REVIEW ARTICLE

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Treatment of facial nerve synkinesis with botulinum toxin. A systematic review

Leczenie synkinez nerwu twarzowego z użyciem toksyny botulinowej. Przegląd systematyczny

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ABSTRACT:

Introduction: Facial synkinesis is a common chronic complication of facial nerve palsy, caused by aberrant nerve regeneration and leading to involuntary co-contractions, hypertonicity, and psychosocial burden. Botulinum toxin type A (botox) is widely used to reduce synkinetic activity, yet protocols vary considerably. This systematic review evaluates the efficacy, safety, and clinical practices of botox for facial synkinesis.

Aim: The aim of this systematic review are to critically evaluate the existing evidence for BoNT-A in the management of facial nerve synkinesis.

Methods: A search of PubMed, Embase, ScienceDirect, and Web of Science identified original English-language studies involving adult patients with facial synkinesis treated with botox. Exclusion criteria included reviews, case reports, abstracts, guidelines, protocols, and pediatric studies. Two reviewers independently performed study selection, data extraction, and risk of bias assessment using the Newcastle–Ottawa Scale, with consensus from a third reviewer.

Results: Forty-four studies (1994–2025; 1980 patients) were included. Synkinesis most commonly followed Bell's palsy, Ramsay Hunt syndrome, or postoperative facial nerve injury. Botox dosing, injection sites, and guidance techniques varied widely, reflecting individualized treatment. Across studies, BoNT-A consistently improved synkinesis severity, facial symmetry, and quality-of-life metrics as assessed using scales such as Sunnybrook, House-Brackmann, SAQ, and FaCE. Benefits appeared within weeks and were maintained with repeated treatments. Adverse effects were mild and transient, including ptosis, dry eye, bruising, and temporary weakness, with no systemic complications reported.

Conclusions: Botulinum toxin injection is an effective and safe therapy for facial synkinesis, improving both functional outcomes and patient-reported quality of life. However, heterogeneous protocols and outcome measures limit comparability. Future studies should implement standardized dosing strategies and validated assessment tools to support evidence-based treatment guidelines.

KEYWORDS: botox, botulinum toxin, facial nerve, synkinesis, systematic review

STRESZCZENIE:

Wprowadzenie: Synkinezy nerwu twarzowego są częstym powikłaniem porażenia tego nerwu, co wynika z nieprawidłowej regeneracji i prowadzi do mimowolnych skurczów obniżających komfort życia. Toksyna botulinowa (botoks) jest powszechnie stosowana w celu redukcji synkinez, choć protokoły terapii są niejednolite. Niniejszy przegląd systematyczny ocenia skuteczność i bezpieczeństwo botoksu w leczeniu synkinez nerwu VII.

Cel: Celem niniejszego przeglądu systematycznego jest krytyczna ocena dostępnych dowodów dotyczących stosowania toksyny botulinowej typu A (BoNT-A) w leczeniu synkinez nerwu twarzowego.

Metody: Przeszukano bazy danych PubMed, Embase, ScienceDirect oraz Web of Science i identyfikowano badania dotyczące dorosłych leczonych toksyną botulinową z powodu synkinez nerwu twarzowego. Wykluczono przeglądy, opisy przypadków, abstrakty, wytyczne, protokoły i badania pediatryczne. Dwóch recenzentów niezależnie dokonało selekcji i ekstrakcji danych oraz oceny jakości (Newcastle-Ottawa Scale).

Wyniki: Włączono 44 badania (1994–2025; 1980 pacjentów). Synkinezy najczęściej następowały po porażeniu Bella, zespole Ramsaya Hunta lub urazach jatrogenicznych. Dawki i miejsca wstrzyknięć istotnie się różniły. We wszystkich pracach

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odnotowano zmniejszenie nasilenia synkinez, poprawę symetrii twarzy i jakości życia ocenianych m.in. skalami Sunnybrook, House'a-Brackmanna, SAQ i FaCE. Efekty pojawiały się po kilku tygodniach i utrzymywały przy kolejnych zabiegach. Działania niepożądane były łagodne i krótkotrwałe (opadanie powieki, suchość oka, zasinienia, przejściowe osłabienie) i nie zaobserwowano powikłań ogólnych.

Wnioski: Toksyna botulinowa jest skuteczną i bezpieczną metodą leczenia synkinez nerwu twarzowego. Różnorodność protokołów ogranicza jednak porównywalność badań. Potrzebne są standaryzowane schematy leczenia i jednolite narzędzia oceny.

SŁOWA KLUCZOWE: botoks, nerw twarzowy, przegląd systematyczny, synkinezy, toksyna botulinowa

ABBREVIATIONS

BoNT-A – botulinum toxin type A
EMG – electromyographic
FACE – Facial Assessment by Computer Evaluation
FaCE – Facial Clinimetric Evaluation Scale
NOS – Newcastle-Ottawa Quality Assessment Scale
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SAQ – Synkinesis Assessment Questionnaire
SFGS – Sunnybrook Facial Grading System

INTRODUCTION

Facial paralysis is a devastating condition that profoundly impacts quality of life, affecting approximately 15 to 40 individuals per 100,000 annually [1], with Bell's palsy representing its most frequent cause. While many patients experience excellent recovery (with about 80% of patients recovering spontaneously and completely within 3 months [2]), a significant part of the patient population develops long-term, debilitating complications following peripheral facial nerve palsy [2], with synkinesis representing the most functionally and psychologically impairing sequela [3]. Derived from the Greek meaning „moving together," synkinesis is the involuntary, simultaneous contraction of 1 facial muscle group accompanying the deliberate movement of another [3]. Common manifestations include involuntary eye closing or cheek twitching during a smile. The primary etiology centers on aberrant nerve regeneration following injury, where regenerating axons are misdirected, causing a single neural impulse to activate multiple, inappropriate muscles [3, 4]. Contributing factors include peripheral ephaptic transmission between neighboring regenerating axons and synaptic reorganization within the facial nerve nucleus [3], as well as possible maladaptive cortical plasticity with structural remodeling of cortical gray matter observed in patients with chronic synkinesis [5, 6]. The resulting facial symptoms create a vicious cycle for the patient. Synkinesis manifests as involuntary movements alongside hypertonicity and contracture, leading to a noticeable tightening or „pulled" appearance of the face at rest [3]. These deficits cause tangible functional problems, impacting speech, articulation, and chewing, alongside significant psychosocial morbidity. Patients with facial paralysis demonstrate significantly higher depression scores, lower self-reported attractiveness, lower mood, and reduced quality of life compared to healthy controls, with 42.1% of patients screening positive for probable depression [7]. Moreover, patients screening positive for subclinical anxiety and depression demonstrate significantly worse quality of life scores that do not necessarily correlate with the objective severity of the paralysis [8].

Current treatment options are multimodal, ranging from facial neuromuscular retraining to surgical interventions such as selective neurectomy [3]. However, chemodenervation with Botulinum Toxin Type A (BoNT-A) has emerged as the most common and effective minimally invasive therapeutic strategy [9]. The mechanism of BoNT-A is specific: it acts at the neuromuscular junction by cleaving the SNAP-25 protein, thereby inhibiting the release of acetylcholine [10], resulting in localized, temporary muscle weakening that effectively reduces hypertonicity and involuntary synkinesis. The procedure demands precise target identification, often guided by clinical observation or electromyography, with individualized dosage and treatment intervals tailored to each patient's unique synkinesis pattern [9]. Accurate assessment of synkinesis is crucial for establishing treatment response. The historic House--Brackmann scale has inherent limitations and demonstrates poor reliability for synkinesis detection compared to more comprehensive grading systems[11]. Clinicians now employ objective scales, such as the Sunnybrook Facial Grading System (SFGS), which incorporates a dedicated synkinesis subscore [11], alongside the Synkinesis Assessment Questionnaire (SAQ), a validated patient-reported outcome measure that reliably captures the functional and psychological impact of synkinesis [12]. Despite widespread clinical adoption of BoNT-A for synkinesis management, with a meta-analysis demonstrating mean improvements of 11.6 points on the SAQ following treatment [9], a significant gap persists in the current evidence base. The literature is characterized by non-standardized BoNT-A protocols with substantial variation in reported dosages, injection sites, and treatment intervals; inconsistent outcome measures mixing objective and subjective scales without clear correlation; and variation in defining successful therapeutic response [9]. Furthermore, while early treatment within 1 year of facial paralysis onset demonstrates superior facial grading system improvement, most studies lack standardized protocols for BoNT-A administration [13].

AIM

Therefore, the imperative goals of this systematic review are to critically evaluate the existing evidence for BoNT-A in the management of facial nerve synkinesis. We specifically aim to

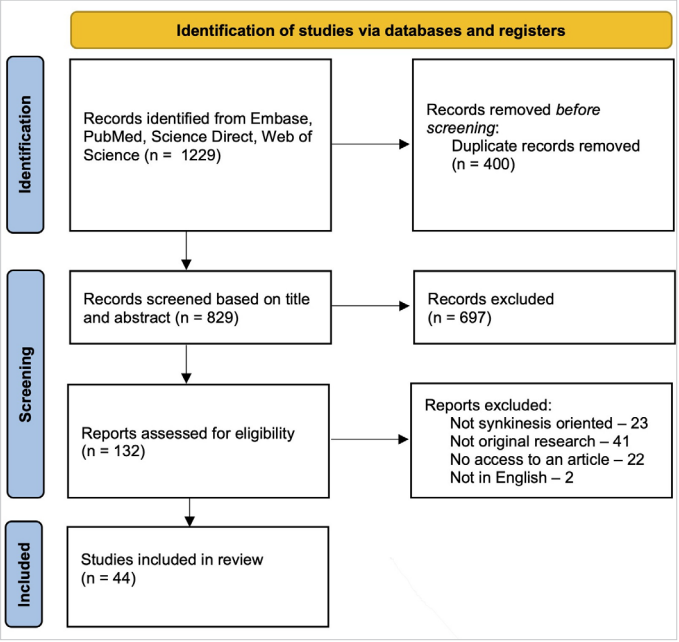

Fig. 1. Study flowchart.

determine its efficacy, identify the most robust best practices regarding injection technique and dosage, and establish clearer, evidence-based guidance for clinicians managing this complex condition, ultimately improving outcomes for patients suffering from this devastating complication of facial nerve dysfunction.

METHODS

This systematic review adhered to the PRISMA 2020 Guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Inclusion criteria were defined as: (1) original studies, (2) manuscripts written in English, (3) adult patients with facial nerve synkinesis, and (4) patients treated with injections of botulinum toxin. Exclusion criteria were: (1) study types such as book chapters, case reports/case series, conference abstracts, guidelines, letters to the editor, protocols, and reviews, (2) the pediatric population. Major electronic databases: Embase, PubMed, Science Direct, and Web of Science were searched, with data from each of them collected on October 2, 2025. For each source, we applied an appropriate search strategy comprising the listed terms: "facial AND synkinesis AND (botulinum OR botox)". Two independent reviewers conducted the screening process. This was carried out in 4 stages: duplicates removal, eligibility assessment based on title and abstract, search for full-texts, and full-publications appraisal. At the end of each step, the results were compared between 2 reviewers, and in case of any inconsistencies, they were resolved by consensus with a third reviewer. Data from each included study were extracted by 2 independent reviewers. Extracted data included: general study data, study design, measured outcomes, patient population data, synkinesis etiology, and procedure data. The extracted data was entered into a spreadsheet. The risk of bias assessment was performed with the use of the Newcastle-Ottawa Quality Assessment Scale (NOS). Each study included in this review was evaluated by 2 independent reviewers; any discrepancies were discussed and resolved by consensus with a third reviewer.

RESULTS

The initial database search produced 1229 records. After 400 duplicates were removed, 829 articles were left for the abstract screening. The assessment of studies based on title and abstract left 85 articles for full-text appraisal. Ultimately, 44 articles (published between 1994 and 2025) were included. These trials included a total of 1980 patients. The study selection process is presented in Fig. 1., and the characteristics of included studies are presented in Tab. I. Risk of bias assessment using the NOS is presented in Fig. 2.

A review of 44 published entries on the causes of synkinesis reveals a complex and often inconsistent landscape. The analyzed studies offered a wide range of descriptions regarding patient backgrounds, with many opting for more narrative summaries instead of using standardized classifications. Patient characteristics are presented in Tab. II.

This inconsistency made it difficult to draw direct comparisons or perform accurate quantitative assessments across the board. Still, certain trends emerged with notable clarity. Idiopathic facial palsy (widely recognized as Bell's palsy) surfaced as one of the most frequently cited causes. Viral infections also played a prominent role, especially Ramsay Hunt syndrome, which is associated with herpes zoster oticus. Together, these 2 conditions accounted for a large portion of the identified cases. Surgical complications stood out as another significant contributor. Synkinesis often developed following medical procedures that resulted in unintended facial nerve damage. A substantial number of these cases were traced to operations involving the removal of tumors such as vestibular schwannomas, sometimes referred to as acoustic neuromas, as well as meningiomas and other procedures near the lateral base of the skull. In addition, traumatic facial injuries were a recurring factor in the reported cases. Several studies documented patient groups with mixed origins of facial palsy. These ranged from small case collections to broader datasets. One study cited thirteen patients with Bell's palsy, 4 with Ramsay Hunt syndrome, and 2 who had undergone acoustic nerve surgery [17]. Another study reported proportions such as 41% idiopathic, 17% Ramsay Hunt, 31% related to surgery, and nearly 7% due to trauma [23]. A third source listed over half of its cases as Bell's palsy, with the rest divided equally between Ramsay Hunt and vestibular schwannoma origins [33]. Interestingly, not all reports focused solely on synkinesis following facial paralysis. Some included individuals with other facial movement disorders, such as hemifacial spasm or blepharospasm, which added further complexity to the sample groups. Because of the wide variability in how causes were reported and classified, it was not possible to calculate precise prevalence rates for each underlying condition. However, the broader pattern remains clear. Most individuals affected by synkinesis appear to share a common clinical path involving abnormal facial nerve regeneration following idiopathic events, viral infections, or complications from facial nerve surgery.

The injected botox dosage varied across studies, reflecting a lack of standardization in administration protocols. Data concerning the botox injection procedures is presented in Tab. III.

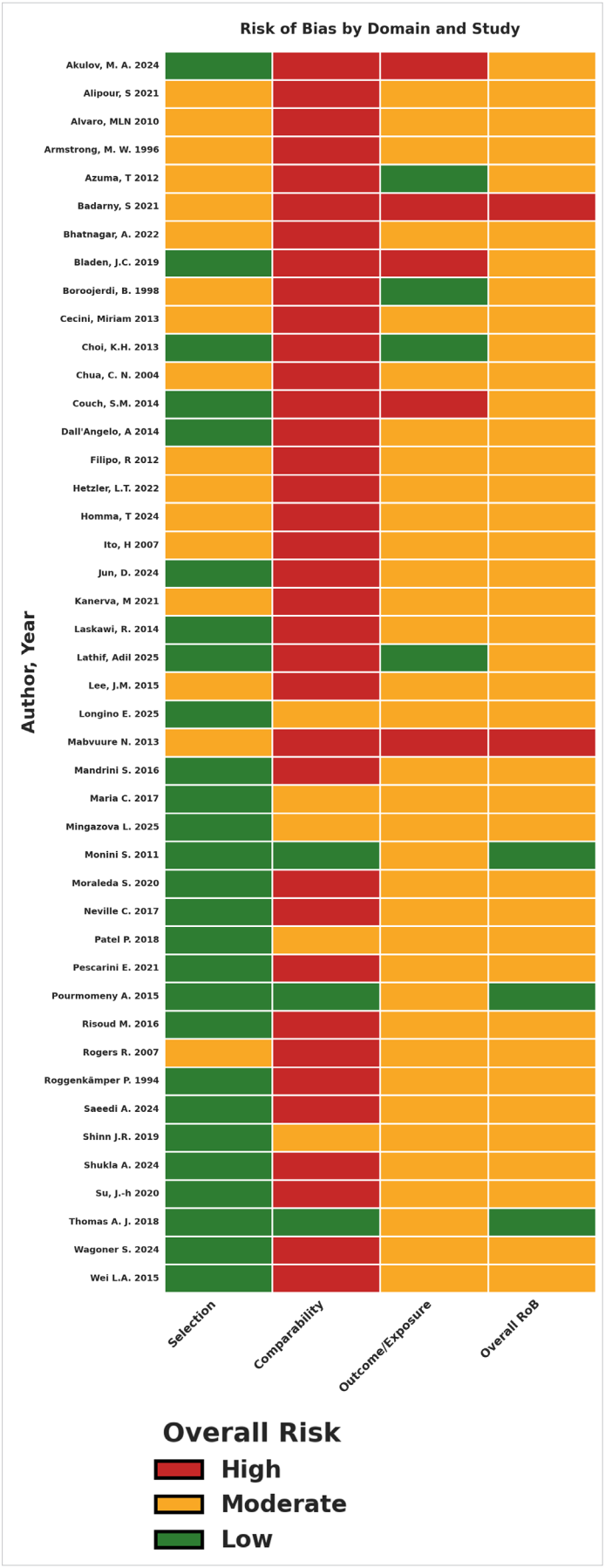

Fig. 2. Studies' risk of bias assessment using Newcastle-Ottawa Quality Assessment Scale.

While several papers omitted the total dosage entirely, those that did include this information reported a wide range. Mean total doses cited included 31.9 ±13.1 U [45], 59.1 ±11 U [54], 20.2 ±11.7 IU [48], and 54 U, with the latter ranging from 31 to 108 U [57]. In some cases, dosages were reported separately for the affected and unaffected sides. One study, for example, administered an average of 17.12 U to the paralyzed side and 52.6 U to the non-paralyzed side [24]. Data on dosing per injection site was often unspecified, but when mentioned, it varied from broad ranges (e.g., 1.5–3 U or 0.5–5 U) to fixed doses (such as 2.5 U per point). Occasionally, individual muscles were singled out, with the orbicularis oculi receiving, on average, 5.6 ±2.3 IU in 1 report [48]. Injection strategies were typically tailored to individual clinical presentations, with location choices guided by symptom distribution and observed synkinetic activity. Most protocols focused on treating hyperactive or synkinetic muscles on the affected side, although some extended treatment to the unaffected side to improve facial symmetry. Targeted muscles included the orbicularis oculi, platysma, depressor anguli oris, risorius, perinasal region, contralateral forehead, and various lip elevators. Injections were delivered through different routes such as subcutaneous, intramuscular, and intraoral, with the latter often used for muscles such as the buccinator [33, 57]. Injection techniques varied considerably between studies. While some explicitly stated that no electromyographic (EMG) guidance was used, others incorporated EMG or ultrasound to improve precision. The tools used were similarly diverse, with 30G and 27G needles being the most frequently mentioned, commonly paired with tuberculin or insulin syringes. Overall, the method of administration was often customized to align with each patient's clinical profile.

The reporting of posttreatment monitoring varied significantly across studies. Some researchers applied structured evaluation schedules, with assessments occurring at multiple set intervals. Others opted for broader observation windows, noting durations that extended to as long as 18 years [57]. In contrast, several studies limited their data collection to brief observation points, offering only a single check at preintervention and again 2 weeks later. Even when the number of posttreatment reviews was specified, interpretations varied across studies. Of the 15 studies that included specific counts, the highest number reported was 4, with an arithmetic average of 1.93. In certain cases, researchers shifted focus from the monitoring process to treatment frequency, reporting figures such as a median or mean number of visits per patient. There was also considerable variation in how treatment intervals were structured. A small group of studies, specifically 4, reported administering only a single injection. In contrast, 7 studies did not indicate any specific timing for the interventions. Among those that did report repeated treatments, the most commonly described intervals ranged between 3 and 6 months. Typical timeframes included statements such as a "Median of 3 months" [15], injections given "Every 16 weeks" [16], or treatments scheduled "Every 3 months or as requested by the patient." Other studies referred more generally to a "Mean of 4 months", or broader estimates falling between 4 and 6 months. In 7 of the reviewed studies, information regarding how long the treatment effects lasted was not reported at all. Among the studies that did include such data, the majority

Tab. I. Characteristics of included studies

FIRST AUTHOR	YEAR	COUNTRY	STUDY DESIGN	SAMPLE SIZE	OBJECTIVE OUTCOME MEASURES	SUBJECTIVE OUTCOMES MEASURES	MEASURING TIMEPOINTS (FOLLOW-UPS)	NUMBER OF FOLLOW-UPS
Akulov [14]	2024	Russia	Comparative study	86 patients (57 main group, 29 control group)	Sunnybrook Facial Grading Scale (SFGS); House--Brackmann scale	Facial Disability Index (FDI scale)	6 months, 1, 2, 3, and 5 years	5 control points
Alipour [15]	2021	Germany	Retrospective analysis	73 patients	Change in dosage and injection pattern, time intervals between treatments	Not assessed, no standardized assessment was used	Data analyzed from 1998 to 2018	Median number of treatments was 18
Alvaro [16]	2010	Spain	Observational study	48 patients	House-Brackmann scale; Facial Grading System	Visual analogue scale (for satisfaction, aesthetics, expectations)	1, 3, 6, and 12–18 months	4 control points
Armstrong [17]	1996	UK	Prospective observational	24 patients (72 treatments)	House-Brackman grading	Cosmetic improvement classification (favourable, sub-optimal, etc.)	1 week, 1 month, then 3-monthly or by request	2 initial reviews, then as needed
Azuma [18]	2012	Japan	Prospective clinical study	13 patients (8 Bell palsy, 5 herpes zoster oticus)	Asymmetry of eye opening width (% eye opening)	Not specified	10 months	Visits once or twice a month
Badarny [19]	2021	Israel	Retrospective cohort study	87 consecutive patients (2441 treatments)	Analysis of injection dosage over time	5-point Likert scale (0–4)	Mean 10 years (range 6–11)	Mean 28.8 visits per patient
Bhatnagar [20]	2022	India	Prospective study	50 patients	SFGS (SB scores)	Not specified (Assessed facial symmetry, speech, drooling)	Baseline, 3, 6, 9, and 12 months	4 (after baseline)
Bladen [21]	2019	UK	Retrospective comparative study	51 patients	Blepharospasm disability score (BDS)	Subjective improvement score (SIS); Duration of maximal effect (DME)	Minimum of 10 years	Data from "first year" and "final year" compared
Boroojerdi [22]	1998	Germany	Clinical trial	10 patients	Videographic control (lid width); Schirmer test	5-point scale (synkinesia); 3-point scale (hyperlacrimation)	2–4 weeks after injection	One (at 2–4 weeks post-injection)
Cecini [23]	2013	Italy	Observational controlled longitudinal study	29 patients	Facial Assessment by Computer Evaluation (FACE) software	SFGS (SB score)	Before injection and 2 weeks (mean 15 days) after	One (post--injection)
Choi [24]	2013	South Korea	Prospective clinical study	42 patients	Dynamic facial asymmetry ratio	SFGS (SB); 20-item questionnaire	1 month after administration; mean 28.4-month follow-up	Mean follow-up duration of 28.4 months
Chua [25]	2004	UK	Prospective interventional study	5 patients	Assessment of lid position	3-point scale (reduction in synkinesia)	One week and 2–3 months post-injection	Two (1 week, 2–3 months)
Couch [26]	2014	USA	Retrospective review	9 patients	SFGS	Facial Clinimetric Evaluation Scale (FaCE Scale)	Pre-treatment and 1 month (30 days) post-treatment	1
Dall'Angelo [27]	2014	Italy	Retrospective study	45 patients	SFGS	Specific platysmal evaluation (aesthetic loss, cramps, pain)	Before treatment and a median of 18 days after	1 (post-treatment)
Filipo [28]	2012	Italy	Prospective study	41 patients	SFGS (SB); Modified SG for hyperkinesis	Self-administered synkinesis questionnaire (SASAQ)	10 days and 1 month (post-treatment)	2

Tab. I. cd. Characteristics of included studies

FIRST AUTHOR	YEAR	COUNTRY	STUDY DESIGN	SAMPLE SIZE	OBJECTIVE OUTCOME MEASURES	SUBJECTIVE OUTCOMES MEASURES	MEASURING TIMEPOINTS (FOLLOW-UPS)	NUMBER OF FOLLOW-UPS
Hetzler [29]	2022	USA	Retrospective chart review	34 patients	SFGS	FaCE Scale, FDI, Synkinesis Assessment Questionnaire (SAQ), Naive observer survey	Data collected August 2018–June 2020	Not specified (multiple chemo-denervation visits)
Homma [30]	2024	Japan	Clinical study	48 patients	Integrated electromyography (iEMG)	SFGS	>6 months after 1st, 2nd, and 3rd injections	3
Ito [31]	2007	Japan	Prospective, open-trial study	11 patients	Schirmer test	Clinical efficacy judged by medical examination	Every 2 months; final assessment in August 2004	Total observation period was 43 months
Jun [32]	2024	South Korea	Retrospective study	21 patients	4-scale scoring system (for synkinesis); Angle of oral commissure (for mouth asymmetry)	Not specified	Initial and final evaluations	Not specified (Initial *vs.* Final comparison)
Kanerva [33]	2021	Finland	Retrospective study	83 patients	Objective cheek contraction visible in the mouth	Patient-reported symptoms and desire to continue treatment	At the "next visit" (typically 3–4 months)	One (assessment at the next visit)
Laskawi [34]	2014	Germany	Retrospective analysis	80 patients	Total dosage, number of injection points, dose per point	Not specified (study analyzed injection parameters, not patient outcomes)	Analyzed up to the 40th injection	Minimum of 10 injections per patient
Lathif [35]	2025	Australia	Prospective cohort	20 patients	Consonant analysis of a recorded reading sample; Clinician-rated intelligibility	Patient-rated intelligibility; Speech Handicap Index (SHI); FDI; Oral Competence Questionnaire (OCQ)	Before BTX (within 48 hours) and 4 weeks after BTX	1 at 4 weeks
Lee [36]	2015	South Korea	Prospective study	17 patients	Photographs	SFGS (SB); 20-item questionnaire	After 1st, 2nd, and 3rd injection (over 2 years)	3 injection points, plus visits every 2 months
Longino [37]	2025	USA	Prospective cohort study	100 patients	SAQ; FaCE Scale	Patient-reported improvement in synkinesis severity and quality of life; CES-D (depression) and FNAES (appearance anxiety) scores	Pre-treatment and 4 weeks post-treatment	1
Mabvuure [38]	2013	UK	Feasibility study and retrospective outcomes analysis	19 patients	Photogrammetric analysis of eye surface area using ImageJ software; Ratio of synkinetic eye to normal eye during volitional movements	Not specified	Pre-treatment and post-treatment photographs	2
Mandrini [39]	2016	Italy	Retrospective case-series study	27 patients	SFGS	Not specified	Baseline and before each BoNT-A + mirror biofeedback session	Up to 12 sessions per patient
Maria [40]	2017	South Korea	Observational cohort study	142 patients	SFGS (SB score); Babak and Kimberly (BK) classification; Video analysis of synkinetic movements	Patient-reported discomfort and facial movement interference	Baseline and 1 year after	2

Tab. I. cd. Characteristics of included studies

FIRST AUTHOR	YEAR	COUNTRY	STUDY DESIGN	SAMPLE SIZE	OBJECTIVE OUTCOME MEASURES	SUBJECTIVE OUTCOMES MEASURES	MEASURING TIMEPOINTS (FOLLOW-UPS)	NUMBER OF FOLLOW-UPS
Mingazova [41]	2025	Russia	Comparative observational study	Not specified	House-Brackmann Facial Nerve Grading Scale; SFGS; SAQ	Patient-reported improvement	Baseline, 7–10 days, 1 month, 3 months, 6 months, 12 months	Up to 6
Monini [42]	2011	Italy	Randomized controlled trial	20 patients	SFGS	Not specified	Baseline (day 0), post-BTX-A (day 7), and late evaluation (day 90)	3
Moraleda [43]	2020	Spain	Prospective observational survey study	70 patients	None reported	Patient-reported improvement; Overall satisfaction (0–10 scale); Willingness to repeat treatment	After 2 prior sessions	3–29 sessions
Neville [44]	2017	UK	Prospective observational study	51 patients	SAQ	Not specified	Pre-treatment and 2 weeks post-treatment	Up to 5 cycles per patient
Patel [45]	2018	USA	Prospective cohort study with crossover comparison	23 patients	SAQ	Patient-reported facial tightness and lip movement (SAQ items 5 and 6); Duration of botulinum toxin effect	Pre-treatment and 2 weeks post-injection	Up to 4 cycles per patient
Pescarini [46]	2021	UK and Italy	Observational clinical practice study	33 patients	FDI; SAQ	Visual Analogue Scale	Pre-treatment and after 2 weeks	1
Pourmomeny [47]	2015	Iran	Randomized clinical trial	34 patients	Photoshop-based digital facial symmetry analysis; Videotape evaluation of synkinesis	Facial Grading System	Pre-treatment and after 4 months	1
Risoud [48]	2016	France	Retrospective observational monocenter study	30 patients	Mean dose per muscle per session; Dose kinetics over multiple sessions	Not specified	Doses recorded for first 3 sessions and final session	3–4 sessions
Rogers [49]	2007	USA	Retrospective observational study	8 patients	Automated Facial Image Analysis	Facial Grading System	5–9 weeks after Botox	1
Roggenkämper [50]	1994	Germany	Retrospective case series	23 patients	Duration of effect (weeks) after injection; Force of lid closure (grams) before and after treatment; Dose–effect ratio (weeks per IU)	Patient-reported improvement; Satisfaction with treatment	Duration of effect tracked after each injection	1–5+ per patient
Saeedi [51]	2024	USA	Prospective pre–post interventional study	16 patients	Standardized photographic measurement	SAQ	Day of injection; within 2–4 weeks after injection	1
Shinn [52]	2019	USA	Prospective cohort study	99 patients	Botulinum treatment patterns; Treatment course metrics; EMG data used for targeting	SAQ	Day of injection – 2 weeks after; IQR 8.9–59.7 months	5–29
Shukla [53]	2024	USA	Retrospective clinical study	25 patients	MRD1, MRD2, and palpebral fissure height measured using Emotrics software	Not specified	Pre- and post-treatment photographs (average follow-up: 23 days)	2

Tab. I. cd. Characteristics of included studies

FIRST AUTHOR	YEAR	COUNTRY	STUDY DESIGN	SAMPLE SIZE	OBJECTIVE OUTCOME MEASURES	SUBJECTIVE OUTCOMES MEASURES	MEASURING TIMEPOINTS (FOLLOW-UPS)	NUMBER OF FOLLOW-UPS
Su [54]	2020	China	Retrospective study	234 patients	Emotrics software; t-test	Difference of smile angle; difference of palpebral fissure height; difference of brow height	Not specified	Not specified
Thomas [55]	2018	USA	Randomized clinical trial	28 patients	SAQ	SAQ	At 1, 2, and 4 weeks after treatment	3
Wagoner [56]	2024	USA	Retrospective cohort study	29 patients	Facial symmetry metrics measured in millimeters using Emotrics software	Not specified	Pre- and post--intervention Photographs (≥1 month apart)	2
Wei [57]	2015	USA	Retrospective medical records review	42 patients	SFGS	SAQ	from 5 months to 18 years	Not specified

BDS – Blepharospasm disability score; BK – Babak and Kimberly; DME – duration of maximal effect; EMG – electromyography; FACE – Facial Assessment by Computer Evaluation; FaCE Scale – Facial Clinimetric Evaluation Scale; FDI – Facial Disability Index; iEMG – integrated electromyography; OCQ – Oral Competence Questionnaire; SAQ – Synkinesis Assessment Questionnaire; SASAQ – self-administered synkinesis questionnaire; SFGS – Sunnybrook Facial Grading Scale; SHI – Speech Handicap Index; SIS – subjective improvement score.

indicated that the effects typically persisted somewhere between 3 and 6 months. Some offered more precise figures, such as "3 to 4 months", "3 to 6 months," or "4 to 6 months", while another cited a "Median of 4 months." Additional findings pointed to a "Mean duration of maximal effect" at 10.5 weeks [21], and another study described an "Average of 23.9 weeks" [22], both of which align closely with the general six-month timeframe. One report offered a less specific summary, noting simply that the treatment response lasted "several months" [17].

Across the 44 included studies (1994–2025; 1980 patients), BoNT-A consistently produced clinically meaningful improvements in facial function, symmetry, and synkinesis severity. Validated scales such as the SFGS, House-Brackmann scale, SAQ, Facial Clinimetric Evaluation Scale (FaCE), and digital tools (Emotrics, FACE software, automated image analysis) demonstrated reductions in involuntary contractions and improved voluntary movement symmetry [44, 51, 52]. Additional improvements were confirmed in later cohorts using Emotrics and FACE software [53, 55, 56]. Patient-reported measures (Facial Disability Index, FaCE, satisfaction scores, visual analogue scales) confirmed enhanced aesthetics, improved social functioning, and better quality of life [37, 44, 52]. Short-term studies (2–4 weeks) reported rapid gains in SAQ and FaCE scores [44, 51, 53]. Long-term cohorts demonstrated sustained benefit over years of repeated therapy without dose escalation [15, 19, 21].

Additional long-term stability was shown in five-year and ten-year follow-ups [14, 25]. Outcomes varied with age, etiology, and mental health comorbidities. Older age, prior treatments, and depression were linked to reduced improvement [37]. Anxiety history correlated with greater SAQ improvement [37]. Studies combining BoNT-A with rehabilitation showed superior outcomes compared to toxin alone [16, 18, 39]. Thread lifting combined with BoNT-A also improved symmetry and durability [47].

Overall, BoNT-A consistently improved both objective measures of facial function and subjective quality-of-life outcomes, confirming its role as a cornerstone therapy for facial synkinesis. Adverse events were generally mild, transient, and dose-related, with no systemic complications reported across studies. Ptosis, diplopia, incomplete lid closure, dry eye, tearing, bruising, lagophthalmos, and transient facial weakness were the most common [17, 23, 33]. Armstrong et al. highlighted higher complication rates in high-dose groups [17]. Chua et al. confirmed that low-dose regimens reduced ptosis risk [25]. Hematomas, redness, swelling, and fullness at injection sites were reported in some articles [23, 28, 57]. Choi et al. described pseudo-Bell's palsy in contralateral hypertrophy cases [24]. Most adverse effects resolved spontaneously within 1–6 weeks [17, 23, 33]. Long-term cohorts showed decreasing rates of minor adverse events over time, suggesting improved safety with experience and titration [15, 19, 21]. Five-year and ten-year studies confirmed stable safety profiles [18, 25]. Several studies reported no significant complications when injections were performed with careful technique (small aliquots, superficial placement, avoiding pretarsal orbicularis) [18, 37, 39].

DISCUSSION

The 44 included studies varied considerably in design, population, and reporting. Cohorts ranged from small feasibility studies with fewer than 10 patients to large observational series exceeding 200 participants [17, 23, 33]. Follow-up durations spanned from 2 weeks to more than a decade [15, 19, 57], and outcome measures were inconsistently applied. This heterogeneity reflects the diverse clinical contexts in which botulinum toxin is used, but it limits direct comparison and quantitative synthesis. Despite these differences, a consistent signal of benefit was observed across studies.

Injection strategies were highly individualized, targeting the muscles most responsible for synkinetic activity. Commonly treated sites included the orbicularis oculi, orbicularis oris, buccinator, platysma, and perinasal muscles [24, 33, 48]. Techniques ranged from simple subcutaneous injections to EMG-guided or

Tab. II. Patient population characteristics.

FIRST AUTHOR	YEAR	NUMBER OF PATIENTS			AGE		SYNKINESIS ETIOLOGY
		TOTAL	MEN	WOMEN	MEAN [YEARS]	SD	
Akulov [14]	2024	86	43 (28 in group 1, 15 in group 2)	43 (29 in group 1, 14 in group 2)	Group 1: 42.8; Group 2: 48.6	Group 1: ±8.7 Group 2: ±11.1	Facial neuropathy after neurosurgery (acoustic neuroma or meningioma resection)
Alipour [15]	2021	84	19 (23%)	65 (77%)	49	±14.9	Idiopathic (38.1%), Postoperative (31.8%), Infectious (23.8%), Posttraumatic (6.4%)
Alvaro [16]	2010	48	14	34	48	Not specified	Severe Bell's palsy
Armstrong [17]	1996	Not specified	Not specified	24	Not specified	Not specified	Bell's palsy (n = 13), Ramsay Hunt syndrome (n = 4), acoustic nerve surgery (n = 2), hemifacial spasm (n = 2), and other (n = 3)
Azuma [18]	2012	13	7	6	65	±8.25	Bell palsy (n = 8); Herpes zoster oticus (n = 5)
Badarny [19]	2021	87	36	51	59.5	±11.5	Facial synkinesis (n = 19), Hemifacial spasm (n = 42), Blepharospasm (n = 26)
Bhatnagar [20]	2022	50	29	21	47,56	±10.9	Bell's palsy (n = 35), Post-traumatic (n = 6), Post-acoustic tumor resection (n = 5), Post-mastoid surgery (n = 4)
Bladen [21]	2019	51	14	37	63	±14.25	Blepharospasm (n = 17), Hemifacial spasm (n = 17), Aberrant facial nerve regeneration (AFR) (n = 17)
Boroojerdi [22]	1998	10	2	8	59	±14.75	Aberrant regeneration after facial palsy (Idiopathic, Zoster oticus, acoustic neurinoma)
Cecini [23]	2013	29	5	24	47.4	±14.75	Idiopathic (41.4%), Ramsay Hunt (17.2%), postsurgical (31%), trauma (6.9%), Guillain-Barré (3.4%)
Choi [24]	2013	42	20	22	48.3	±20.3	Bell's palsy (n = 24), herpes zoster oticus (n = 8), traumatic (n = 7), facial nerve transection (n = 3)
Chua [25]	2004	5	2	3	55.6	±11.5	Ramsay Hunt's syndrome (n = 1), Post-acoustic neuroma excision (n = 1), Bell's palsy (n = 3)
Couch [26]	2014	9	1	8	59.8	±14.8	Bell's palsy (n = 7), post-acoustic neuroma resection (n = 1), Ramsay Hunt syndrome (n = 1)
Dall'Angelo [27]	2014	45	10	35	44	±15	Bell's palsy (40%), Ramsay Hunt (15.6%), post--surgical (neuroma/meningioma), post-traumatic
Filipo [28]	2012	41	13	28	47	±16	Bell's palsy (n = 28), iatrogenic (n = 9), herpes zoster (n = 3), other (n = 1)
Hetzler [29]	2022	34	31	3	55	±15.5	Bell's palsy (14), Ramsey Hunt (4), acoustic neuroma (12), vestibular nerve section (1), facial neuroma (1), trauma (2)
Homma [30]	2024	48	12	36	62.6	±11.25	Bell's palsy (n = 23), Ramsay Hunt (n = 15), damage during surgery (n = 10)
Ito [31]	2007	11	3	8	59	±11.75	Bell's palsy (n = 7), Ramsay Hunt (n = 1), CIDP (n = 1), Traumatic (n = 2)
Jun [32]	2024	21	3	18	40.6	±11.9	Mid-face trauma, including cosmetic procedures (n = 16) and non-cosmetic blunt trauma (n = 5)
Kanerva [33]	2021	83	16	67	59	±14.25	Bell's palsy (52%), Ramsay Hunt (12%), vestibular schwannoma (12%), hemifacial spasms (5%), other (19%)
Laskawi [34]	2014	80	Not specified	Not specified	Not specified	Not specified	Synkinesis (n = 19), Blepharospasm (n = 30), Hemifacial spasm (n = 31)
Lathif [35]	2025	20	18	2	45	±13	Porażenie Bella (n = 12); zespół Ramsaya Hunta (n = 4); jatrogenny uraz chirurgiczny (n = 4)
Lee [36]	2015	17	7	10	49,3	±5,1	Jednostronne porażenie twarzy (bez wskazania konkretnej etiologii)
Longino [37]	2025	100	9	91	56,4	±12,3	Porażenie idiopatyczne/porażenie Bella (47%); operacja bocznej podstawy czaszki (31%); zespół Ramsaya Hunta (11%); operacja ślinianki przyusznej (3%); uraz (1%); inne (7%)

Tab. II. cd. Patient population characteristics.

FIRST AUTHOR	YEAR	NUMBER OF PATIENTS			AGE		SYNKINESIS ETIOLOGY
		TOTAL	MEN	WOMEN	MEAN [YEARS]	SD	
Mabvuure [38]	2013	19	3	16	Not specified	Not specified	Facial palsy
Mandrini [39]	2016	27	5	22	45	±16	Bell's palsy (13), Ramsay Hunt (4), post-neuroma surgery (8), post-traumatic (2)
Maria [40]	2017	142	58	84	42.3	±4	Bell's palsy: 74 Traumatic: 29 Ramsay Hunt: 27 Iatrogenic: 8 Middle ear mass: 4
Mingazova [41]	2025	Not specified	Not specified	Not specified	Not specified	Not specified	Bell's palsy
Monini [42]	2011	20	8	12	Not specified	Not specified	Viral, post-surgical (vestibular schwannoma, facial schwannoma), zoster, post-traumatic
Moraleda [43]	2020	70	19	51	54	Not specified	Bell's palsy; Post-surgical; Herpes zoster; Congenital
Neville [44]	2017	51	9	42	Not specified	Not specified	Facial palsy
Patel [45]	2018	23	4	19	46	±10.4	Vestibular schwannoma; Bell's palsy; Ramsay Hunt; Trauma
Pescarini [46]	2021	33	4	29	53	Not specified	Bell's palsy; Ramsay Hunt syndrome; Acoustic neuroma
Pourmomeny [47]	2015	34	6	28	36.11	Not specified	Bell's palsy
Risoud [48]	2016	30	9	21	46.8	±17.1	Idiopathic; Acoustic neuroma surgery; Temporal bone fracture; Post-herpes zoster; congenital; meningoencephalitis, cholesteatoma, chondro-sarcoma, glomus tumor
Rogers [49]	2007	8	2	6	51.6	±11.1	Bell palsy; Ramsay Hunt; Surgery; Tumor
Roggenkämper [50]	1994	23	5	18	68.9	±16.8	Viral infection; Zoster paresis; trauma; Cerebral stroke; Acoustic neurinoma surgery; Face-lifting
Saeedi [51]	2024	16	9	7	48	±9.71	Idiopathic 12; Herpes zoster 3; Post-vestibular schwannoma resection 1
Shinn [52]	2019	99	19	80	54	Not specified	Bell's palsy; Vestibular schwannoma; Ramsay Hunt; trauma; other
Shukla [53]	2024	25	6	19	48.7	±16.9	Idiopathic (60%), iatrogenic (24%), traumatic (12%), tumor (4%)
Su [54]	2020	234	21	27	58.2	±13.5	Hemifacial spasm
Thomas [55]	2018	28	8	20	49.1	±18.5	Not specified
Wagoner [56]	2024	29	8	21	58.1	±11.5	Not specified
Wei [57]	2015	42	4	38	53	±30.5	Bell's palsy

ultrasound-guided approaches [24, 37, 57], with needle sizes typically between 25G and 32G [33, 57]. Reported total doses varied widely (from <10 U to >100 U per session) [45, 48, 54], though per-site aliquots were usually small (1–5 U) [24, 48]. Long-term studies noted that while the number of muscles injected often increased over time, the dose per muscle remained stable [15, 19, 55], underscoring the importance of individualized mapping rather than the escalation of per-site dosage. Several studies explored multimodal approaches, combining botulinum toxin with rehabilitation techniques such as mirror biofeedback, neuromuscular retraining, or Wisconsin School exercises [16, 18, 39]. Others integrated botox with surgical procedures (selective neurectomy, facelift) or thread lifting [16, 39]. These combined strategies frequently yielded superior or longer-lasting improvements compared to toxin alone [18, 47], suggesting that chemodenervation may serve as a facilitator of rehabilitation or an adjunct to surgical correction rather than a stand-alone therapy in all cases. Outcome assessment lacked standardization. Objective tools included the SFGS [11], House-Brackmann scale [11], and digital analyses (Emotrics, FACE software, automated image analysis) [44, 51, 52]. Subjective measures such as the SAQ [12], Facial Disability Index [37, 44], and patient satisfaction scores [37, 52] captured psychosocial impact. While most studies demonstrated parallel improvement across objective and subjective domains [37, 44, 51], some reported discordance [37], highlighting the need for consensus on validated, multidimensional outcome measures that integrate both functional and quality-of-life aspects.

Tab. III. Data concerning botox injection procedure.

FIRST AUTHOR	YEAR	TIME OF ONSET TO THE FIRST PROCEDURE	TYPE OF BOTULINUM TOXIN	INTERVAL BETWEEN INJECTIONS	DOSAGE TOTAL (PER PROCEDURE)	DOSAGE PER INJECTION SITE	DURATION OF RESPONSE	INJECTION TECHNIQUE	ADVERSE EFFECTS
Akulov [14]	2024	Prescribed "early after facial nerve injury"	Incobotulinum-toxinA (Inco-BoNT)	4–6 months	Not specified	Not specified	Not specified	Not specified	Incidence of dry eye and Bogorad symptom increased in Group 1.
Alipour [15]	2021	Not specified	Onabotu-linumtoxin (OnaBoNT), IncoBoNT) Abo-botulinumtoxin (AboBoNT)	Median of 3.0 months	Initial dose (Ona/Inco): 24 U; Initial (Abo): 69 U	Dose per muscle remained stable	Stable median interval of 3.0 months	Performed without electromyographic guidance	Not analyzed; treatment was adapted for "unfavourable outcome... such as asymmetry or muscle dysfunction"
Alvaro [16]	2010	At the start of reinnervation or synkinesis onset	BoNT-A (Botox)	Every 16 weeks	Not specified	2.5 units per point	4–6 months	Injections in synkinetic muscles, hypertonic area, and the healthy side	Not specified
Armstrong [17]	1996	Patients had "established facial nerve palsies"	BoNT-A (Dysport)	3-monthly or on patient request	Eye: 20–100 U (median 40 U); Mouth: 60–240 U (median 120 U)	Eye: 10 U, 20U, or 40 U aliquots; Mouth: 20 U, 40 U, or 80 U aliquots	Lasted "several months"	Injections around the eye and into the normal side around the mouth	Ptosis, diplopia , facial weakness, drooling. Complications were "generally mild and transient".
Azuma [18]	2012	Mean 23 months (range 6–96)	BoNT-A (Botox)	Single treatment	15 units	2.5 units (at 6 points)	10 months (long-lasting effect of combined therapy)	Injected into ipsilateral orbicularis oculi muscle	None observed (no ptosis or diplopia)
Badarny [19]	2021	Not specified (First 3 treatments excluded as "titration")	Botox and Dysport	Mean 136 days	Not specified (Doses remained stable)	Not specified	3–4 months	Brands interchanged as needed (1:4 Botox: Dysport ratio)	Ptosis, lacrimation, diplopia, over weakness (all minor)
Bhatnagar [20]	2022	Minimum of 2 years after onset	BoNT-A	Not specified (a single session combined with threads)	Average 15.8 ±6.3 injections (for contralateral side)	1.5–2 units per point	6 months	Injected into the contralateral (non-paralyzed) side	Not specified (mentioned side effects can range from bruising to infection)
Bladen [21]	2019	Not specified	OnaBoNT	Fixed (12 weeks) or Flexible (mean 3.4 injections/ year)	Not specified	Not specified	Mean duration of maximal effect (DME) was 10.5 weeks	Not specified	Ptosis (30%), dry eye (14%), lagophthalmos (8%)
Boroojerdi [22]	1998	Varied (1–30 years)	BoNT-A (Dysport)	Not specified (Effect lasted approx. 6 months)	Average 75 MU (synkinesia); Average 20 MU (hyperlacrimation)	Not specified	Average 23.9 weeks (approx. 6 months)	4 points in orbicularis oculi (synkinesia); into lacrimal gland (hyperlacrimation)	Incomplete lid closure, ptosis, double vision, conjunctivitis
Cecini [23]	2013	Mean 38 months	BoNT-A (Botox)	Effect lasts 3–4 months	Mean 17.5 IU (range 7–29 IU)	2.5 IU	3–4 months	Injected into orbicularis oculi, platysma, and/or zygomaticus	2 hematomas; no other side effects observed
Choi [24]	2013	Mean 15.2 months	BoNT-A (Botox)	Average 10.6 months (for patients needing repeat injections)	Paralysed side (mean 17.12 U); Non-paralysed side (mean 52.6 U)	Paralysed side (1.5–2.5 U); Non-paralysed side (2.5–5 U)	(See interval: 10.6 months)	Concomitant injection of both sides (paralysed and non-paralysed)	Ptosis (4 patients), pseudo Bell's palsy (2 patients), diplopia (1 patient)
Chua [25]	2004	Not specified	BoNT-A (Dysport)	Mean 3 months (for higher doses); 2 months (for lowest dose)	120, 80, or 40 units	Not specified (divided doses)	Mean 3 months	Injected into pretarsal orbicularis at 2 or 4 sites	Ptosis (2 patients); none at the 40-unit dose

Tab. III. cd. Data concerning botox injection procedure.

FIRST AUTHOR	YEAR	TIME OF ONSET TO THE FIRST PROCEDURE	TYPE OF BOTULINUM TOXIN	INTERVAL BETWEEN INJECTIONS	DOSAGE TOTAL (PER PROCEDURE)	DOSAGE PER INJECTION SITE	DURATION OF RESPONSE	INJECTION TECHNIQUE	ADVERSE EFFECTS
Couch [26]	2014	Not specified	OnaBoNT (Botox)	Not specified (average 17.9 total treatments)	Average 14.8 units	Varies (11.1 U orbicularis oculi, 2.7 U zygomaticus)	Not specified	Injections into multiple muscles, including orbicularis oculi, zygomaticus major, etc.	No adverse events occurred during follow-up
Dall'Angelo [27]	2014	Median 18 months	OnaBoNT (BoNT-A) (Botox)	Median 4 months (patient reported)	Median platysmal dose 8.2 IU; Median total dose 17.7 IU	Approx. 2.5 IU	Median 4 months	Subcutaneously in platysmal bands	No adverse reactions occurred; transient bruising in 3 patients
Filipo [28]	2012	Not specified	BoNT-A (Botox)	Not specified (Duration of effect 3–6 months)	Not specified (Mean 7.9 injection points per patient)	1–8 U, depending on muscle	3–6 months	Subcutaneous, 45° angle, varied needle lengths by area	Eye dryness (3), hematoma (3), mild lagophthalmos (1), ptosis (1)
Hetzler [29]	2022	Average 5.2 years (Range 9 months–35 years)	OnaBoNT (Botox)	Not specified	Not specified	1 U (Range 0.5–1.25 U)	Not specified	Injected into perinasal muscles (DS, MM, LLSAN, NM)	Not specified (mentions risk of lip drop with lateral injection)
Homma [30]	2024	Minimum 12 months after onset	BoNT-A	At least 6 months	Not specified (Dose per muscle listed in supplement)	2.5 units	3–4 months	Injection site determined by patient complaints and synkinesis	3 total (corner of mouth ptosis, eyebrow ptosis); all temporary
Ito [31]	2007	1–22 years	BoNT-A (Botox)	Mean 14.5 weeks	Average 5.76 U (Range 2–10 U)	0.5–1.25 U per point	Remission defined as 6 months symptom--free	Subcutaneous injection into orbicularis oculi and oris	Mild subcutaneous hemorrhage (2 of 107 injection points)
Jun [32]	2024	Physical rehabilitation (first-line) was used for > 6 months; surgery was performed approx. 1 year after onset	BoNT-A (Botox)	Not specified	10–15 units	Not specified	Not specified	Injected into points of strongest synkinetic movement; sometimes injected on the unaffected side for symmetry	Sagging of the mouth corner (if the dose is too high
Kanerva [33]	2021	Not specified (Median 14.5 previous BT visits for returning patients)	BoNT-A (Botox)	3–4 months	Not specified (Buccinator dose range 1.25–7.5 IU)	Most common dose was 2.5 IU (84% of patients)	3 months (mentioned for hemifacial spasm patients)	Intraorally at the most posterior contracting part	Mostly mild; weakness of the mouth corner, saliva leakage, food pile up, difficulty chewing
Laskawi [34]	2014	Not specified	Botox (Allergan)	Mean 5.0 months (for synkinesis group)	Synkinesis group: Initial mean 14.3 U; 40th injection mean 28.3 U	Showed only a very slight increase (nearly constant)	Not specified (intervals were time-based, not symptom-based)	Individually adjusted injection points	Not specified
Lathif [35]	2025	Median 8.0 years (Range 1.0–31.0 years)	BoNT-A (Allergan/ AbbVie)	Not specified	Median 36.3 units	Not specified (Doses tailored to muscle; 3–4 points per muscle)	Not specified (Follow-up was at 4 weeks)	Tailored to severity; small boluses across 3–4 points per muscle	Not specified
Lee [36]	2015	Mean 26 months	BoNT-A (Botox)	6–8 months (for 3 injections)	1st: 17.4 U; 2nd: 36.5 U; 3rd: 15.6 U (mean)	1.5–3 U	3–5 months (toxin alone); 2 years (combined therapy)	Injected for synkinesis (ipsilateral) and hypertrophy (contralateral)	4 patients; hematoma, ptosis, and diplopia (lasted 6 weeks)

Tab. III. cd. Data concerning botox injection procedure.

FIRST AUTHOR	YEAR	TIME OF ONSET TO THE FIRST PROCEDURE	TYPE OF BOTULINUM TOXIN	INTERVAL BETWEEN INJECTIONS	DOSAGE TOTAL (PER PROCEDURE)	DOSAGE PER INJECTION SITE	DURATION OF RESPONSE	INJECTION TECHNIQUE	ADVERSE EFFECTS
Longino [37]	2025	7.6 ±6.2 years	OnaBoNT (Botox, Allergan)	Single treatment	Mean 39.9 units	Not specified	Assessed at 4 weeks post-injection	Targeted muscles based on synkinetic pattern	Not specified
Mabvuure [38]	2013	Not specified	Not specified	Single treatment	Not specified	Not specified	Evaluated via post-treatment photographs	Not specified	Not specified
Mandrini [39]	2016	Median 17.3 months	OnaBoNT	Minimum 5 months	Mean 18.6 ±5.9 IU	1.5–3 IU	Evaluated before each new session	Subcutaneous injection with an insulin syringe (25G needle); sites included orbicularis oculi, platysma (paretic side), and frontalis (healthy side)	Not specified
Maria [40]	2017	37.6 ±6.8 months	Nabota	Not specified	Mean 17.4 ±13.9 U	1.5–3 U	Evaluated over 1 year	Tuberculin syringe with 27G needle	Patients with >3 types of synkinesis, some experienced worsened paralysis or numbness
Mingazova [41]	2025	<1 month (acute Bell's palsy); 3 months–19 years (chronic cases)	BoNT-A (Relatox)	Group I: single injection; Group II: repeated every 3–4 months for 1–3 years	100 U reconstituted in 2 mL saline (5 U per 0.1 mL)	1.25–2.5 U per point; 15–20 points per session	3–4 months	Subcutaneous injections using 30G needle	Temporary dry eye (orbicularis oculi injection)
Monini [42]	2011	At least 1 year	BoNT-A	Single treatment	10–40 U	5 U/mL concentration	Evaluated over 90 days	BTX-A diluted (100 U in 2 mL saline)	Not specified
Moraleda [43]	2020	Not specified	OnaBoNT (64%); IncoBoNT (36%)	Mean 4 months	Mean 46 U (range: 10–72.5 U)	Not specified	Over 4-month	Individualized based on symptoms	Not specified
Neville [44]	2017	Not specified	BoNT-A	Minimum 4 months	Not specified	0.5–5 U per site	Follow-up at 16 days post-injection	Not specified	Lip ptosis, dry eye, lagophthalmos, excessive contralateral zygomaticus injection
Patel [45]	2018	~36 months	OnaBoNT	Every 3 months	31.9 ±13.1 U	2.5 U	66.2 ±13.4 days	EMG – guided injection using 27G needle electrode. Buccinator injected via buccal mucosa below Stenson's duct	Not specified
Pescarini [46]	2021	Mean 6.4 years	Xeomin (BoNT-A)	Single treatment	5 units	5 units	Assessed at 2 weeks post-injection	Ultrasound-guided injection into PBD muscle using 31G needle, 1 cm deep, with anatomical landmarks and chin retrusion maneuver	Not specified
Pourmomeny [47]	2015	5 ±6.93 years	Dysport (BoNT-A)	Single treatment	1 vial of 500 U diluted in 2.5 mL saline; injected into 3–7 muscle points per patient	Not specified	Evaluated after 4 months	Tuberculin syringe with 30-gauge needle	Not specified

Tab. III. cd. Data concerning botox injection procedure.

FIRST AUTHOR	YEAR	TIME OF ONSET TO THE FIRST PROCEDURE	TYPE OF BOTULINUM TOXIN	INTERVAL BETWEEN INJECTIONS	DOSAGE TOTAL (PER PROCEDURE)	DOSAGE PER INJECTION SITE	DURATION OF RESPONSE	INJECTION TECHNIQUE	ADVERSE EFFECTS
Risoud [48]	2016	12 ±12.1 years	OnaBoNT	Every 4–6 months	Mean 20.2 ±11.7 IU	Orbicularis oculi: 5.6 ±2.3 IU Depressor anguli oris: 3.8 ±1.4 IU Platysma: 9.0 ±5.7 IU Mentalis: 3.8 ±2.0 IU	Not specified	Intramuscular injection using 1-mL syringe and 26-gauge needle. Fan-like needle movement to follow muscle fiber pathways; no EMG guidance used	Not specified
Rogers [49]	2007	12–36 months	OnaBoNT	Single treatment	6–24 U	6–12 U	At 5–9 weeks post-injection	Targeted injections into specific muscles based on synkinesis type	Not specified
Roggenkämper [50]	1994	≥12 months	Occulinum, Allergan Inc.	~19 weeks	Not specified	1.25–2.5 IU	13.1 ±6.82 weeks	Periocular injections into orbicularis oculi	Tearing, lid lag, punctate keratitis, numbness
Saeedi [51]	2024	Not specified	OnaBoNT	Single treatment	32–49 U	10–13 U	Not specified	Individualized injection map and photographic/clinical planning	Not specified
Shinn [52]	2019	Not specified	OnaBoNT	~91 days	12.5–32.5 U	2–3 U	62–76 days	1.5-inch × 27-gauge hypodermic needle electrode with Luer-lock hub; BT dilution 2.5 U per 0.1 mL; dosing delivered with a 1-mL syringe for precision.	Not specified
Shukla [53]	2024	Median 29 months	OnaBoNT	Not specified	Upper eyelid group: 5.4 ±1.8 units; Lower/lateral only group: 7.5 ±3.4 units	Upper eyelid: 1.3 ±0.6 units; Lateral eyelid: 1.9 units (upper group) *vs* 3.4 units (lower/lateral only group); Lower eyelid: ~2.3–2.7 units	~23 days post-injection	Superficial subcutaneous injection to preseptal and orbital orbicularis oculi; pretarsal area avoided	Not specified
Su [54]	2020	4.6 ± 8.2	Lanbotulinumtoxin A(Lantox); OnaBoNT (Botox, Allergan)	At least 4 months	59.1 ±11 units	1.25–3.75 MU	Not specified	Periocular region and other facial regions with severe symptoms	Not specified
Thomas [55]	2018	Not specified	OnaBoNT, AboBoNT,and IncoBoNT	12 weeks minimum	Not specified	Not specified	Assessed over 4 weeks	Not specified	Redness, bruising, swelling, fullness at injection sites
Wagoner [56]	2024	72.3 ±82.4 months	Not specified	Not specified	Not specified	Not specified	Mean 33.9 ±25.9 months	Chemodenervation targeted areas: contralateral forehead, ipsilateral eye, depressor anguli oris, risorius, contralateral lip elevators, platysma	Not specified
Wei [57]	2015	7 years	OnaBoNT injections (Botox, Allergan, Irvine, CA, U.S.A.)	Not specified	54 units (range, 31–108 units)	Not specified	Not specified	An intraoral approach with a 32-gauge needle, a concentration of 2.5 units per milliliter	Transient eyelid ptosis, tearing, and lagophthalmos

AboBoNT – Abobotulinumtoxin; BoNT-A – botulinum toxin type A; DME – mean duration of maximal effect; EMG – electromyography; IncoBoNT – IncobotulinumtoxinA; OnaBoNT – Onabotulinumtoxin.

Risk of bias was formally assessed using the NOS. Most studies scored low to moderate, reflecting limitations in selection, comparability, and outcome assessment. Randomized controlled trials provided stronger evidence but were few and small in scale [9, 13]. Common weaknesses included reliance on patient-reported outcomes without blinding [17, 23, 33], short follow-up periods [15, 53], and lack of adjustment for confounders such as age, etiology, or baseline severity [37]. These methodological constraints reduce certainty in pooled conclusions and emphasize the need for larger, multicenter randomized trials [9, 13].

CONCLUSIONS

This systematic review summarizes and synthesizes existing studies concerning facial nerve synkinesis treatment with botulinum toxin. Patients with facial synkinesis present variable symptoms, and treatment should be tailored to each individual patient. Different treatment protocols, patient presentation, and inconsistent outcome measures complicate the formulation of definitive treatment guidelines. In further studies, objective outcome measures should be used, and a predefined treatment protocol should be employed.

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