.111). Finally, the time from poisoning to lung transplantation was significantly shorter in deceased patients (11.67 ± 6.66 days) compared with survivors (40.89 ± 13.07 days; U = 0.000, p = 0.009).

Discussion

Acute paraquat poisoning remains a serious clinical challenge due to its high mortality rate and destructive nature [18]. While the toxin can affect multiple organs such as the kidneys, liver, and gastrointestinal tract, severe and irreversible pulmonary damage, often leading to progressive fibrosis, is the main cause of death in these patients [19]. Unfortunately, no effective medical treatment currently exists to halt paraquat-induced lung fibrosis. In this critical situation, the only potentially life-saving therapeutic option is the replacement of the damaged organ. This can be achieved through two primary methods: 1) extracorporeal membrane oxygenation (ECMO) and 2) lung transplantation. ECMO serves as a temporary supportive measure, acting as a bridge to preserve the patient's life until a lung transplant can be performed [20]. Studies have shown that ECMO alone cannot reduce mortality; rather, it must

be used as part of a comprehensive strategy with the ultimate goal of lung transplantation [21]. However, lung transplantation as a treatment option is accompanied by significant limitations that must be carefully considered: Time Constraints: The need for an urgent surgical procedure due to the rapid progression of pulmonary injury makes finding a suitable donor within a short timeframe extremely difficult. Reports indicate that some patients who were candidates for transplantation died due to a lack of a suitable organ.

Resource Limitations: A successful lung transplant requires a highly specialized surgical team, advanced intensive care facilities, and significant financial resources. These constraints mean the procedure is only feasible in specialized centers with the appropriate infrastructure.

Despite these challenges, available data from case reports and case series show promising results. A review of 12 reported cases since 1968 reveals that 9 patients (75%) survived after lung transplantation, which is a highly encouraging survival rate. It is noteworthy that all three deceased cases were reported between 1968 and 1985, suggesting a considerable improvement in outcomes with recent advancements in surgical techniques, post-operative care, and treatment protocols [22-24]. Precise timing of the transplant is a crucial factor in determining the clinical outcome. Autopsy studies on deceased patients who underwent transplantation on days 6 and 10 after poisoning revealed the presence of fibrosis in the transplanted lung. This finding suggests that residual paraquat in the blood or body tissues can cause damage to the new lung. Therefore, transplantation should be performed after systemic clearance of the toxin, which can be accelerated using methods such as hemoperfusion and hemodialysis [25]. nversely, a study by Lee et al. (2023) emphasizes that excessive delay can increase the risk of post-operative infections. This study suggests that once renal and hepatic function returns, transplantation can be performed, and it is not necessary to wait for paraquat concentration to reach zero [15].

Finally, the type of transplant procedure may also influence the outcome. Of the surviving patients, only one underwent a single-lung transplant, while the rest received a bilateral transplant. In contrast, two of the three deceased patients had a single-lung transplant, and the third had a staged procedure. This observation raises the hypothesis that bilateral lung transplantation may be associated with higher survival, although further studies are required to confirm this claim [26].

Table 1. Paraquat poisoned patient with detail.

Case report year	1968 (Matthew et al; 1968)	1973 (Cooke et al; 1973)	1985 (The Toronto Lung Transplant group, 1985)	1997 (Walder et al; 1997)	2014 (Jiao et al; 2021)	2015 (Tang et al; 2015)	2018 (Jiao et al; 2021)	2019 (Jiang et al; 2019)	2020 (Jial et al; 2021)	2021 (Jiao et al; 2021)	2022 (Wu et al; 2022)	2023 (Congcong Li et al; 2023)
year/gender	15/male	18/male	31/male	17/male	24/female	21/female	45/male	26/female	38/male	30/male	18/female	17/male
poison volume (concentration)	I moufful (20%)	1 moufful	Exposure 10 years	NR (suicid)	50 mL (20%)	50 mL (20%)	60 mL (20%)	20 mL (20%)	50 mL (20%)	60 mL (20%)	NR (Be poisone)	30-50ml(25%)
Preoperative liver function	dysfunction	dysfunction	NR	NR	stabilized	recovery	stabilized	NR	stabilized	stabilized	NR	NR
Preoperative renal function	mild jaundice	oliguria	oliguria	oliguria	stabilized	recovery	stabilized	NR	stabilized	stabilized	NR	oliguria
days to ECMO	-	-	14(R[a]), 24(L[b])	44	44	44	38	35	27	28	34	26
ECMO mode	-	-	V-V[a]	CPB	V-V[a]	V-V[a]	V-V	V-V[a] & V-A	V-A	V-V	NR	V-V
days to LT	6	10	19(R[a]), 41(L[b])	44	56	56	38	58	27	28	34	27
LT Type	left	single	right then left	left	bilateral	bilateral	bilateral	bilateral	bilateral	bilateral	bilateral	bilateral
complications infection	no	NR	yes	no	yes	no	yes	yes	yes	yes	NR	yes
bronchial stenosis/ fistula	no	NR	yes	yes	nO	no	yes	NR	no	yes	NR	no
respiratory stress/ failure	yes	NR	yes	no	no	no	no	NR	no	no	NR	yes
Other	pneumothorax	NR	anuria myopathy	pneumothorax myopathy	no	no	thrombus pancreatitis	NR	no	no	NR	pneumothorax myopathy
Outcome	death	death	death	survive	survive	survive	survive	survive	survive	survive	survive	survive
survival time from toxicosis	19 days	12 days	110 days	>20 months	>5 years	>Iyear	>3 years	>1 year	>7months	>7months	>I year	>I year
paraquat concentration												
serum (μg/L)	400 (day 7)	NR	30 (dayl7) 200 (day2l)	0 (day4,l8,50)	NR	248.96 (day46) 30.53 (day56)	NR	NR	NR	NR	0 (dayl3)	NR
urine (μg/L)	2,106 (dayl)	NR	NR	0 (day 4,18,50)	248,960[b]	NR	229,200[b]	NR	148,600[b]	126,400[b]	70 (dayl3)	NR
tissue (μg/L)	0 (day17) removed lung 8.50 (dayl9)	NR	muscle (day2l) 0.27 μg/mL	59th day: lung 134, muscle 328	NR	lung 0.38 (day56)	NR	NR	NR	NR	0 (dayl9) NR	NR

NR, not reported; a, Right lung; b, Left lung.
[a] ECMO was instituted preoperatively.
[b] **At first admission, CPB, cardiopulmonary bypass**

In summary, given the high mortality of acute paraquat poisoning in the stage of irreversible pulmonary fibrosis, lung transplantation remains the only effective treatment option to increase a patient's chance of survival. However, the success of this method depends on overcoming logistical and clinical challenges by implementing standardized treatment protocols. These protocols should include the use of ECMO as a bridge, optimized transplant timing, and toxin clearance techniques. Based on the promising results, future studies should focus on establishing precise patient selection criteria and comparing outcomes of single versus bilateral transplantation to determine the optimal therapeutic strategy.

Limitations

The present systematic review has several limitations, that is, the lack of information in registry studies, heterogeneous etiologies of poisoning, and reporting bias. The exclusion of publications not written in English or Persian may reduce the methodological and reporting quality of this review. Morrison et al. stated that language bias due to language restrictions does not seem to affect summarized treatment effects, but that the precision of pooled estimates improved with the inclusion of trials in languages other than English. The large number of case reports is also a limitation, as they often describe only successful cases.

Conclusion

This study confirms that lung transplantation is a viable life-saving option for patients with acute paraquat poisoning who progress to irreversible pulmonary fibrosis. The promising overall survival rate of 75% observed in these 12 patients report underscores the potential of this aggressive therapeutic approach.

Our findings reveal several key factors influencing survival outcomes. Preoperative liver function and the type of lung transplantation performed were significantly associated with survival. The 100% survival rate among patients with recovered or stabilized liver function, coupled with the perfect survival rate among those who received a bilateral lung transplant, highlights the importance of patient selection and surgical strategy. Furthermore, our results emphasize the critical role of optimal timing for transplantation. Patients who died had a significantly shorter time from poisoning to both ECMO initiation and lung transplantation compared to survivors. This finding strongly suggests that rushing the transplant procedure—before the body has had sufficient time to clear the circulating toxin—may lead to graft injury and poorer outcomes. This underscores the need to use ECMO as a true bridge, allowing adequate time for systemic toxin clearance and organ recovery, particularly of the liver, before proceeding with the definitive procedure. While other variables such as gender, age, and initial poison volume did not show a statistically significant association with survival, their clinical relevance cannot be dismissed. The presence of respiratory stress/failure was also a significant predictor of mortality, reinforcing the notion that only ECMO can effectively support these patients while they wait for their transplant. In summary, the high mortality of paraquat poisoning can be significantly reduced through lung transplantation. However, success hinges on two critical factors: careful patient selection based on organ function recovery and a well-timed surgical intervention facilitated by ECMO as a bridge. Future research should focus on establishing standardized protocols for patient selection and optimal timing of transplantation to maximize survival in this challenging patient population.

Acknowledgment

None.

Funding

None.

Conflicts of Interest

The authors report there are no competing interests to declare.

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