

The Effect of Intravenous Lipid Emulsion in Tricyclic Antidepressant Poisoning: A Systematic Review

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INTRODUCTION

Tricyclic antidepressant (TCA) poisoning is a medical emergency that may cause seizures, altered consciousness, hypotension, and life-threatening

ABSTRACT

Tricyclic antidepressant (TCA) poisoning may cause severe hypotension, QRS complex prolongation, arrhythmias, seizures, and cardiac arrest. Intravenous lipid emulsion (ILE) has been proposed as an adjunctive rescue treatment, but its role remains uncertain. We conducted a Preferred Reporting Items for Systematic Reviews and Meta-Analyses-guided systematic review without meta-analysis to evaluate clinical outcomes and safety of ILE in adult patients with TCA poisoning. PubMed/MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, Google Scholar, Persian-language databases, and gray-literature sources were searched through December 2025. Methodological quality was assessed using design-specific Joanna Briggs Institute critical appraisal checklists for case reports and case series. Uncontrolled case-based evidence was synthesized narratively using descriptive case-level proportions with exact 95% confidence intervals (CIs). Twenty-four studies published between 2009 and 2023 were included: 20 case reports, three case series, and one registry-derived case series, representing 42 cases of uncontrolled case-based evidence. Survival was reported in 41 of 42 cases (97.6%). Survival was reported in all documented arrest cases receiving ILE, although concurrent resuscitative interventions preclude attribution. Hypotension resolved in 14 of 17 cases (82.4%), whereas wide-QRS and arrhythmia resolution occurred in 6 of 14 cases (42.9%) and 4 of 9 cases (44.4%), respectively. Reported adverse events included acute respiratory distress syndrome, hypertriglyceridemia with laboratory interference, and mild liver abnormalities. The evidence was limited by publication bias, lack of comparator groups, selective reporting, concurrent treatments, and absent systematic safety monitoring. Therefore, the findings do not establish the effectiveness or safety of ILE in all TCA poisoning cases. More research is needed before ILE can be supported for routine or first-line use, but ILE may be considered as rescue therapy in selected patients with refractory, life-threatening toxicity alongside standard therapies, with careful monitoring for potential harms.

KEYWORDS: *Intravenous lipid emulsion, overdose, poisoning, systematic review, tricyclic antidepressants*

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arrhythmias. Cardiotoxicity results mainly from myocardial sodium-channel blockade, leading to conduction delay and QRS widening. QRS durations of ≥ 100 ms and ≥ 160 ms are associated with increased risks of seizures and ventricular arrhythmias, respectively, whereas serum TCA concentrations have limited prognostic value.^[1]

Intravenous lipid emulsion (ILE), used primarily for local anesthetic systemic toxicity, has been proposed as an adjunct for poisoning by lipophilic drugs through a “lipid sink/shuttle” mechanism. Because many TCAs, particularly amitriptyline, are highly lipophilic, ILE may be considered as a rescue adjunct in selected severe overdoses.^[2-4]

Evidence supporting ILE in TCA poisoning is limited mainly to case reports and small observational studies reporting survival and transient hemodynamic or electrocardiographic (ECG) improvement in refractory amitriptyline and mixed overdoses.^[5] Experimental studies have shown inconsistent results, including no clear hemodynamic benefit, possible poorer survival, and no advantage over sodium bicarbonate.^[6] Accordingly, American Academy of Clinical Toxicology (AACT) recommendations advise against using ILE as first-line therapy for life-threatening amitriptyline toxicity, although it may be considered in selected refractory cases when standard treatments fail.^[7]

Safety concerns remain important, as acute ILE use has been associated with pulmonary and metabolic adverse effects. Accordingly, the American College of Medical Toxicology (ACMT) recommends that ILE be considered only as an adjunct in selected severe cases and not as a replacement for standard therapies.^[8]

Previous reviews have evaluated ILE across diverse poisonings, with limited focus on TCA toxicity. This review provides a TCA-specific, case-level synthesis of clinical severity, ILE dosing and timing, treatment responses, survival, adverse events, concurrent therapies, and reporting completeness. By using explicit availability denominators and design-specific critical appraisal, it distinguishes reported clinical patterns from causal evidence and clarifies the limited adjunctive role of ILE alongside standard treatment.

METHODS

This systematic review evaluated the reported clinical outcomes and safety of ILE in adults with TCA poisoning. The review was conducted from August 2025 to January 2026 and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive

literature search was conducted in PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library from database inception through December 2025. Supplementary searches were performed in Google Scholar and the Persian-language databases (Magiran and SID) using relevant English and Persian keywords. The search strategy combined controlled vocabulary and free-text terms related to three main concepts: TCAs, poisoning or overdose, and ILE. Search terms included “tricyclic antidepressants,” “TCA,” “poisoning,” “overdose,” “intravenous lipid emulsion,” “ILE,” “lipid rescue,” and the names of individual TCAs, including amitriptyline, imipramine, clomipramine, and nortriptyline. The terms were combined using Boolean operators. The complete electronic search strategies are provided in Supplementary Tables 1-4.

Human studies were eligible if they involved adults aged 18 years or older with TCA poisoning who received ILE and had reported clinical outcomes. Case reports, case series, and other observational reports were considered eligible. Studies were excluded if they involved pregnant patients, participants younger than 18 years, co-ingestion of non-TCA substances, insufficient extractable data, or overlapping or duplicate patient populations. Studies reporting mixed poisoning populations were eligible only when data for individual patients with isolated TCA poisoning could be extracted separately. Individual cases involving confirmed co-ingestion of non-TCA substances were excluded. Administration of standard supportive or resuscitative treatments was not considered a reason for exclusion; instead, these treatments were recorded as concurrent interventions.

All retrieved records were collated, and duplicate records were removed. Two reviewers independently screened titles and abstracts and assessed the full texts of potentially eligible studies. When eligibility could not be determined from the title or abstract, the full article was reviewed. Disagreements were resolved by consensus or consultation with a third reviewer. Data were independently extracted by two reviewers using a prespecified standardized form. Extracted variables included the first author, publication year, study design, country, sample size, patient age and sex, specific TCA involved, ILE formulation, dose, timing, infusion regimen, and reported clinical outcomes. The outcomes of interest included survival, hemodynamic changes, electrocardiographic findings, seizure outcomes, and adverse events. Concurrent supportive and resuscitative treatments were also systematically extracted, including sodium bicarbonate, vasopressors or inotropes, antiarrhythmic agents, endotracheal intubation or mechanical ventilation, cardiopulmonary resuscitation,

benzodiazepines or other anticonvulsants, defibrillation or cardioversion, extracorporeal membrane oxygenation, intravenous fluids, and gastrointestinal decontamination. Each variable was classified as explicitly reported as present, explicitly reported as absent, partially or aggregately reported, or not reported.

Because the included evidence consisted of case reports and case series, methodological quality was assessed using design-specific Joanna Briggs Institute (JBI) critical appraisal tools. The 20 case reports were assessed using the eight-item JBI Critical Appraisal Checklist for Case Reports.^[9] The three case series and one registry-derived case series were assessed using the ten-item JBI Critical Appraisal Checklist for Case Series.^[10] Each item was rated as “Yes,” “No,” “Unclear,” or “Not applicable.” Two reviewers independently performed the assessments, and disagreements were resolved through discussion or consultation with a third reviewer. No arbitrary numerical quality threshold was applied; instead, item-level findings were considered when interpreting the evidence.

All analyses were conducted at the case level, with each unique TCA-related exposure treated as a single observation. Continuous variables were summarized using medians and interquartile ranges (IQRs), with ranges reported where informative. Categorical variables were presented as frequencies and percentages using the number of cases with available data as the denominator. Exact 95% Clopper–Pearson CIs were calculated for binomial proportions.

Survival was summarized as a descriptive clinical outcome among cases with reported survival status. It was not considered a primary effectiveness endpoint because the included evidence was uncontrolled and patients received substantial concurrent supportive and resuscitative treatments. For outcomes that could not be attributed to individual TCA cases in the registry-derived study, analyses were restricted to cases with extractable case-level information. The registry findings were otherwise summarized descriptively.

Return of spontaneous circulation (ROSC) was not consistently reported as a separate outcome. Therefore, among patients with documented cardiac arrest, survival was reported as a conservative indicator consistent with successful resuscitation and at least one episode of ROSC. Response outcomes, including hypotension reversal, wide-QRS resolution, arrhythmia resolution, and seizure cessation, were evaluated only in cases with the relevant abnormality at baseline and documented post-ILE status.

Exploratory subgroup analyses were conducted according to the timing from TCA ingestion to hospital

presentation, total administered ILE volume (≤ 500 vs. >500 mL), and cardiac-arrest status. These analyses were considered hypothesis generating, and no formal hypothesis testing was performed.

No missing data were imputed. Missing or unreported information was not interpreted as an absent or negative finding. Because the included evidence consisted of heterogeneous and uncontrolled case reports and case series, a quantitative meta-analysis was not performed. Findings were synthesized narratively, with attention to heterogeneity, incomplete reporting, concurrent treatments, publication bias, and selective outcome reporting. All analyses were performed using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria). This systematic review was not registered in PROSPERO or any other systematic review registry. A separate review protocol was not prepared. Therefore, there were no amendments to registration information or a review protocol.

Ethics

This review used data from published studies and did not involve direct interaction with human participants or the collection of identifiable patient data. The study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.ARI.MUI.REC.1404.149).

RESULTS

Study selection

A total of 613 records were identified through database and supplementary searches. After the removal of 249 duplicates, 364 records underwent title and abstract screening, of which 242 were excluded. Full-text reports were sought for 122 records; 67 could not be retrieved, and 55 were assessed for eligibility. Following the exclusion of 31 reports, 24 studies were included in the systematic review. Further details of the selection process and reasons for exclusion are presented in the PRISMA flow diagram [Figure 1]. The search was executed in the databases and captured records indexed through the end of 2025. Although the search did retrieve studies published in 2024 and 2025, upon full-text screening against our pre-defined eligibility criteria, none of these recent records met the inclusion threshold. The most common reasons for exclusion were insufficient outcome reporting and the use of fat emulsion types other than ILE. Consequently, the publication date range of the final included studies was 2009–2023.

Quality assessment and risk of bias

Detailed JBI critical appraisal results are presented in Supplementary Tables 5–8. All 20 case reports adequately described patient characteristics, clinical

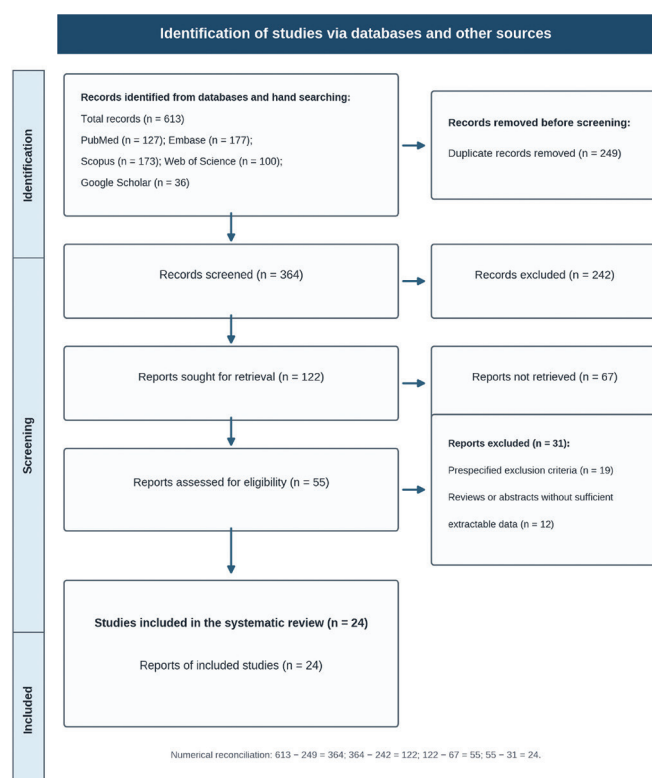


Figure 1: PRISMA 2020 flow diagram of study selection. The flow diagram summarizes the study-selection process. A total of 613 records were identified through database and hand searches. After removal of 249 duplicate records, 364 records were screened, and 242 were excluded on the basis of title and abstract. Reports were sought for 122 records; 67 reports could not be retrieved, and 55 reports were assessed for eligibility. Thirty-one reports were excluded: 19 according to the prespecified exclusion criteria and 12 because they were reviews or abstracts without sufficient extractable data. Ultimately, 24 reports representing 24 studies were included in the systematic review

history, presenting condition, diagnostic assessment, treatment, post-intervention condition, and key clinical lessons. Harms or unanticipated events were adequately addressed in 15 of the 20 reports, whereas five did not explicitly report this domain. Among the three case series and one registry-derived case series, three reported clear inclusion criteria, but only one clearly demonstrated consecutive and complete case inclusion. Demographic, clinical, and outcome reporting was otherwise generally adequate. Overall, the evidence remained vulnerable to selection and publication bias, incomplete reporting of adverse events, confounding by concurrent treatments, and selective reporting of favorable outcomes.

Baseline characteristics

The 24 included studies were published between 2009 and 2023 and comprised 20 case reports, three case series, and one registry-derived case series. All 20 case reports contributed one case each. The three case series contributed four, two, and one eligible TCA cases, respectively, whereas the registry-derived case series contributed 15 cases, resulting in a total of 42 cases.

The reports originated from 13 countries and one multinational online registry. Amitriptyline was the most frequently reported TCA. Other reported agents included imipramine, dosulepin/dothiepin, doxepin, nortriptyline, and amoxapine. Study-level characteristics and the specific TCA agents involved are presented in Table 1. Documentation of baseline severity domains varied across studies. Hypotension status was documented in all 24 studies, level-of-consciousness status in 22/24 studies, seizure status in 15/24 studies, and cardiac arrest status in 10/24 studies. ECG findings were documented in 23/24 studies, including QRS-widening status in 23/24 studies. Post-ILE documentation was less consistent. Blood pressure status and ECG findings were documented after ILE in 22/24 studies, whereas post-ILE QRS status was documented in 20/24 studies. Post-ILE seizure and arrest status were rarely recorded.

A case-level summary of demographics and baseline severity is reported in Table 2. Age was reported in 25/42 cases (59.5%), with a median age of 36 years (IQR: 25–45). Sex was reported in 26/42 cases (61.9%); among those, 20/26 (76.9%) were female. Baseline clinical severity was substantial among the 42 included cases, although reporting was incomplete across sources. Decreased level of consciousness was documented in 25/42 cases (59.5%) and was present in all reported instances (25/25, 100%). Hypotension was reported in 26/42 cases (61.9%), occurring in 21/26 (80.8%). Seizures were reported in 19/42 cases (45.2%) and were present in 15/19 (78.9%). Cardiac arrest status was available in 14/42 cases (33.3%), with arrest documented in 8/14 (57.1%). Tachycardia (heart rate >100 beats/min) was reported in 23/42 cases (54.8%) and was present in 17/23 (73.9%). Baseline electrocardiographic findings were frequently abnormal where documented. Any abnormal ECG was reported in 27/42 cases (64.3%) and was abnormal in 24/27 (88.9%). Wide QRS was reported in 26/42 cases (61.9%) and was present in 21/26 (80.8%). Arrhythmias were reported in 19/42 cases (45.2%) and were present in 13/19 (68.4%). Prolonged QT was reported in 14/42 cases (33.3%) and was present in 9/14 (64.3%). Among cases with extractable numeric values, the median heart rate was 130 beats/min (IQR: 107–140; 16/42, 38.1%), the median QRS duration was 178 ms (IQR: 136–196; 15/42, 35.7%), and the median QT interval was 488.5 ms (IQR: 432.8–535.0; available in 8/42 cases, 19.0%).

Pattern of intravenous lipid emulsion use

ILE concentration was explicitly reported in 18/42 cases (42.9%); when reported, it was almost always a 20% lipid emulsion (17/18, 94.4%), with 10% emulsion reported in 1/18 (5.6%). The brand name Intralipid

Table 1: Study-level characteristics and reporting availability

Study (first author, year)	Country	Design	n (TCA cases)	Specific TCA involved	Baseline domains documented	Outcomes/post-ILE domains documented
Al-Duaij, 2009 ^[11]	USA	Case report	1	Imipramine	DLOC, hypotension, seizure, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, arrhythmia, ECG
Engels, 2010 ^[12]	Canada	Case report	1	Amitriptyline	DLOC, hypotension, seizure, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: LOC, BP, ECG
Boegevig, 2011 ^[13]	Denmark	Case report	1	Dosulepin	DLOC, hypotension, seizure, ECG, WQRS, arrhythmia, QT	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Huge, 2011 ^[14]	Germany	Case report	1	Amitriptyline	DLOC, hypotension, arrest, ECG, WQRS, arrhythmia	Survival; Post-ILE: BP, QRS, arrhythmia, ECG
Blaber, 2012 ^[15]	UK	Case report	1	Dothiepin (dosulepin)	DLOC, hypotension, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Harvey, 2012 ^[16]	New Zealand	Case report	1	Amitriptyline	DLOC, hypotension, arrest, ECG, WQRS	Survival; post-ILE: BP, QRS, ECG
Hellig, 2012 ^[17]	South Africa	Case report	1	Amitriptyline	DLOC, hypotension, seizure, ECG, WQRS, QT	Survival; post-ILE: BP, QRS, ECG
Kiberd, 2012 ^[18]	Canada	Case report	1	Amitriptyline	Hypotension, seizure, arrest, ECG, WQRS	Survival; post-ILE: BP, QRS, ECG
Perza, 2013 ^[19]	USA	Case report	1	Doxepin	DLOC, hypotension, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Agarwala, 2014 ^[20]	USA	Case report	1	Amitriptyline	DLOC, hypotension, seizure, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Cave, 2014 ^[21]	Multi-country	Registry-derived case series	15	Amitriptyline and dosulepin/dothiepin	DLOC, hypotension	Survival
Eren Cevik, 2014 ^[22]	Turkey	Case series	4	Amitriptyline	DLOC, hypotension, seizure, arrest, ECG, WQRS, arrhythmia, QT	Survival
Radley, 2015 ^[23]	UK	Case report	1	Amitriptyline	DLOC, hypotension, ECG, WQRS	Survival; post-ILE: BP, QRS, ECG
İzci, 2015 ^[24]	Turkey	Case report	1	Amitriptyline	DLOC, hypotension, seizure, ECG, WQRS, QT	Survival; post-ILE: BP, QRS, ECG
Tse, 2015 ^[25]	Hong Kong	Case series	2	Amitriptyline	Hypotension, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Mason, 2016 ^[26]	USA	Case report	1	Nortriptyline	DLOC, hypotension, seizure, ECG, WQRS, arrhythmia, QT	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Ramasubbu, 2016 ^[27]	UK	Case report	1	Amitriptyline	DLOC, hypotension, seizure, ECG, WQRS, arrhythmia, QT	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Sabah, 2017 ^[28]	Bangladesh	Case report	1	Amitriptyline	DLOC, hypotension, ECG, WQRS, QT	Survival; post-ILE: BP, QRS, ECG
Berthe, 2017 ^[29]	Belgium	Case report	1	Amitriptyline	DLOC, hypotension, seizure, ECG, WQRS	Survival; post-ILE: BP, QRS, ECG
Lawner, 2019 ^[30]	USA	Case report	1	Nortriptyline	DLOC, hypotension, ECG, WQRS	Survival; post-ILE: BP, QRS, ECG,
Angel-Isaza, 2020 ^[31]	Colombia	Case report	1	Amitriptyline	DLOC, hypotension, seizure, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Akdemir, 2021 ^[32]	Turkey	Case report	1	Amitriptyline	DLOC, hypotension, seizure, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Estrada-Atehortua, 2022 ^[33]	Colombia	Case series	1	Amitriptyline	DLOC, hypotension, seizure, arrest, ECG, WQRS, arrhythmia	Survival; post-ILE: BP, QRS, arrhythmia, ECG
Matsuoka, 2023 ^[34]	Japan	Case report	1	Amoxapine	DLOC, hypotension, seizure, ECG, WQRS, QT	Survival; post-ILE: BP, QRS, ECG

n=Number of TCA cases, BP=Blood pressure, ECG=Electrocardiogram, ILE=Intravenous lipid emulsion, DLOC=Decreased level of consciousness, NR=Not reported, QRS=QRS complex, QT=QT interval, TCA=Tricyclic antidepressant, UK=United Kingdom, USA=United States of America, WQRS=Wide QRS complex, ROSC=Return of spontaneous circulation

was explicitly documented in 2/42 cases (4.8%). All ILE formulation, dosing, and timing characteristics are summarized in Table 3. Regimen structure (bolus

versus infusion) was identifiable in 27/42 cases (64.3%). Within the full case set, a bolus followed by infusion was reported in 21/42 cases (50.0%), infusion-only

Table 2: Case-level summary of demographics and baseline severity

Variable	Available data=n/42 (%)	Finding among available cases, n (%)	NR/missing=n/42 (%)
Age (years)	25/42 (59.5)	Median (IQR) 36 (25–45)	17/42 (40.5)
Sex	26/42 (61.9)	Female: 20/26 (76.9); Male: 6/26 (23.1)	16/42 (38.1)
Decreased level of consciousness	25/42 (59.5)	Present: 25/25 (100.0); Absent: 0/25 (0.0)	17/42 (40.5)
Hypotension	26/42 (61.9)	Present: 21/26 (80.8); Absent: 5/26 (19.2)	16/42 (38.1)
Seizures	19/42 (45.2)	Present: 15/19 (78.9); Absent: 4/19 (21.1)	23/42 (54.8)
Cardiac arrest	14/42 (33.3)	Present: 8/14 (57.1); Absent: 6/14 (42.9)	28/42 (66.7)
Tachycardia (HR >100 bpm)	23/42 (54.8)	Present: 17/23 (73.9); Absent: 6/23 (26.1)	19/42 (45.2)
Abnormal ECG	27/42 (64.3)	Present: 24/27 (88.9); Absent: 3/27 (11.1)	15/42 (35.7)
Arrhythmia	19/42 (45.2)	Present: 13/19 (68.4); Absent: 6/19 (31.6)	23/42 (54.8)
QRS widening	26/42 (61.9)	Present: 21/26 (80.8); Absent: 5/26 (19.2)	16/42 (38.1)
QT prolongation	14/42 (33.3)	Present: 9/14 (64.3); Absent: 5/14 (35.7)	28/42 (66.7)
Heart rate (bpm)	16/42 (38.1)	Median (IQR) - 130 (107–140)	26/42 (61.9)
QRS duration (ms)	15/42 (35.7)	Median (IQR) - 178 (136–196)	27/42 (64.3)
QT interval (ms)	8/42 (19.0)	Median (IQR) - 488.5 (432.8–535.0)	34/42 (81.0)

ECG=Electrocardiogram, HR=Heart rate, IQR=Interquartile range, NR=Not reported, QRS=QRS complex, QT=QT interval

Table 3: Intravenous lipid emulsion regimen characteristics

Variable	Available data=n/42 (%)	Finding among available cases	NR/missing=n/42 (%)
ILE concentration	18/42 (42.9)	20: 17/18 (94.4); 10: 1/18 (5.6)	24/42 (57.1)
Brand name	2/42 (4.8)	Intralipid: 2/2 (100.0)	40/42 (95.2)
Regimen pattern	27/42 (64.3)	Bolus + infusion: 21/27 (77.8); infusion only: 4/27 (14.8); bolus only: 2/27 (7.4)	15/42 (35.7)
Bolus status	27/42 (64.3)	Present: 23/27 (85.2); explicitly absent: 4/27 (14.8)	15/42 (35.7)
Initial bolus=absolute volume	20/42 (47.6)	Median 100 mL (IQR 100–100); range: 75–250 mL	22/42 (52.4)
Bolus=weight-based	6/42 (14.3)	1.5 mL/kg in 5 cases; repeated 3.125 mL/kg boluses ×4 with 10 emulsion in 1 case	36/42 (85.7)
Repeat bolus/re-bolus	5/42 (11.9)	Explicitly reported in 5 cases	37/42 (88.1); absence cannot be inferred
Infusion status	27/42 (64.3)	Present: 25/27 (92.6); explicitly absent: 2/27 (7.4)	15/42 (35.7)
Infusion rate	11/42 (26.2)	0.25 mL/kg/min: 8 cases; 0.5 mL/kg/min: 3 cases	31/42 (73.8)
Infusion duration for weight-based regimens	11/42 (26.2)	0.25 mL/kg/min: 10–120 min (median: 30 min); 0.5 mL/kg/min: 120 min	31/42 (73.8)
Fixed infusion rate	2/42 (4.8)	Approximately 16 mL/h and approximately 100 mL/h	40/42 (95.2); absence cannot be inferred
Total ILE volume	19/42 (45.2)	Median: 500 mL (IQR: 500–1000); range: 125–4300 mL	23/42 (54.8)
Time from ingestion to ILE administration	4/42 (9.5)	Median 11.5 h (IQR: 8.73–17.5); range: 1.92–34 h	38/42 (90.5)

ILE=Intravenous lipid emulsion, IQR=Interquartile range, NR=Not reported

regimens (no bolus stated) in 4/42 (9.5%), and bolus-only regimens in 2/42 (4.8%), while regimen structure was not extractable in the remaining 15/42 cases (35.7%). Overall, a bolus dose was reported in 23/42 cases (54.8%), was explicitly absent in 4/42 (9.5%), and was not reported in 15/42 (35.7%).

When bolus dosing was reported as an absolute volume (20/42 cases, 47.6%), the initial bolus was tightly clustered at 100 mL (median: 100 mL [IQR: 100–100], range: 75–250 mL). Weight-based bolus dosing was explicitly reported in 6/42 cases (14.3%), most commonly 1.5 mL/kg (5/6 cases); one case used repeated 3.125 mL/kg boluses (×4) with a 10% emulsion. Repeat

bolus or re-bolus dosing was explicitly documented in 5/42 cases (11.9%), including repeated boluses during the infusion course and delayed re-dosing in selected reports.

An infusion component was described in 25/42 cases (59.5%), was absent in 2/42 (4.8%), and was not reported in 15/42 (35.7%). A weight-based infusion rate was specified in 11/42 cases (26.2%), most commonly 0.25 mL/kg/min (8 cases), and less commonly 0.5 mL/kg/min (3 cases). Where duration could be extracted (the same 11/42 cases), infusions at 0.25 mL/kg/min typically lasted 10–120 min (median: 30 min), while 0.5 mL/kg/min was reported for 120 min.

Two reports described prolonged fixed-rate infusions (2/42, 4.8%), including approximately 16 mL/h (with additional bolus dosing) and approximately 100 mL/h as a longer course.

A usable total administered ILE volume was extractable in 19/42 cases (45.2%), with a median of 500 mL (IQR: 500–1000) and a range of 125–4300 mL, reflecting substantial heterogeneity and occasional prolonged infusion strategies. Time from ingestion to ILE administration was rarely reported 4/42 (9.5%), with a median of 11.5 h (IQR: 8.73–17.5) and a range of 1.92–34 h, indicating that timing was inconsistently documented across the included case evidence.

Concurrent treatments

Concurrent supportive and resuscitative treatments were incompletely and heterogeneously reported across the 42 included cases [Table 4]. Sodium bicarbonate was explicitly documented in 26/42 cases (61.9%), endotracheal intubation or mechanical ventilation in 21/42 (50.0%), vasopressors or inotropes in 16/42 (38.1%), gastrointestinal decontamination in 13/42 (31.0%), benzodiazepines or other anticonvulsants in 11/42 (26.2%), cardiopulmonary resuscitation in 8/42 (19.0%), defibrillation or cardioversion in 7/42 (16.7%), intravenous fluids or volume resuscitation in 7/42 (16.7%), and antiarrhythmic agents in 4/42 (9.5%). ECMO was not explicitly reported in any included case. Only one report explicitly stated that CPR was not performed; for most interventions, nonuse was not documented. Therefore, unreported information was classified as missing rather than absent, and these proportions represent minimum documented frequencies rather than true treatment-prevalence estimates.

Survival

Across the 42 included TCA-related cases, 41 patients survived (97.6%, exact 95% CI: 87.4–99.9), with one

reported death (2.4%, exact 95% CI: 0.06–12.6). The single fatality occurred in Lawner *et al.*, 2019. As a robustness check, excluding the registry-derived case series yielded a similar survival estimate (26/27; 96.3%, exact 95% CI: 81.0–99.9), indicating that the high observed survival was not driven solely by the registry component. Clinical outcomes across the included cases, including survival, arrest status, response endpoints, and reported adverse events, are summarized in Table 5.

Return of spontaneous circulation in cardiac arrest

Cardiac arrest status was reported for 14/42 cases (33.3%), with cardiac arrest present in 8/14 (57.1%). A standalone “ROSC” variable was not consistently reported across case narratives; however, all eight cardiac arrest cases survived (8/8; 100%), which is consistent with successful resuscitation and at least one episode of ROSC in each of these cases (exact 95% CI: 63.1–100).

Pre/post response endpoints

Pre/post response endpoints were evaluated only when both baseline status and post-ILE status were documented, which substantially limited the analyzable denominators within the 42-case dataset. Post-ILE hypotension status was available in 21/42 cases (50.0%); among cases with baseline hypotension and post-ILE documentation (17 cases), hypotension reversed in 14/17 (82.4%) (exact 95% CI: 56.6–96.2), whereas hypotension persisted in 3/17 (17.6%). Post-ILE wide-QRS status was available in 15/42 cases (35.7%); among cases with baseline wide QRS and post data (14 cases), QRS normalized in 6/14 (42.9%) (exact 95% CI: 17.7–71.1) and remained wide in 8/14 (57.1%). Post-ILE arrhythmia status was available in 9/42 cases (21.4%); among cases with baseline arrhythmia and post data (9 cases), arrhythmias resolved in 4/9 (44.4%) (exact 95% CI: 13.7–79.0) and persisted

Table 4: Concurrent supportive and resuscitative treatments reported among the included cases

Concurrent treatment	Available data, n/42 (%)	Present among available cases, n/N (%)	Explicitly absent, n/N (%)	NR/missing, n/42 (%)
Sodium bicarbonate	26/42 (61.9)	26/26 (100.0)	0/26 (0.0)	16/42 (38.1)
Vasopressors or inotropes	16/42 (38.1)	16/16 (100.0)	0/16 (0.0)	26/42 (61.9)
Antiarrhythmic agents	4/42 (9.5)	4/4 (100.0)	0/4 (0.0)	38/42 (90.5)
Endotracheal intubation or mechanical ventilation	21/42 (50.0)	21/21 (100.0)	0/21 (0.0)	21/42 (50.0)
CPR	9/42 (21.4)	8/9 (88.9)	1/9 (11.1)	33/42 (78.6)
Benzodiazepines or other anticonvulsants	11/42 (26.2)	11/11 (100.0)	0/11 (0.0)	31/42 (73.8)
Defibrillation or cardioversion	7/42 (16.7)	7/7 (100.0)	0/7 (0.0)	35/42 (83.3)
ECMO	0/42 (0.0)	0/0 (NE)	0/0 (NE)	42/42 (100.0)
Intravenous fluids or volume resuscitation	7/42 (16.7)	7/7 (100.0)	0/7 (0.0)	35/42 (83.3)
Gastrointestinal decontamination	13/42 (31.0)	13/13 (100.0)	0/13 (0.0)	29/42 (69.0)

CPR = Cardiopulmonary resuscitation; ECMO = Extracorporeal membrane oxygenation; NE = Not estimable; NR = Not reported

Table 5: Summary of clinical outcomes=evidence limitations=and clinical interpretation

Outcome	Available cases	Result (95% CI)	Key evidence limitations	Clinical interpretation
Survival	42	41/42 (97.6%; 95% CI 87.4–99.9)	Uncontrolled case reports/series; no comparator group; substantial publication and selection bias; multiple concurrent treatments	Reported survival was high, but a causal survival benefit from ILE cannot be established. Overall certainty: Very low
Survival among cardiac-arrest cases	8	8/8 (100.0%; 95% CI 63.1–100)	ROSC was not consistently reported as a standalone endpoint; survival was used as a conservative proxy. Resuscitative co-interventions were substantial	The finding is compatible with successful resuscitation but cannot be attributed independently to ILE. Overall certainty: Very low
Hypotension reversal	17	14/17 (82.4%; 95% CI 56.6–96.2)	Small denominator; paired pre/post data were incomplete; vasopressors, fluids, sodium bicarbonate, and other therapies were administered concurrently	Hemodynamic improvement was frequently reported, but the independent contribution of ILE remains uncertain. Overall certainty: Very low
Wide-QRS resolution	14	6/14 (42.9%; 95% CI 17.7–71.1)	Small denominator, wide confidence interval, incomplete serial ECG reporting, and concurrent sodium bicarbonate administration	Electrophysiologic improvement was inconsistent and cannot be separated from the effect of standard therapy. Overall certainty: Very low
Arrhythmia resolution	9	4/9 (44.4%; 95% CI 13.7–79.0)	Very small denominator, wide confidence interval, heterogeneous arrhythmias, and incomplete post-ILE documentation	No reliable conclusion can be drawn regarding an antiarrhythmic effect of ILE. Overall certainty: Very low
Seizure cessation	3	1/3 (33.3%; 95% CI 0.8–90.6)	Extremely sparse reporting; concurrent anticonvulsant and supportive treatment; very imprecise estimate	The available evidence is insufficient to assess whether ILE contributes to seizure cessation. Overall certainty: Very low
Adverse events	Not systematically monitored	ARDS, hypertriglyceridemia/lipemia with laboratory interference; and mild liver-test abnormalities were reported; registry data also described bronchospasm and hyperamylasemia	Safety reporting was incomplete and inconsistent; some registry adverse events were not TCA-stratified; causality was uncertain	The incidence of ILE-related adverse effects cannot be estimated. Careful respiratory, metabolic, and laboratory monitoring is warranted. Overall certainty: Very low

ARDS=Acute respiratory distress syndrome, CI=Confidence interval, ECG=Electrocardiogram, ILE=Intravenous lipid emulsion, QRS=QRS complex, ROSC=Return of spontaneous circulation, TCA=Tricyclic antidepressant

in 5/9 (55.6%). Seizure cessation was rarely documented after ILE; post-ILE seizure status was available in 7/42 cases (16.7%), but only three of these had seizures at baseline, among whom seizure cessation was reported in 1/3 (33.3%) (exact 95% CI: 0.8–90.6). Overall, in the subset of baseline-positive cases with post-intervention documentation, hemodynamic reversal (hypotension) was reported more frequently than electrophysiologic normalization (wide QRS or arrhythmia), whereas seizure outcomes were too sparsely reported to support stable inference. The distribution of response rates across hemodynamic and electrophysiologic endpoints is detailed in Table 6.

Adverse events

Reported adverse events by case and source confirming the nature and context of each event are detailed in Table 7. Across the 42 included cases, explicit adverse event reporting related to ILE was infrequent and inconsistently documented, limiting any inference about

incidence. In the detailed case narratives (where case-level safety descriptions were available), reported events were predominantly metabolic or respiratory and were generally described as transient. One TCA case (Radley, 2015) developed acute respiratory distress syndrome (ARDS) after ILE during management of severe amitriptyline toxicity; the report raised concern that ILE may have contributed, although confounding from critical illness and aspiration/infection risk was emphasized, so causality remains uncertain. One amitriptyline case (Tse, 2015) developed marked hypertriglyceridemia with gross lipemia, with triglycerides rising from 1.95 mmol/L pre-ILE to a peak of 22.13 mmol/L at one hour and falling to 2.94 mmol/L by 14 h; during the lipemic period, laboratory analysis of electrolytes and liver function tests was not feasible for several samples, indicating clinically meaningful laboratory interference. Mild liver function derangement was reported in two amitriptyline cases in the same poison-center series, although attribution to ILE was

Table 6: Clinical outcomes across included cases

Outcome	Analyzable data	Positive event/ response	Negative event/ nonresponse	Exact 95% CI for positive proportion	Missing/NR/not assessable
Survival	42/42	41/42 (97.6%)	Death: 1/42 (2.4%)	87.4–99.9	0/42
Cardiac arrest present	14/42	8/14 (57.1%)	No arrest: 6/14 (42.9%)	28.9–82.3	28/42 NR
Survival among documented arrest cases (proxy for at least one ROSC)	8/8 arrest cases	8/8 (100.0%)	Death: 0/8 (0.0%)	63.1–100.0	Standalone ROSC was NR/inconsistently reported
Hypotension reversal	17/42	14/17 (82.4%)	Persistent hypotension: 3/17 (17.6%)	56.6–96.2	25/42 not assessable
Wide-QRS resolution	14/42	6/14 (42.9%)	Persistent wide QRS: 8/14 (57.1%)	17.7–71.1	28/42 not assessable
Arrhythmia resolution	9/42	4/9 (44.4%)	Persistent arrhythmia: 5/9 (55.6%)	13.7–78.8	33/42 not assessable
Seizure cessation	3/42	1/3 (33.3%)	Persistent/recurrent seizure: 2/3 (66.7%)	0.8–90.6	39/42 not assessable

CI=Confidence interval, NR=Not reported, QRS=QRS complex, ROSC=Return of spontaneous circulation

Table 7: Explicitly reported adverse events by case/source

Source	Adverse event (s)	Brief description	Reporting classification
Radley <i>et al.</i> , 2015 ^[23]	ARDS	ARDS was reported after ILE; attribution was uncertain because of confounding by critical illness	Explicitly reported event
Tse <i>et al.</i> , 2015 ^[25] , Case 2	Mild LFT derangement	Mild liver enzyme/bilirubin abnormalities were reported; causality was uncertain	Explicitly reported event
Tse <i>et al.</i> , 2015 ^[25] , Case 3	Hypertriglyceridemia/lipemia; laboratory interference; LFT derangement	Triglycerides increased from 1.95 to 22.13 mmol/L at 1 h and decreased to 2.94 mmol/L by 14 h; lipemia prevented analysis of electrolytes/LFTs	Explicitly reported event
Cave <i>et al.</i> , 2014 ^[21]	Bronchospasm; hyperamylasemia; laboratory interference		Explicitly listed; details incomplete in manuscript

ARDS=Acute respiratory distress syndrome, ILE=Intravenous lipid emulsion, LFT=Liver function test

uncertain and may have reflected hypotension or critical illness. In the available TCA case evidence, pancreatitis, fat overload syndrome, and embolic complications were not reported.

Exploratory analyses

Exploratory subgroup analyses were conducted to describe clinical and reporting patterns rather than to estimate treatment effects. Time from TCA ingestion to hospital presentation was available for eight cases. Survival was reported in all five cases presenting within 2 h of ingestion and in all three cases presenting more than 2 h after ingestion. Total administered ILE volume was available for 19 cases. Survival was reported in all 12 cases receiving a total volume of ≤ 500 mL and in all seven cases receiving >500 mL. Documented hypotension improvement appeared more frequent than QRS or arrhythmia improvement in several descriptive strata; however, outcome-specific denominators were small and differed across endpoints, precluding formal comparisons. Cardiac arrest status was available for 14 cases: survival was reported in all eight cases with documented cardiac arrest, whereas one death occurred among the six cases in which cardiac arrest was explicitly absent.

These findings should be considered hypothesis-generating only because of the small subgroup sizes, substantial missing data, heterogeneous outcome reporting, concurrent treatments, and likely selection and reporting bias. Detailed exploratory subgroup results are presented in Table 8.

DISCUSSION

Principal findings

Across 24 studies including 42 TCA-related cases, amitriptyline was the most frequently reported agent, and ILE was generally used as an adjunctive rescue therapy alongside standard treatments. Survival was reported in 41/42 cases, including all eight documented cardiac-arrest cases, although outcomes could not be attributed to ILE because of concurrent interventions. Hypotension improvement was reported more often than QRS or arrhythmia improvement, while seizure and safety outcomes were sparsely documented. Three cases from two sources described potentially relevant adverse events, but causality remained uncertain. Overall, this case-level review provides a TCA-specific synthesis of ILE regimens, responses, co-interventions, and harms, but the evidence remains highly uncertain because of uncontrolled study designs, missing data, reporting bias, and confounding.

Table 8: Exploratory subgroup analyses with exact 95% confidence intervals

Exploratory subgroup	Survival	Hypotension reversal*	Wide-QRS resolution*	Arrhythmia resolution*	Seizure cessation*
Time from TCA ingestion to hospital presentation ≤2 h (n=5)	5/5 (100.0%; 47.8–100.0)	3/3 (100.0%; 29.2–100.0)	NR	NR	NR
Time from TCA ingestion to hospital presentation >2 h (n=3)	3/3 (100.0%; 29.2–100.0)	1/1 (100.0%; 2.5–100.0)	2/2 (100.0%; 15.8–100.0)	1/1 (100.0%; 2.5–100.0)	NR
Dose ≤500 mL (n=12)	12/12 (100.0%; 73.5–100.0)	7/7 (100.0%; 59.0–100.0)	4/6 (66.7%; 22.3–95.7)	2/2 (100.0%; 15.8–100.0)	1/1 (100.0%; 2.5–100.0)
Dose >500 mL (n=7)	7/7 (100.0%; 59.0–100.0)	3/4 (75.0%; 19.4–99.4)	1/3 (33.3%; 0.8–90.6)	1/3 (33.3%; 0.8–90.6)	NR
Arrest (n=8)	8/8 (100.0%; 63.1–100.0)	4/5 (80.0%; 28.4–99.5)	1/4 (25.0%; 0.6–80.6)	2/4 (50.0%; 6.8–93.2)	NR
No arrest (n=6)	5/6 (83.3%; 35.9–99.6)	2/3 (66.7%; 9.4–99.2)	0/1 (0.0%; 0.0–97.5)	0/1 (0.0%; 0.0–97.5)	NR

NR=Not reported, QRS=QRS complex, TCA=Tricyclic antidepressant

Clinical interpretation

The high reported survival proportion should be interpreted cautiously because the evidence was derived from uncontrolled published cases subject to publication bias, selective reporting, incomplete follow-up, and confounding by concurrent treatments. Although hemodynamic improvement was reported more frequently than electrophysiologic recovery, these findings are only hypothesis-generating, and the proposed lipid sink/shuttle and cardiotoxic mechanisms remain unconfirmed. Sodium bicarbonate remains the cornerstone of treatment for TCA-induced QRS widening and hemodynamic instability; ILE should be considered only as an adjunct in selected severe or refractory cases and should not replace standard therapy.

Influence of concurrent treatments

Concurrent supportive and resuscitative treatments made it impossible to isolate the independent contribution of ILE. Therefore, reported survival and clinical improvements should be interpreted as descriptive observations rather than evidence of efficacy. ILE should be considered only as an adjunctive rescue therapy in selected severe or refractory cases and should not replace or delay established treatments.

Consistency with prior evidence and guidance

Controlled evidence for ILE in TCA poisoning remains limited. Animal studies have shown amitriptyline sequestration without consistent hemodynamic benefit, and a controlled swine study found no improvement in hypotension compared with sodium bicarbonate.^[6] Accordingly, professional guidance assigns ILE only a limited adjunctive role. AACT discourages first-line use but allows consideration after standard treatments fail,^[7] while ACMT supports individualized use in severe instability without defining ILE as standard care.^[8] The 2025 AHA guidelines prioritize sodium bicarbonate and standard resuscitative measures for life-threatening TCA cardiotoxicity and consider ILE reasonable

only in selected refractory sodium-channel blocker poisoning.^[35] The findings of this review support this cautious approach: ILE was generally used alongside multiple treatments in severe or refractory cases, and its independent contribution could not be determined. Therefore, ILE should be regarded as an individualized rescue adjunct rather than routine, early, or first-line therapy. A comparison of AACT, ACMT, AHA, and the present review is provided in Table 9.

Dose, timing, and practice variation

ILE dosing strategies varied substantially across the included reports. Among cases with available concentration data, a 20% lipid emulsion predominated, and a bolus followed by infusion was the most commonly documented regimen. The reported initial bolus was commonly 100 mL or 1.5 mL/kg, whereas the most frequently documented weight-based infusion rate was 0.25 mL/kg/min. Total administered volumes ranged from 125 to 4300 mL, indicating marked variability in reported clinical practice. Time from TCA ingestion to ILE administration was reported in only 4/42 cases (9.5%). Given the substantial missing data and extremely small number of cases with timing information, no reliable comparison of earlier versus later ILE administration was possible, and no conclusions could be drawn regarding the optimal timing of ILE.

Safety considerations

Safety reporting was limited and inconsistent, so the few documented complications should not be interpreted as evidence of ILE safety. Reported events included ARDS, hypertriglyceridemia and lipemia with laboratory interference, and mild liver biochemical abnormalities, although causality was uncertain. Pancreatitis and fat-overload syndrome were not reported, but incomplete monitoring prevents assuming that they did not occur. Future studies should use predefined safety outcomes and systematic respiratory, metabolic, pancreatic, hepatic, and laboratory monitoring.

Table 9: Comparison of professional recommendations with the findings of the present review

Guidance document	Recommendation relevant to TCA poisoning	Strength or basis	Findings of the present review	Interpretation
AACT-led collaborative evidence-based recommendations, 2016 ^[7]	ILE is not recommended as first-line therapy in life-threatening amitriptyline toxicity. It may be considered only after other therapies fail or as a last-resort intervention. The recommendation is neutral for cardiac arrest caused by amitriptyline or other TCAs, and ILE is discouraged in non-life-threatening TCA toxicity	The recommendation for rescue use in refractory amitriptyline toxicity was graded 2D and was based mainly on very-low-quality evidence. The guidance was developed by a multi-association lipid emulsion therapy workgroup	ILE was generally administered in severe or refractory presentations and usually alongside intensive standard treatment. Survival was reported in 41/42 cases; however, the evidence was uncontrolled. Hypotension reversal was reported in 14/17 cases, whereas wide-QRS resolution and arrhythmia resolution were reported in 6/14 and 4/9 cases, respectively	The review is consistent with considering ILE only as a rescue option in refractory, life-threatening toxicity. It does not support routine or first-line use and cannot resolve the uncertainty regarding ILE during cardiac arrest
ACMT position statement, 2017 ^[8]	There is no standard-of-care requirement either to administer or to withhold ILE. It may be considered individually in serious hemodynamic or other instability caused by a highly lipid-soluble xenobiotic, particularly when the patient does not respond to standard resuscitation measures. Consultation with a medical toxicologist is advised where possible	Expert position statement rather than a TCA-specific treatment guideline. It also states that no validated evidence-based ILE dosing regimen exists	The included cases showed substantial heterogeneity in ILE concentration, dose, timing, infusion duration, total administered volume, monitoring, and adverse-event reporting. Multiple concurrent treatments were common, preventing separation of the independent effect of ILE	The findings support ACMT's cautious and individualized approach. They do not establish a mandatory indication for ILE or a validated TCA-specific administration regimen
AHA guidelines, 2025 ^[35]	Sodium bicarbonate should be used for adults with life-threatening cardiotoxicity from TCA or tetracyclic antidepressant poisoning. ILE may be reasonable only for life-threatening sodium-channel-blocker poisoning that remains refractory to other treatments. ECLS is reasonable for refractory cardiogenic shock, and class Ib antiarrhythmics such as lidocaine may be considered in selected sodium-channel-blocker poisonings	Sodium bicarbonate: Class 1, Level B-NR in adults. ILE after failure of other treatment modalities: Class 2b, Level C-EO. ECLS for refractory cardiogenic shock: Class 2a, Level C-EO	Sodium bicarbonate and other supportive or resuscitative therapies were frequently administered concurrently with ILE. Clinical improvement was more commonly documented for hypotension than for QRS or arrhythmia outcomes, and the independent contribution of ILE could not be determined	The review supports the AHA treatment hierarchy: sodium bicarbonate and standard resuscitation remain primary, whereas ILE has only a limited adjunctive role in refractory life-threatening toxicity and should not delay ECLS when indicated and available

AACT=American Academy of Clinical Toxicology, ACMT=American College of Medical Toxicology, AHA=American Heart Association, ECLS=Extracorporeal life support, ILE=Intravenous lipid emulsion, QRS=QRS complex, TCA=Tricyclic antidepressant

Limitations

This review was constrained by an evidence base dominated by single-case reports and small case series, with substantial selection and publication bias, heterogeneous co-interventions, and incomplete reporting of severity, treatment timing, and outcomes. Inconsistent documentation of concurrent treatments and their timing prevented estimation of both their true frequency and the independent contribution of ILE. Pre/post responses were assessable only in selectively reported subsets, while registry data were not fully TCA-stratified, particularly for adverse events. The predominance of amitriptyline cases also limits generalizability to other TCAs. Another limitation of this review was the high number of reports that could not be retrieved. Of the 122 reports sought for retrieval, 67 (54.9%) could not be obtained

despite efforts to access the full texts, including contacting authors by email and using our university library services. Resource-access limitations in Iran contributed to the inability to retrieve these reports. This poses a substantial risk of selection bias, as the findings of the unavailable reports may systematically differ from those of the included studies. Consequently, our synthesized findings may not fully represent the entire body of evidence, and the conclusions should therefore be interpreted with caution. A practical summary of the potential indications, timing, monitoring requirements, adverse effects, and limitations of ILE use in severe TCA poisoning is presented in Table 10.

Implication of the critical appraisal

The JBI appraisal identified substantial methodological limitations, including uncontrolled study designs,

Table 10: Practical considerations for intravenous lipid emulsion in tricyclic antidepressant poisoning

Clinical domain	Practical considerations
Role and patient selection	ILE is not recommended for routine or first-line treatment of TCA poisoning. It may be considered as an individualized rescue adjunct in selected patients with refractory, life-threatening hypotension, shock, malignant ventricular dysrhythmia, or cardiac arrest despite standard treatment, preferably after consultation with a medical toxicologist or poison control center ^[7,8,35]
When ILE is not indicated	ILE should not be used prophylactically, in asymptomatic patients, or in mild or moderate toxicity responding to supportive care. Lipophilicity of the TCA or a large reported dose alone is not an indication ^[3,7,8]
Timing and standard treatment	No evidence-based ingestion-to-ILE interval has been established. Decisions should be based on clinical severity and failure of established therapy. ILE must not replace or delay sodium bicarbonate, airway management, ventilation, vasopressors, benzodiazepines, defibrillation, or high-quality cardiopulmonary resuscitation ^[7,8,35]
Formulation and dosing	No validated TCA-specific regimen exists. When ILE is selected, a 20% lipid emulsion may be administered according to an institutional or toxicology protocol. ACMT guidance describes a 1.5 mL/kg bolus over 2–3 minutes followed by 0.25 mL/kg/min, with early reassessment and cautious consideration of repeat dosing ^[3,8]
Clinical monitoring and response	Monitor cardiac rhythm, heart rate, QRS duration, QT interval, blood pressure, perfusion, oxygenation, respiratory and neurological status, seizure activity, vasopressor requirements, and return of spontaneous circulation. Improvement should not automatically be attributed to ILE because concurrent treatments may have contributed ^[3,8]
Laboratory monitoring and safety	When feasible, monitor triglycerides, glucose, electrolytes, renal and liver function, acid–base status, and pancreatic enzymes when indicated. Potential complications include hypertriglyceridemia, lipemia and laboratory interference, pancreatitis, acute lung injury or ARDS, bronchospasm, fat-overload syndrome, liver-test abnormalities, hypersensitivity, and embolic or extracorporeal-circuit complications ^[3,21,23,25,36]
Evidence limitations	Evidence is based mainly on uncontrolled case reports and small case series with publication bias, heterogeneous co-interventions, incomplete reporting, and inconsistent safety monitoring. ILE use should therefore remain selective and adjunctive, and efficacy cannot be inferred from the high survival reported in published cases

ACMT=American College of Medical Toxicology, ARDS=Acute respiratory distress syndrome, ILE=Intravenous lipid emulsion, TCA=Tricyclic antidepressant

frequent concurrent treatments, incomplete case selection, and inconsistent adverse-event reporting. Therefore, reported improvements cannot be attributed to ILE, and the findings remain hypothesis-generating rather than supportive of routine or first-line use in TCA poisoning.

Certainty of evidence and strength of recommendations

Evidence for ILE in TCA poisoning remains highly uncertain because it is based mainly on uncontrolled case reports and small series with heterogeneous regimens, incomplete reporting, concurrent treatments, and substantial bias. Its independent contribution cannot be determined, and current evidence does not support routine or first-line use. ILE may be considered only as an individualized rescue adjunct in refractory, life-threatening cases after standard treatments have been optimized; sodium bicarbonate remains the cornerstone of therapy and should not be delayed or replaced.

CONCLUSION

In published human cases of TCA poisoning, ILE has been used mainly as a rescue adjunct and is associated with high reported survival and frequent descriptions of hemodynamic improvement. However, the evidence is dominated by uncontrolled case reports/series with

substantial reporting bias and incomplete outcome documentation. Accordingly, the findings do not establish the effectiveness or safety of ILE in all TCA poisoning cases. More research is needed to support the routine or first-line use of ILE in TCA toxicity; it may be considered for refractory, life-threatening presentations alongside standard therapies, with careful monitoring for potential harms.

Data availability statement

The data-extraction form, extracted case-level data, and analytic code used in this systematic review are not publicly available but may be obtained from the corresponding author upon reasonable request. All data analyzed in this review were derived from the published studies cited in the manuscript and its supplementary materials.

Author contributions

A.S. contributed to the conceptualization and methodology of the study, literature screening, data extraction, quality assessment, formal analysis, and visualization. A.O. contributed to conceptualization, methodology, study screening, and supervision. N.A. contributed to study screening, data extraction, data analysis, visualization, and preparation of the original manuscript draft. A.T. developed the literature search strategy and contributed to visualization. R.M., M.K., and A.M.S. contributed to study screening and

validation of the extracted data. N.E.M. contributed to methodology, supervision, and critical revision of the manuscript. All authors reviewed and approved the final version of the manuscript and agreed to be accountable for the accuracy and integrity of the work.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Vasquez V, Lara B, Basauri S. Tricyclic antidepressant poisoning. *ARS Med (Santiago)* 2023;48:31-8.
- Rothschild L, Bern S, Oswald S, Weinberg G. Intravenous lipid emulsion in clinical toxicology. *Scand J Trauma Resusc Emerg Med* 2010;18:51.
- Jaffal K, Chevillard L, Mégarbane B. Lipid emulsion to treat acute poisonings: Mechanisms of action, indications, and controversies. *Pharmaceutics* 2023;15:1396.
- Nendumba G, Blackman S, De Lissnyder N, Cillis M, Honore PM. Use of intravenous lipid emulsions in drug-induced toxicities: A 2025 narrative review. *Ann Intensive Care* 2025;15:181.
- Bilvanisi S, Gülen M, Sabak M, Demiryürek Ş, Demiryürek AT. Intravenous lipid emulsion therapy in drug overdose and poisoning: An updated review. *Eurasian J Med* 2024;56:205-12.
- Litonius E, Niiya T, Neuvonen PJ, Rosenberg PH. No antidotal effect of intravenous lipid emulsion in experimental amitriptyline intoxication despite significant entrapment of amitriptyline. *Basic Clin Pharmacol Toxicol* 2012;110:378-83.
- Gosselin S, Hoegberg LC, Hoffman RS, Graudins A, Stork CM, Thomas SH, et al. Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning. *Clin Toxicol (Phila)* 2016;54:899-923.
- American College of Medical Toxicology. ACMT Position Statement: Guidance for the Use of Intravenous Lipid Emulsion. *J Med Toxicol.* 2017 Mar;13(1):124-125. doi:10.1007/s13181-016-0550-z. Epub 2016 Apr 27. Erratum in: *J Med Toxicol* 2016;12:416. [doi:10.1007/s13181-016-0554-8].
- Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. JBI Critical Appraisal Checklist for Case Reports. Adelaide: Joanna Briggs Institute; 2017. Available from: https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-checklist_for_Case_Reports2017_0.pdf. [Last accessed on 2026 August 12].
- Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies: An introduction to the JBI critical appraisal tool. *JBI Evid Synth* 2020;18:2127-33.
- Al-Duaij N, George M, O'Donnell K, Burns Ewald M. Lipid emulsion therapy in massive imipramine overdose [abstract]. *Clin Toxicol (Phila)* 2009;47:460.
- Engels PT, Davidow JS. Intravenous fat emulsion to reverse haemodynamic instability from intentional amitriptyline overdose. *Resuscitation* 2010;81:1037-9.
- Boegevig S, Rothe A, Tfelt-Hansen J, Hoegberg LC. Successful reversal of life threatening cardiac effect following dosulepin overdose using intravenous lipid emulsion. *Clin Toxicol (Phila)* 2011;49:337-9.
- Huge V, Baschnegger H, Moehle P, Peraud A, Briegel J. Amitriptyline-induced cardiac arrest: Treatment with fat emulsion. *Anaesthesist* 2011;60:541-5.
- Blaber MS, Khan JN, Brebner JA, McColm R. Lipid rescue for tricyclic antidepressant cardiotoxicity. *J Emerg Med* 2012;43:465-7.
- Harvey M, Cave G. Case report: Successful lipid resuscitation in multi-drug overdose with predominant tricyclic antidepressant toxidrome. *Int J Emerg Med* 2012;5:8.
- Hellig J, von Watzdorf I, Lahri S, Vallabh K, Allgaier RL. Chewing the fat: A case report on intravenous lipid emulsion to reverse cardiotoxicity from intentional amitriptyline overdose. *Afr J Emerg Med* 2012;2:159-62.
- Kiberd MB, Minor SF. Lipid therapy for the treatment of a refractory amitriptyline overdose. *CJEM* 2012;14:193-7.
- Perza MN, Schneider LA, Rosini JM. Suspected tricyclic antidepressant overdose successfully treated with lipids. *J Emerg Nurs* 2013;39:296-8.
- Agarwala R, Ahmed SZ, Wiegand TJ. Prolonged use of intravenous lipid emulsion in a severe tricyclic antidepressant overdose. *J Med Toxicol* 2014;10:210-4.
- Cave G, Harvey M, Willers J, Uncles D, Meek T, Picard J, et al. LIPAEMIC report: Results of clinical use of intravenous lipid emulsion in drug toxicity reported to an online lipid registry. *J Med Toxicol* 2014;10:133-42.
- Eren Cevik S, Tasyurek T, Guneyzel O. Intralipid emulsion treatment as an antidote in lipophilic drug intoxications. *Am J Emerg Med* 2014;32:1103-8.
- Radley D, Droog S, Barragry J, Bigham C. Survival following massive amitriptyline overdose: The use of intravenous lipid emulsion therapy and the occurrence of acute respiratory distress. *J Intensive Care Soc* 2015;16:181-2.
- İzci F, İzci S, Acar E, İzci V. The treatment of a patient with intravenous lipid emulsion infusion after amitriptyline overdose which caused in QRS interval prolongation: A case report. *New Symposium* 2015;53:37-40.
- Tse CW, Chan YC, Lau FL. Intravenous lipid emulsion as antidote: Experience in Hong Kong. *Hong Kong J Emerg Med* 2015;22:100-7.
- Mason R, Hurley W, Utarnachitt RB. Intravenous fat emulsion (IFE) improvement of QT-interval in tricyclic antidepressant overdose. *Emerg Med Open J* 2016;2:23-6.
- Ramasubbu B, James D, Scurr A, Sandilands EA. Serum alkalisation is the cornerstone of treatment for amitriptyline poisoning. *BMJ Case Rep* 2016;2016:bcr2016214685.
- Sabah KM, Chowdhury AW, Islam MS, Saha BP, Kabir SR, Kawser S. Amitriptyline-induced ventricular tachycardia: A case report. *BMC Res Notes* 2017;10:286.
- Berthe G, Tonglet M, Bertrand X, Degesves S. How I treat a poisoning with tricyclic antidepressants: Potential role of a treatment with lipid emulsion. *Rev Med Liege* 2017;72:6-9.
- Lawner BJ, Mbah N, Bailey S, Erickson H, Poremba M. Interfacility critical care transport of an elderly patient with confirmed tricyclic antidepressant toxicity and hemodynamic collapse. *Air Med J* 2019;38:377-81.
- Angel-Isaza AM, Bustamante-Cristancho LA, Uribe-B FL. Successful outcome following intravenous lipid emulsion rescue therapy in a patient with cardiac arrest due to amitriptyline overdose. *Am J Case Rep* 2020;21:e922206.

32. Akdemir HU, Cenik Y, Uras M, Ünal Akdemir N. Successful treatment with intravenous lipid emulsion of severe tricyclic antidepressant intoxication. *J Exp Clin Med* 2021;38:43-6.
33. Estrada-Atehortua AF, Quiroz-Alvarez JE, Arroyave-Peña T. Use of lipid emulsions in tricyclic antidepressant intoxication from the emergency department: A series of cases. *Rev Toxicol* 2022;39:36-40.
34. Matsuoka M, Imai T, Iwabuchi S, Kinoshita K. Successful treatment of amoxapine-induced intractable seizures with intravenous lipid emulsion. *J Emerg Med* 2023;64:62-6.
35. Cao D, Arens AM, Chow SL, Easter SR, Hoffman RS, Lagina AT 3rd, *et al.* Part 10: Adult and pediatric special circumstances of resuscitation: 2025 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2025;152:S578-672.
36. Hayes BD, Gosselin S, Calello DP, Nacca N, Rollins CJ, Abourbih D, *et al.* Systematic review of clinical adverse events reported after acute intravenous lipid emulsion administration. *Clin Toxicol (Phila)* 2016;54:365-404.

SEARCH LINES WITHIN EACH DATABASE

Supplementary Table 1: PubMed database

Line	Query
#1	"Cyclic Antidepress*" OR "Tricyclic Antidepress*" OR "TCA" OR Amitriptyline OR Imipramine OR Clomipramine OR Desipramine OR Nortriptyline OR Doxepin OR Protriptyline OR Trimipramine OR Amoxapine OR Dothiepin OR Maprotiline OR Dibenzepin OR Opipramol OR Dosulepin OR Lofepramine OR Butriptyline OR Iprindole OR Melitracen OR Noxiptiline OR Quinupramine OR Clomipramine
#2	Poisoning OR Overdos* OR Toxic* OR Intoxication OR "adverse effect" OR Complication
#3	(#1 AND #2) OR "Antidepressant Toxicity"
#4	("Antidepressive Agents, Tricyclic/adverse effects"[Majr] OR "Antidepressive Agents, Tricyclic/poisoning"[Majr] OR "Antidepressive Agents, Tricyclic/toxicity"[Majr])
#5	(#3 OR #4)
#6	Intralipid OR "Lipid Emulsion" OR "ILE" OR "Lipid Rescue" OR "Fat Emulsion" OR "Lipid Injection" OR "Liposyn" OR "SMOFlipid" OR "intravenous lipid" OR "Lipid Infusion" OR Intrafat OR "phospholipid emulsion" OR "Lipophilic drug*" OR Lipofundin OR lipovenoes OR "lipid suspension"
Combine	(#5 AND #6) 127 documents found

ILE = Intravenous lipid emulsion, Majr = MeSH major topic, MeSH = Medical subject headings, TCA = Tricyclic antidepressant

Supplementary Table 2: Scopus database

Query
(((TITLE-ABS-KEY ("Cyclic Antidepress*" OR "Tricyclic Antidepress*" OR "TCA" OR Amitriptyline OR Imipramine OR Clomipramine OR Desipramine OR Nortriptyline OR Doxepin OR Protriptyline OR Trimipramine OR Amoxapine OR Dothiepin OR Maprotiline OR Dibenzepin OR Opipramol OR Dosulepin OR Lofepramine OR Butriptyline OR Iprindole OR Melitracen OR Noxiptiline OR Quinupramine OR Clomipramine) AND TITLE-ABS-KEY (Poisoning OR Overdos* OR Toxic* OR Intoxication OR "adverse effect" OR Complication)) OR TITLE-ABS-KEY (Antidepressant PRE/2 Toxic*)) AND TITLE-ABS-KEY (Intralipid OR "Lipid Emulsion" OR "ILE" OR "Lipid Rescue" OR "Fat Emulsion" OR "Lipid Injection" OR "Liposyn" OR "SMOFlipid" OR "intravenous lipid" OR "Lipid Infusion" OR Intrafat OR "phospholipid emulsion" OR "Lipophilic drug*" OR Lipofundin OR lipovenoes OR "lipid suspension")) 173 documents found
ILE=Intravenous lipid emulsion, PRE/2=Scopus proximity operator requiring terms to appear in the specified order within two words, TCA=Tricyclic antidepressant, TITLE-ABS-KEY=Title, abstract, and keyword fields

Supplementary Table 3: Web of science (core collection)

Line	Search Query	Results
#1	"Cyclic Antidepress*" OR "Tricyclic Antidepress*" OR "TCA" OR Amitriptyline OR Imipramine OR Clomipramine OR Desipramine OR Nortriptyline OR Doxepin OR Protriptyline OR Trimipramine OR Amoxapine OR Dothiepin OR Maprotiline OR Dibenzepin OR Opipramol OR Dosulepin OR Lofepramine OR Butriptyline OR Iprindole OR Melitracen OR Noxiptiline OR Quinupramine OR Clomipramine (Topic)	62,632
#2	Poisoning OR Overdos* OR Toxic* OR Intoxication OR "adverse effect" OR Complication (Topic)	2,669,369
#3	TS=(Antidepress* NEAR/1 Toxicity)	127
#4	#2 AND #1	5908
#5	#4 OR #3	5960
#6	TS=(Intralipid OR "Lipid Emulsion" OR "ILE" OR "Lipid Rescue" OR "Fat Emulsion" OR "Lipid Injection" OR "Liposyn" OR "SMOFlipid" OR "intravenous lipid" OR "Lipid Infusion" OR Intrafat OR "phospholipid emulsion" OR "Lipophilic drug*" OR Lipofundin OR lipovenoes OR "lipid suspension")	32,338
#7	#5 AND #6	100

ILE=Intravenous lipid emulsion, NEAR/1=Proximity operator within one word, TCA=Tricyclic antidepressant, TS=Topic search

Line	Query	Results
#1	“cyclic antidepress*”:ti, ab, kw OR “tricyclic antidepress*”:ti, ab, kw OR “tca”:ti, ab, kw OR amitriptyline: ti, ab, kw OR imipramine: ti, ab, kw OR desipramine: ti, ab, kw OR nortriptyline: ti, ab, kw OR doxepin: ti, ab, kw OR protriptyline: ti, ab, kw OR trimipramine: ti, ab, kw OR amoxapine: ti, ab, kw OR dothiepin: ti, ab, kw OR maprotiline: ti, ab, kw OR dibenzepin: ti, ab, kw OR opipramol: ti, ab, kw OR dosulepin: ti, ab, kw OR lofepramine: ti, ab, kw OR butriptyline: ti, ab, kw OR iprindole: ti, ab, kw OR melitracen: ti, ab, kw OR noxiptiline: ti, ab, kw OR quinupramine: ti, ab, kw OR clomipramine: ti, ab, kw OR “tca”/exp/mj OR “amitriptyline”/exp/mj OR “imipramine”/exp/mj OR “desipramine”/exp/mj OR “nortriptyline”/exp/mj OR “doxepin”/exp/mj OR “protriptyline”/exp/mj OR “trimipramine”/exp/mj OR “amoxapine”/exp/mj OR “dothiepin”/exp/mj OR “maprotiline”/exp/mj OR “dibenzepin”/exp/mj OR “opipramol”/exp/mj OR “dosulepin”/exp/mj OR “lofepramine”/exp/mj OR “butriptyline”/exp/mj OR “iprindole”/exp/mj OR “melitracen”/exp/mj OR “noxiptiline”/exp/mj OR “quinupramine”/exp/mj OR “clomipramine”/exp/mj	87,510
#2	poisoning: ti, ab, kw OR overdos*:ti, ab, kw OR toxic*:ti, ab, kw OR intoxication: ti, ab, kw OR “adverse effect”:ti, ab, kw OR complication: ti, ab, kw OR “poisoning”/exp/mj OR “overdose”/exp/mj OR toxic OR “intoxication”/exp/mj OR “adverse effect”/exp/mj OR “complication”/exp/mj	3,518,363
#3	#1 AND #2	12,846
#4	antidepress* NEAR/1 toxicity	85
#5	#3 OR #4	12,859
#6	“tricyclic antidepressant agent”/exp/mj/dd_ae OR (“tricyclic antidepressant agent”/exp/mj AND “intoxication”/de) OR “tricyclic antidepressant agent”/exp/mj/dd_to	8823
#7	#5 OR #6	18,021
#8	intralipid: ti, ab, kw OR “lipid emulsion”:ti, ab, kw OR “ile”:ti, ab, kw OR “lipid rescue”:ti, ab, kw OR “fat emulsion”:ti, ab, kw OR “lipid injection”:ti, ab, kw OR “liposyn”:ti, ab, kw OR “smoflipid”:ti, ab, kw OR “intravenous lipid”:ti, ab, kw OR “lipid infusion”:ti, ab, kw OR intrafat: ti, ab, kw OR “phospholipid emulsion”:ti, ab, kw OR “lipophilic drug*”:ti, ab, kw OR lipofundin: ti, ab, kw OR lipovenoes: ti, ab, kw OR “lipid suspension”:ti, ab, kw OR “intralipid”/exp OR “lipid emulsion”/exp OR “fat emulsion”/exp OR “liposyn”/exp OR “smoflipid”/exp OR “lipid infusion”/exp OR “intrafat”/exp OR “lipofundin”/exp OR “lipovenoes”/exp	39,724
#9	#7 AND #8	177

ab=Abstract, de=Descriptor, dd_ac=Adverse drug effect subheading, dd_to=Drug toxicity subheading, exp=Exploded subject heading, ILE=Intravenous lipid emulsion, kw=Keyword, mj=Major focus, NEAR/1=Proximity operator within one word, TCA=Tricyclic antidepressant, ti=Title

JBICRITICAL APPRAISAL AND RISK-OF-BIAS ASSESSMENT

Supplementary Table 5: Joanna Briggs Institute critical appraisal of the 20 included case reports

[illegible]

Supplementary Table 6: Joanna Briggs Institute critical appraisal of the four included case series

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall appraisal
Cave <i>et al.</i> , 2014 (LIPAEMIC registry)	Yes	Unclear	Unclear	No	No	Yes	Yes	Yes	Yes	Yes	Include
Cevik <i>et al.</i> , 2014	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Include
Tse <i>et al.</i> , 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Estrada-Atehortua <i>et al.</i> , 2022	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	NA	Include

NA=Not applicable

Supplementary Table 7: Item-level summary: Case reports

Item	Yes	No	Unclear	N/A	Total
Q1	20	0	0	0	20
Q2	20	0	0	0	20
Q3	20	0	0	0	20
Q4	20	0	0	0	20
Q5	20	0	0	0	20
Q6	20	0	0	0	20
Q7	15	5	0	0	20
Q8	20	0	0	0	20

JBİ appraisal item definitions and item-level summaries. Case-report item definitions Q1=Were the patient's demographic characteristics clearly described? Q2=Was the patient's history clearly described and presented as a timeline? Q3=Was the current clinical condition on presentation clearly described? Q4=Were diagnostic tests or assessment methods and results clearly described? Q5=Were the intervention (s) or treatment procedure (s) clearly described? Q6=Was the post-intervention clinical condition clearly described? Q7=Were adverse events (harms) or unanticipated events identified and described? Q8=Does the case report provide takeaway lessons? JBİ=Joanna Briggs Institute, N/A=Not available

Supplementary Table 8: Item-level summary: Case series

Item	Yes	No	Unclear	N/A	Total
Q1	3	1	0	0	4
Q2	3	0	1	0	4
Q3	2	0	2	0	4
Q4	1	1	2	0	4
Q5	1	1	2	0	4
Q6	4	0	0	0	4
Q7	4	0	0	0	4
Q8	4	0	0	0	4
Q9	4	0	0	0	4
Q10	3	0	0	1	4

Case-series item definitions. Q1=Were there clear criteria for inclusion in the case series? Q2=Was the condition measured in a standard, reliable way for all participants? Q3=Were valid methods used for identification of the condition for all participants? Q4=Did the case series have consecutive inclusion of participants? Q5=Did the case series have complete inclusion of participants? Q6=Was there clear reporting of participant demographics? Q7=Was there clear reporting of clinical information? Q8=Were outcomes or follow-up results clearly reported? Q9=Was there clear reporting of presenting site (s)/clinic (s) demographic information? Q10=Was statistical analysis appropriate? N/A=Not available