REVIEW

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Long-term functional mobility and gait-related outcomes after single-event multilevel surgery in ambulatory children with cerebral palsy: A systematic review

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ABSTRACT

Background: Single-event multilevel surgery (SEMLS) is widely used to manage multilevel lower-limb deformities and gait impairment in ambulatory children with cerebral palsy. However, the long-term relationship between gait correction, functional mobility, biomechanical outcomes, and the need for additional surgery remains incompletely defined. This systematic review evaluated long-term functional mobility and gait-related outcomes after SEMLS or related multilevel surgical procedures in ambulatory children and adolescents with cerebral palsy.
Methods: A systematic literature search was conducted in PubMed and Scopus. Long-term follow-up was defined as postoperative follow-up exceeding 12 months. Eligible studies included original clinical studies evaluating SEMLS, multilevel gait improvement surgery, or procedure-specific interventions performed as part of a multilevel surgical approach in ambulatory individuals with cerebral palsy. Functional mobility outcomes included Functional Mobility Scale (FMS), Gillette Functional Assessment Questionnaire Walking Scale (FAQWS), Gross Motor Function Classification System (GMFCS), assistive device use, and wheelchair use. Gait-related outcomes included global gait indices, three-dimensional gait analysis, spatiotemporal parameters, kinematic and kinetic variables, and biomechanical measures. Methodological quality was assessed using MINORS, and findings were synthesized narratively.
Results: Of 480 identified records, 10 studies met the inclusion criteria. Functional mobility outcomes showed maintenance or improvement of ambulatory ability after SEMLS, although outcomes varied according to baseline GMFCS level and walking distance. Patients with GMFCS levels I–II generally demonstrated more favorable household and community mobility than those with GMFCS level III. Global gait indices, including GPS, GDI, EVGS, and GGI, generally improved after SEMLS. However, residual abnormalities such as pelvic tilt, swing-phase knee motion, postoperative back-kneeing, and recurrent crouch gait were also reported. Several long-term cohorts reported additional orthopedic surgery because of recurrence, residual deformity, or newly developed biomechanical problems.
Conclusion: SEMLS was associated with favorable long-term functional mobility and gait-related outcomes in ambulatory cerebral palsy. However, postoperative outcomes remained heterogeneous across functional level, gait domain, surgical composition, and follow-up duration.

Keywords: Ambulatory children, cerebral palsy, functional mobility, gait analysis, long-term outcomes, orthopedic surgery, SEMLS, single-event multilevel surgery.
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INTRODUCTION

Cerebral palsy is a non-progressive disorder of movement and posture that frequently results in progressive musculoskeletal impairment during growth.[1,2] In ambulatory children with cerebral palsy, altered muscle tone, impaired selective motor control, muscle weakness, contractures, torsional deformities, and lever-arm dysfunction may contribute to abnormal gait patterns and limitations in functional mobility.[3,4] These impairments can affect walking efficiency, independence, participation, and quality of life, particularly in children with bilateral or spastic diplegic cerebral palsy who remain ambulatory but develop multilevel lower-limb deformities over time.[5]

Orthopedic management of gait impairment in ambulatory cerebral palsy has evolved from repeated single-level procedures to single-event multilevel surgery (SEMLS).[6,7] SEMLS aims to address multiple musculoskeletal deformities during one operative episode, thereby reducing the need for repeated hospital admissions and separate rehabilitation periods. Surgical planning is commonly guided by clinical examination, imaging, and instrumented gait analysis, with procedures directed at deformities involving the hip, knee, ankle, and foot.[8,9] In contemporary practice, SEMLS is widely used to improve gait function in ambulatory children with cerebral palsy, particularly those classified within Gross Motor Function Classification System levels I to III.[10,11]

Previous studies have reported improvements in gait-related outcomes after SEMLS, including changes in global gait indices, spatiotemporal parameters, and segmental kinematics. Improvements have been reported using measures such as the Gait Profile Score, Gait Deviation Index, Movement Analysis Profile, Gillette Gait Index, Edinburgh Visual Gait Score, and three-dimensional gait analysis variables.[12,13] However, postoperative gait changes are not always uniform across all joints or gait phases. Some studies have shown improvement in overall gait quality while also reporting persistent or worsened abnormalities in specific components of gait, including pelvic tilt, knee motion, or recurrent sagittal plane deviations.[14,15]

Although gait analysis is central to the assessment of SEMLS, laboratory-based gait outcomes may not fully represent functional mobility in daily life.[16,17] Functional mobility depends not only on gait mechanics, but also on walking distance, environmental demands, assistive device use, endurance, and baseline motor function. Studies that evaluated functional mobility after SEMLS have used measures such as the Functional Mobility Scale, Gillette Functional Assessment Questionnaire Walking Scale, and Gross Motor Function Classification System. These measures provide information on walking performance in real-world settings, including home, school or work, and community environments.[5,16]

Long-term evaluation is particularly important because the postoperative course after SEMLS may continue to evolve after the early rehabilitation period.[18,19] Early gait improvement may be maintained, partially diminish, or be accompanied by residual deformity, recurrence, new biomechanical problems, or the need for additional orthopedic surgery.[20,21] Several long-term studies have reported that some patients require further procedures after SEMLS, indicating that surgical outcomes should be interpreted within the broader context of longitudinal musculoskeletal management in cerebral palsy.[11,14,16]

In addition, procedure-specific and biomechanical studies have provided further insight into selected mechanisms of postoperative change. Studies evaluating calf muscle lengthening, intramuscular psoas lengthening, conversion of biarticular to monoarticular muscles, and musculoskeletal loading have shown that individual components of multilevel surgery may influence specific kinematic or biomechanical outcomes.[22-24] However, because SEMLS involves simultaneous correction at multiple anatomical levels[25,26], the overall postoperative effect is difficult to attribute to any single procedure alone.[27,28]

Despite the growing body of evidence on SEMLS, the relationship between long-term gait improvement, functional mobility, biomechanical outcomes, patient-centered outcomes, and additional surgery remains incompletely defined. Many studies focus primarily on gait laboratory measures, while fewer studies evaluate functional mobility or quality of life over longer follow-up periods. Therefore, a synthesis of available evidence is needed to clarify long-term functional and gait-related outcomes after SEMLS in ambulatory children and adolescents with cerebral palsy.

The aim of this systematic review was to evaluate long-term functional mobility and gait-related outcomes after SEMLS in ambulatory children and adolescents with cerebral palsy. Secondary objectives were to summarize biomechanical and procedure-specific outcomes, patient-centered outcomes, and the need for additional orthopedic surgery after SEMLS. For this review, long-term follow-up was defined as postoperative follow-up exceeding 12 months.

METHODS

Study Design and Reporting Standards

This study was designed as a systematic review to evaluate long-term functional mobility and gait-related outcomes after single-event multilevel surgery in ambulatory children and adolescents with cerebral palsy. The review focused on original clinical studies reporting postoperative outcomes following SEMLS, multilevel gait improvement surgery, or procedure-specific surgical interventions performed as part of a multilevel surgical approach. For the purpose of this review, long-term follow-up was operationally defined as postoperative assessment performed more than 12 months after surgery, or a reported mean or median postoperative follow-up duration exceeding 12 months. This operational threshold was selected to capture outcomes beyond the early postoperative rehabilitation period and to include studies reporting medium- to longer-term postoperative trajectories.

The conduct and reporting of this systematic review were guided by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 statement (**Figure 1**). The review process included predefined eligibility criteria, systematic literature searching, duplicate removal, title and abstract screening, full-text assessment, structured data extraction, methodological quality assessment, and qualitative evidence synthesis. Because of anticipated clinical and methodological heterogeneity across studies, including differences in participant characteristics, surgical procedures, follow-up duration, and outcome measures, a quantitative meta-analysis was not planned. Findings were therefore synthesized narratively.

The primary outcome domain was functional mobility, including the Functional Mobility Scale, Gillette Functional Assessment Questionnaire Walking Scale, Gross Motor Function Classification System, walking independence, use of assistive devices, wheelchair use, and community ambulation. Secondary outcome domains included gait-related and biomechanical outcomes, such as gait quality indices, spatiotemporal parameters, three-dimensional gait analysis findings, kinematic and kinetic variables, musculoskeletal loading, joint contact forces, and additional orthopedic surgery. Quality of life, patient-reported outcomes, caregiver-reported outcomes, and satisfaction with surgery were considered patient-centered secondary outcomes.

A review protocol was developed before study selection and data extraction to guide the methodological process, define eligibility criteria, and standardize outcome classification. However, the protocol is still in the process of PROSPERO registration. All included studies were derived from the predefined search strategy and final eligibility assessment, and no studies outside the selected evidence set were added to the qualitative synthesis.

Eligibility Criteria

Studies were considered eligible if they evaluated ambulatory individuals with cerebral palsy who underwent single-event multilevel surgery, multilevel gait improvement surgery, or procedure-specific orthopedic interventions explicitly performed as part of a multilevel surgical approach. Ambulatory cerebral palsy was defined as independent or assisted walking before surgery, corresponding to Gross Motor Function Classification System levels I to III when reported. Studies involving cohorts followed into adulthood were eligible when the index surgical intervention was performed during childhood or adolescence, or when the cohort predominantly represented pediatric or adolescent ambulatory cerebral palsy. Studies with limited inclusion of older participants were retained when the clinical context, intervention, and outcome assessment remained directly relevant to pediatric multilevel surgery in ambulatory cerebral palsy.

Eligible diagnoses included spastic diplegic cerebral palsy, bilateral spastic cerebral palsy, or ambulatory cerebral palsy cohorts in which lower-limb gait impairment was the primary surgical indication. Studies were eligible regardless of whether participants had previous orthopedic procedures, provided that the index intervention evaluated in the article consisted of SEMLS, multilevel gait improvement surgery, or a clearly defined component of SEMLS. Studies including patients with non-ambulatory cerebral palsy as the dominant population, isolated upper-limb surgery, selective dorsal rhizotomy as the primary intervention, or non-cerebral palsy neuromotor disorders were excluded.

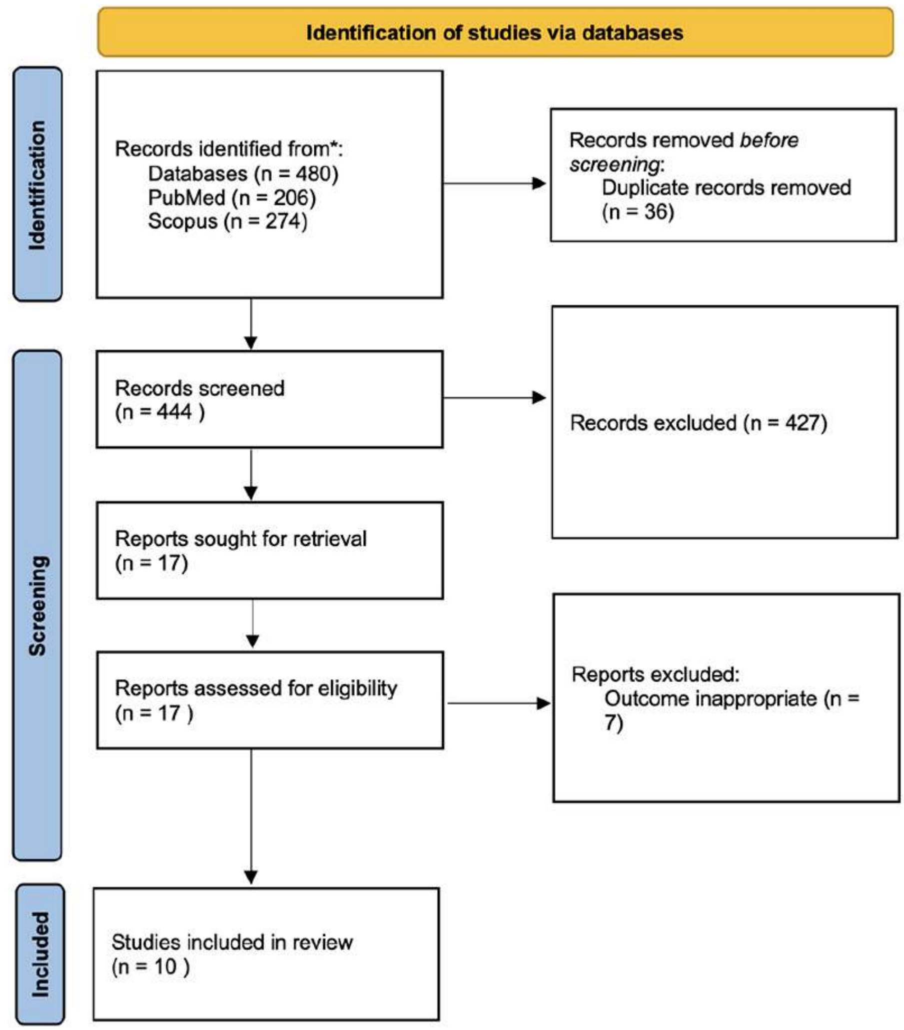

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Eligible interventions included single-event multilevel surgery involving soft-tissue and/or bony procedures performed at multiple anatomical levels during one operative episode. Multilevel gait improvement surgery was considered eligible when it addressed lower-limb deformities or gait dysfunction through combined orthopedic procedures. Procedure-specific studies were also eligible when the investigated procedure was explicitly performed during SEMLS or as a component of multilevel surgery, including calf muscle lengthening, intramuscular psoas lengthening, conversion of biarticular to monoarticular muscles, or biomechanical evaluation following SEMLS.

For the purpose of this review, long-term follow-up was defined as postoperative assessment beyond 12 months, or a reported mean or median postoperative follow-up duration exceeding 12 months. Studies with multiple postoperative assessments were eligible when at least one assessment met this follow-up criterion. Studies with shorter follow-up were excluded unless the reported mean or median postoperative interval exceeded 12 months.

The primary outcomes of interest were functional mobility outcomes, including Functional Mobility Scale scores, Gillette Functional Assessment Questionnaire Walking Scale scores, Gross Motor Function Classification System classification, walking independence, use of assistive devices, wheelchair use, and community ambulation. Patient-centered outcomes, including quality of life, patient-reported outcomes, caregiver-reported outcomes, and satisfaction with surgery, were considered secondary outcomes.

Secondary outcomes included gait-related and biomechanical measures, such as Gait Profile Score, Gait Deviation Index, Gillette Gait Index, Edinburgh Visual Gait Score, spatiotemporal gait parameters, three-dimensional gait analysis variables, lower-limb kinematics, kinetic parameters, muscle forces, joint contact forces, musculoskeletal loading, and the need for additional orthopedic surgery.

Original human clinical studies were eligible for inclusion, including prospective cohort studies, retrospective cohort studies, case series, comparative observational studies, and procedure-specific clinical studies. No restriction was applied based on the presence or absence of a control group. Studies comparing SEMLS with baseline status, typically developing reference data, nonoperative controls, botulinum toxin injection, or other comparator groups were eligible when the SEMLS-related outcomes could be extracted. Review articles, narrative commentaries, editorials, letters without original data, animal studies, cadaveric studies, in vitro studies, technical notes without clinical outcome data, and conference abstracts without sufficient full-text information were excluded from the main synthesis.

Only full-text articles available in English were included. Articles were included in the final qualitative synthesis when they fulfilled the predefined criteria for population, intervention, follow-up duration, and functional mobility or gait-related outcome reporting.

Information Sources

The literature search was conducted using two electronic databases: PubMed and Scopus. These databases were selected to provide broad coverage of biomedical, orthopedic, rehabilitation, gait analysis, and clinical biomechanics literature relevant to cerebral palsy and single-event multilevel surgery. PubMed was used to capture studies indexed within the biomedical and clinical literature, whereas Scopus was used to broaden retrieval across multidisciplinary journals, including orthopedic surgery, rehabilitation science, movement analysis, and biomechanics.

The search was designed to identify original clinical studies evaluating long-term functional mobility and gait-related outcomes after single-event multilevel surgery, multilevel gait improvement surgery, or procedure-specific interventions performed as part of a multilevel surgical approach in ambulatory individuals with cerebral palsy. No additional databases were used. Grey literature, unpublished studies, trial registries, conference abstracts without full-text data, and non-peer-reviewed sources were not included in the final evidence synthesis.

All records retrieved from PubMed and Scopus were combined before duplicate removal. The final set of included articles was derived exclusively from the records identified through these database searches after title and abstract screening, full-text eligibility assessment, and application of the predefined inclusion and exclusion criteria. No studies outside the predefined search results were added to the qualitative synthesis.

Search Strategy

The literature search was conducted in PubMed and Scopus, with the final search completed on April 29, 2026. The search strategy was developed to identify original clinical studies evaluating functional mobility and gait-related outcomes after single-event multilevel surgery or related multilevel orthopedic procedures in ambulatory individuals with cerebral palsy. No restriction on publication year was applied during the database search.

The search strategy combined three core concepts: cerebral palsy, multilevel orthopedic surgery, and functional mobility or gait-related outcomes. The cerebral palsy concept included terms such as "cerebral palsy," "spastic diplegia," "diplegic cerebral palsy," and "bilateral spastic cerebral palsy." The intervention concept included "single-event multilevel surgery," "single event multilevel surgery," "single-stage multilevel surgery," "SEMLS," "multilevel surgery," "multi-level surgery," and "gait improvement surgery." The outcome concept included "gait," "walking," "ambulation," "mobility," "functional mobility," "gait analysis," "Gait Profile Score," "Gait Deviation Index," "Gillette Gait Index," "Edinburgh Visual Gait Score," "Functional Mobility Scale," "Gillette Functional Assessment Questionnaire," "kinematics," "kinetics," "joint loading," "muscle force," and "contact force."

Boolean operators were used to combine search terms within and across these concepts. Synonymous terms within each concept were combined using OR, and the three main concepts were combined using AND. In PubMed, Medical Subject Headings and title/abstract terms were used where applicable. In Scopus, the search was adapted using the TITLE-ABS-KEY field. The search strategy was adapted to the syntax of each database while preserving the same conceptual structure across databases.

Two reviewers independently performed the database searches and screened the retrieved records according to the predefined eligibility criteria. Records were subsequently managed for duplicate removal, title and abstract screening, and full-text assessment as described in the Study Selection section.

Data Extraction

Data extraction was performed using a standardized data extraction form developed for this review. Two reviewers independently extracted data from each included full-text article, and any discrepancies were resolved through discussion and consensus. The extraction process was conducted after completion of the full-text eligibility assessment.

The following key information was extracted from each study: first author and year of publication, country, study design, sample size, participant characteristics, type of surgical intervention, follow-up duration, outcome measures, and main findings. Participant characteristics included cerebral palsy subtype and Gross Motor Function Classification System level when reported. Intervention data included whether the study evaluated single-event multilevel surgery, multilevel gait improvement surgery, or a specific surgical procedure performed as part of a multilevel surgical approach.

Outcome data were extracted according to the focus of each article and included functional mobility outcomes, gait-related outcomes, biomechanical outcomes, and the need for additional surgery when reported. Functional mobility outcomes included measures such as the Functional Mobility Scale, Gillette Functional Assessment Questionnaire Walking Scale, Gross Motor Function Classification System, walking independence, use of assistive devices, and wheelchair use. Patient-centered outcomes included quality of life, patient-reported outcomes, caregiver-reported outcomes, and satisfaction. Gait-related and biomechanical outcomes included gait quality scores, spatiotemporal parameters, three-dimensional gait analysis findings, kinematic and kinetic variables, muscle forces, joint contact forces, and musculoskeletal loading.

For each included study, the main preoperative and postoperative findings were extracted as reported by the original authors. When studies reported multiple follow-up time points, the longest available follow-up was prioritized for the main synthesis, while earlier postoperative findings were retained when relevant to describe changes over time. For comparative studies, findings were extracted for the SEMLS group and comparator group when applicable. For non-comparative studies, within-cohort preoperative and postoperative changes were extracted.

The extracted data were used to construct the study characteristics table and to support the qualitative narrative synthesis. Because of heterogeneity in study design, surgical procedures, follow-up duration, and outcome measures, data were summarized descriptively without quantitative pooling.

Risk of Bias Assessment

The methodological quality and risk of bias of the included studies were assessed independently by two reviewers using the Methodological Index for Non-Randomized Studies (MINORS). This tool was selected because all included articles were non-randomized clinical studies evaluating surgical or gait-related outcomes, including retrospective cohort studies, prospective observational studies, case series, and comparative observational studies. A single risk-of-bias tool was therefore considered appropriate for the full body of included evidence.

For non-comparative studies, the assessment included eight domains: clearly stated aim, inclusion of consecutive patients, prospective collection of data, endpoints appropriate to the study aim, unbiased assessment of study endpoints, adequate follow-up period, loss to follow-up less than 5%, and prospective calculation of study size. For studies with an explicit comparator group, four additional domains were assessed: adequacy of the control group, contemporaneous nature of groups, baseline equivalence of groups, and adequacy of statistical analyses. Studies that only compared postoperative results with preoperative baseline values were assessed as non-comparative studies. Studies using typically developing reference data without a true clinical comparator group were also assessed as non-comparative studies.

Each domain was scored as 0 when not reported, 1 when reported but inadequate, and 2 when reported and adequate. The maximum possible score was 16 for non-comparative studies and 24 for comparative studies. Disagreements between reviewers were resolved through discussion and consensus. When reporting was unclear, scoring was performed conservatively based on the information available in the full-text article.

The risk-of-bias assessment was used to support interpretation of the findings rather than to determine study exclusion. No study was excluded solely on the basis of methodological quality. The final risk-of-bias results were summarized in tabular form and incorporated into the qualitative synthesis.

Data Synthesis

A quantitative meta-analysis was not performed because of substantial clinical and methodological heterogeneity across the included studies. The included articles differed in study design, participant characteristics, cerebral palsy subtype, GMFCS distribution, surgical composition, follow-up duration, outcome measures, and reporting format. In addition, several studies reported outcomes at the limb level, whereas others reported outcomes at the patient level, limiting the appropriateness of statistical pooling.

Therefore, findings were synthesized narratively according to predefined outcome domains. The primary synthesis focused on functional mobility outcomes, including Functional Mobility Scale scores, Gillette Functional Assessment Questionnaire Walking Scale scores, Gross Motor Function Classification System levels, walking independence, use of assistive devices, wheelchair use, and community ambulation. Patient-centered outcomes, including quality of life, patient or caregiver satisfaction, and perceived functional status, were summarized as secondary supportive outcomes.

Gait-related outcomes were synthesized separately and included global gait indices, spatiotemporal parameters, three-dimensional gait analysis findings, kinematic variables, kinetic variables, and visual gait assessment scores. Where applicable, gait quality measures such as the Gait Profile Score, Gait Deviation Index, Gillette Gait Index, Movement Analysis Profile, and Edinburgh Visual Gait Score were described according to the direction and magnitude of postoperative change reported by each study. Biomechanical outcomes, including muscle forces, joint loading, and joint contact forces, were summarized separately because these outcomes represented mechanistic gait-related measures rather than direct functional mobility measures.

The included studies were grouped according to their primary clinical focus. Studies evaluating overall SEMLS or multilevel gait improvement surgery were considered the main evidence base for the review. Procedure-specific studies were synthesized as supportive evidence when the investigated procedure was performed as part of SEMLS or a multilevel surgical approach. Biomechanical or musculoskeletal modeling studies were also treated as supportive evidence because they provided mechanistic information on gait-related outcomes after SEMLS.

When studies reported multiple

postoperative time points, the longest follow-up time point meeting the eligibility criterion of more than 12 months was prioritized for the main synthesis. Earlier postoperative assessments were retained when they provided relevant information on temporal changes after surgery, including maintenance, deterioration, or progression of functional mobility and gait-related outcomes. When studies reported both short-term and longer-term findings, the interpretation emphasized the longer-term postoperative results.

The direction of treatment effect was categorized descriptively as improvement, maintenance, deterioration, or mixed change based on the authors' reported findings. Improvement was defined as postoperative change toward better functional mobility, greater walking independence, reduced gait deviation, improved gait quality scores, or more favorable kinematic, kinetic, or biomechanical parameters. Maintenance was defined as preservation of preoperative or early postoperative functional mobility or gait status at later follow-up. Deterioration was defined as worsening of functional mobility, increased need for assistive devices or wheelchair use, worsening gait indices, or unfavorable changes in kinematic or biomechanical parameters. Mixed change was assigned when a study reported improvement in some outcome domains but deterioration or lack of improvement in others.

The synthesis also considered the need for additional orthopedic surgery after SEMLS as an important contextual outcome. Additional surgery was not interpreted solely as treatment failure, but as an indicator of the long-term clinical course, recurrence, residual deformity, or the need for ongoing orthopedic management in ambulatory cerebral palsy. Findings related to additional surgery were summarized alongside functional and gait-related outcomes when reported.

Because the review included only studies provided in the predefined evidence set, no external studies were added during synthesis. Conclusions were drawn only from the included articles and were interpreted in relation to study design, sample size, follow-up duration, outcome measures, and risk of bias.

RESULTS

Study Selection

The literature search yielded 480 records, including 206 records from PubMed and 274 records from Scopus. After duplicate removal, 444 records remained for title and abstract screening. Of these, 427 records were excluded because they were not relevant to the review question or did not meet the predefined eligibility criteria. Seventeen full-text articles were subsequently retrieved and assessed for eligibility.

Following full-text assessment, seven articles were excluded because their outcomes were not consistent with the objectives of this review. Consequently, 10 articles met the inclusion criteria and were included in the final qualitative synthesis. All included studies reported postoperative functional mobility, gait-related, biomechanical, or procedure-specific outcomes after single-event multilevel surgery, multilevel gait improvement surgery, or surgical procedures performed as part of a multilevel approach in ambulatory individuals with cerebral palsy. No studies outside the predefined search results and eligibility process were added to the final synthesis.

Study Characteristics

The main characteristics of the included studies are summarized in **Table 1**. The final qualitative synthesis included 10 clinical studies evaluating postoperative outcomes after single-event multilevel surgery, multilevel gait improvement surgery, or procedure-specific procedures performed as part of a multilevel surgical approach in ambulatory individuals with cerebral palsy. The included studies were published between 2004 and 2021 and consisted predominantly of retrospective cohort studies, case series, and procedure-specific observational studies. One study used a prospective design, and several studies incorporated comparative elements, including nonoperative control groups, typically developing reference data, or comparison between surgical subgroups.

The study populations consisted mainly of children and adolescents with spastic diplegic or bilateral spastic cerebral palsy who were ambulatory before surgery. When reported, participants were classified within GMFCS levels I to III, although several studies predominantly included GMFCS level II or III patients. Sample sizes varied substantially across studies, ranging from 13 to 258 patients in the SEMLS-related cohorts. Follow-up duration also varied, from a mean of approximately 13.7 months to a median of 18 years. All included studies met the operational definition of long-term follow-up used in this review, defined as an individual postoperative assessment or a reported mean or median follow-up duration exceeding 12 months.

The included studies reported heterogeneous outcome domains. Functional mobility and patient-centered outcomes were assessed using measures such as the Functional Mobility Scale, Gillette Functional Assessment Questionnaire Walking Scale, GMFCS classification, quality-of-life instruments, and satisfaction scores. Gait-related outcomes were assessed using three-dimensional gait analysis, visual gait analysis, spatiotemporal parameters, Gait Profile Score, Gait Deviation Index, Movement Analysis Profile, Gillette Gait Index, and Edinburgh Visual Gait Score. Procedure-specific and biomechanical studies reported joint kinematics, kinetics, muscle forces, joint contact forces, calf muscle lengthening, intramuscular psoas lengthening, and conversion of biarticular to monoarticular muscles.

Risk of Bias Assessment

The methodological quality and risk-of-bias assessment using the Methodological Index for Non-Randomized Studies (MINORS) is summarized in Table 2. Overall, the included studies showed variable methodological quality, reflecting differences in study design, sample size, follow-up duration, outcome assessment, and the presence or absence of comparator groups. Most included studies had clearly stated aims, clinically relevant endpoints, and follow-up periods that were appropriate for the objectives of this review. However, common methodological limitations included retrospective study design, small sample size, absence of prospective sample size calculation, lack of blinded or independent endpoint assessment, and incomplete follow-up in several long-term cohorts.

Table 1. Characteristics of included studies

Study	Study design and population	Intervention and follow-up	Main outcome domains
Visscher et al.[14]	Retrospective case series; 13 children with bilateral spastic cerebral palsy, all GMFCS level II at index surgery	SEMLS; serial 3D gait analysis with long-term follow-up at a mean of 11.1 years	GPS, MAP, lower-limb and pelvic kinematics, statistical parametric mapping, additional surgery
Saraph et al.[6]	Retrospective cohort; 32 ambulatory children with diplegic cerebral palsy	Single-event multilevel gait improvement surgery; postoperative gait analyses at mean 1.0, 2.3, and 4.4 years	Sagittal plane hip, knee, and ankle kinematics; time-distance gait parameters
de Freitas Guardini et al.[15]	Retrospective comparative cohort; 258 patients with spastic diplegic CP, GMFCS I–III, and 88 nonoperative controls	SEMLS compared with no surgical intervention; mean follow-up of approximately 30.7 months in the SEMLS group	GDI, GPS, MAP, gait velocity, predictors of kinematic outcome
Klotz et al.[25]	Retrospective procedure-specific study; 19 patients with bilateral spastic CP and primary genu recurvatum, with 26 limbs analyzed	Aponeurotic calf muscle lengthening during SEMLS; mean follow-up of 13.7 months	Ankle dorsiflexion, knee hyperextension, sagittal kinematics, responder status
Jones et al.[16]	Long-term retrospective single-center cohort; 26 of 39 eligible patients with diplegic CP had complete assessment	Multilevel surgery/SEMLS; median follow-up of 18 years	EVGS, FAQWS, GMFCS, SF-36, functional independence, patient satisfaction, additional surgery
Terjesen et al.[11]	Prospective cohort; 34 ambulatory children and adolescents with spastic diplegic CP	Gait-analysis-based orthopedic multilevel surgery; 5-year gait-analysis follow-up	GPS, selected kinematic parameters, FMS, parental satisfaction, additional surgery
Metaxiotis et al.[26]	Prospective procedure-specific clinical study; 20 ambulatory children with spastic diplegic CP, with 40 limbs analyzed	Multilevel surgery including conversion of biarticular to monoarticular muscles; mean follow-up of 3.1 years	Clinical ROM, 3D gait analysis, kinematics, kinetics, time-distance parameters
Van Rossom et al.[28]	Retrospective comparative biomechanical modelling study; 44 SEMLS patients, 49 botulinum toxin patients, and 15 typically developing controls	SEMLS compared with multilevel botulinum toxin injections; SEMLS postoperative assessment approximately 388 days after intervention	Joint angles, joint moments, muscle forces, joint contact force magnitudes and orientations
Edwards et al.[5]	Case series; 61 patients with diplegic CP, GMFCS I–III, treated with SEMLS before age 18 years	SEMLS; mean long-term follow-up of 8 years	FMS, CP QOL Teen, GPS at 24 months, functional mobility at home, school/work, and community distances
Mallet et al.[27]	Retrospective procedure-specific comparative study; 34 ambulatory children with CP, 47 limbs, GMFCS I–III	SEMLS with or without intramuscular psoas lengthening; mean follow-up of 2.4 years	Clinical hip flexion deformity, hip and knee kinematics, GGI, walking speed, step length, recurrent crouch gait

Table 2. Methodological quality and risk-of-bias assessment using the methodological index for non-randomized studies (MINORS) tool

Study	Study type for MINORS assessment	MINORS score
Visscher et al.[14]	Non-comparative	8/16
Saraph et al.[6]	Non-comparative	10/16
de Freitas Guardini et al.[15]	Comparative	17/24
Klotz et al.[25]	Non-comparative	9/16
Jones et al.[16]	Non-comparative	10/16
Terjesen et al.[5]	Non-comparative	13/16
Metaxiotis et al.[26]	Non-comparative	13/16
Van Rossom et al.[28]	Comparative	16/24
Edwards et al.[5]	Non-comparative	10/16
Mallet et al.[27]	Comparative	18/24

Among the non-comparative studies, MINORS scores ranged from 8 to 13 out of 16. The highest scores were observed in prospective or systematically followed cohorts with clearly defined populations, standardized gait analysis protocols, and complete or near-complete follow-up. Lower scores were generally related to retrospective recruitment, selective inclusion of patients with available follow-up gait analysis, limited reporting of consecutive enrollment, and absence of prospective sample size calculation. Among the comparative studies, MINORS scores ranged from 16 to 18 out of 24. These studies benefited from the inclusion of comparator groups or subgroup comparisons, although the non-randomized design, baseline differences between groups, and potential selection bias limited the strength of causal interpretation.

No study was excluded on the basis of methodological quality. Instead, the risk-of-bias findings were used to guide interpretation of the evidence. In the narrative synthesis, findings from studies with longer follow-up, clearly defined eligibility criteria, standardized outcome assessment, and more complete reporting were interpreted with consideration of their methodological strengths, while findings from smaller procedure-specific or biomechanical studies were interpreted as supportive evidence.

Functional Mobility Outcomes

Functional mobility outcomes were reported in three included studies using the Functional Mobility Scale (FMS), the Gillette Functional Assessment Questionnaire Walking Scale (FAQWS), and the Gross Motor Function Classification System (GMFCS). Follow-up duration in these studies ranged from 5 years to 18 years. The reported functional mobility outcomes are summarized according to the outcome measure used.

Edwards et al. assessed long-term functional mobility using the FMS in 61 patients with diplegic cerebral palsy after SEMLS.[1] The mean age at surgery was 11 years and 8 months, and the mean duration of long-term follow-up was 8 years. Among patients classified as GMFCS levels I and II before surgery, the median FMS score at long-term follow-up was 5 at home, 5 at school or work, and 5 in the community. In this subgroup, 71% of patients walked independently at home, while 57% walked independently at school or work and in the community. Among patients classified as GMFCS level III before surgery, the median FMS score at long-term follow-up was 4 at home, 2 at school or work, and 1 in the community. In this subgroup, 82% of patients walked either independently or with an assistive device at home, 76% walked independently or with an assistive device at school or work, and 61% required a wheelchair for community distances.[5]

Terjesen et al. evaluated functional mobility using the FMS in 34 ambulatory children and adolescents with spastic diplegic cerebral palsy after gait-analysis-based multilevel surgery. FMS was assessed at 5 m, 50 m, and 500 m preoperatively, at 1 year postoperatively, and at 5 years postoperatively. At 1 year after surgery, FMS improved significantly from baseline at the 5-m and 50-m distances, while the improvement at 500 m was not statistically significant. At 5 years after surgery, FMS scores were improved from preoperative values across all three distances. Improvement by at least one FMS category at 5-year follow-up was reported in 7 children at 5 m, 9 children at 50 m, and 16 children at 500 m. In children classified as GMFCS level II, FMS at 5 m remained unchanged because all children were already walking without assistive devices at this distance before surgery, whereas significant improvements were reported at 50 m and 500 m. In children classified as GMFCS level III, FMS improved at all three distances, with the greatest improvement reported at 5 m.[11]

Jones et al. reported functional status using the FAQWS and GMFCS in a long-term cohort of patients with diplegic cerebral palsy who underwent multilevel surgery more than 10 years earlier.[6] Complete assessment was available for 26 patients, with a median follow-up duration of 18 years. Before surgery, 12 patients were classified as GMFCS level II and 14 as GMFCS level III. At the most recent follow-up, no patient had deteriorated in GMFCS level, and one patient had improved by one level. The median FAQWS score increased from 6 preoperatively to 8 at initial postoperative assessment and remained 8 at the most recent long-term follow-up. The improvement in FAQWS from preoperative assessment to most recent follow-up was statistically significant. At the most recent assessment, all patients retained the ability to walk. In addition, 25 of 26 patients were fully independent in transfers.[16]

Across the three studies reporting functional mobility outcomes, FMS was used in two studies, FAQWS in one study, and GMFCS in one study. Functional mobility was reported at household, school or work, and community distances in the FMS-based studies. GMFCS level was reported as stable in the long-term cohort assessed by Jones et al., while distance-specific FMS results showed different mobility patterns between GMFCS I–II and GMFCS III subgroups in the studies by Edwards et al. and Terjesen et al. Functional mobility outcomes were not reported as primary endpoints in the remaining included studies.

Gait-Related Outcomes

Gait-related outcomes were reported in all included studies, although detailed procedure-specific and biomechanical findings are summarized separately in the following section. The reported measures included three-dimensional gait analysis, visual gait analysis, Gait Profile Score (GPS), Gait Deviation Index (GDI), Movement Analysis Profile (MAP), Gillette Gait Index (GGI), Edinburgh Visual Gait Score (EVGS), sagittal plane kinematics, spatiotemporal parameters, and procedure-specific gait variables.

Visscher et al. assessed gait outcomes in 13 children with bilateral spastic cerebral palsy who underwent SEMLS and had serial three-dimensional gait analysis before surgery and at short-, mid-, and long-term follow-up. The mean long-term follow-up was 11.1 years. GPS improved from preoperative assessment to postoperative follow-up, and no significant differences were reported between the short-, mid-, and long-term postoperative assessments. MAP scores improved for hip flexion, knee flexion, ankle dorsiflexion, internal pelvic rotation, and internal foot progression. Statistical parametric mapping showed improvement in knee extension during stance, while knee flexion during swing and pelvic tilt showed postoperative deterioration. Eight of 13 participants underwent additional surgical interventions during the follow-up period.[14]

Saraph et al. reported sagittal plane gait outcomes in 32 ambulatory children with diplegic cerebral palsy after single-event multilevel gait improvement surgery. Postoperative gait analyses were performed at mean intervals of 1.0, 2.3, and 4.4 years after surgery. Walking velocity increased significantly at the first postoperative assessment and remained stable across later assessments. Stride length progressively increased over the postoperative assessments. Hip extension in stance improved gradually and reached statistical significance at the third postoperative assessment. Knee extension in stance showed marked early improvement, followed by some reduction in the magnitude of improvement at later assessments, although the final values remained improved compared with preoperative values. Ankle kinematics showed progressive increases in dorsiflexion at initial contact, midstance, and swing, with reduced plantarflexion at toe-off.[6]

de Freitas Guardini et al. compared 258 patients who underwent SEMLS with 88 nonoperative controls. In the SEMLS group, GDI increased from 51.4 to 58.4, while GPS decreased by 2.5°.[15] In the control group, GDI decreased from 59.6 to 57.9. MAP analysis in the SEMLS group showed postoperative improvement in knee flexion-extension, ankle dorsiflexion-plantarflexion, hip internal-external rotation, and foot progression angle. Pelvic anterior-posterior tilt showed deterioration after surgery. In subgroup analysis, the increase in GDI was greater in patients classified as GMFCS levels I and II than in those classified as GMFCS level III. Patients with greater improvement in GDI had lower preoperative GDI and higher baseline gait velocity.[15]

Klotz et al. evaluated gait outcomes after aponeurotic calf muscle lengthening performed during SEMLS in 19 patients with bilateral spastic cerebral palsy and primary genu recurvatum. A total of 26 limbs were analyzed, with a mean follow-up of 13.7 months. After surgery, ankle dorsiflexion improved significantly during midstance, and knee hyperextension was significantly reduced. Six limbs, representing 23% of the analyzed limbs, were classified as nonresponders because knee hyperextension remained greater than one standard deviation from the age-matched reference group after surgery.[25]

Jones et al. assessed gait using EVGS in 26 patients with complete long-term assessment after multilevel surgery for diplegic cerebral palsy. The median follow-up duration was 18 years.[16] The median preoperative EVGS was 37.5 and improved to 13.5 at midterm postoperative follow-up. At the most recent long-term follow-up, the median EVGS was 16.5. EVGS remained significantly improved at the most recent follow-up compared with the preoperative assessment, although the median score was higher at long-term follow-up than at the midterm postoperative assessment. One patient did not show improvement in EVGS at the most recent follow-up.[16]

Terjesen et al. reported gait outcomes in 34 ambulatory children and adolescents with spastic diplegic cerebral palsy after gait-analysis-based multilevel surgery. The mean GPS improved from 20.7° preoperatively to 15.4° at 5 years postoperatively. No significant change in GPS was reported between the 1-year and 5-year postoperative assessments. Selected kinematic parameters at the ankle, knee, and hip also improved significantly at 5-year follow-up. Additional orthopedic procedures were performed in 14 children during follow-up.[11]

Metaxiotis et al. assessed gait outcomes in 20 ambulatory children with spastic diplegic cerebral palsy who underwent multilevel surgery including conversion of biarticular to monoarticular muscles.[26] Forty limbs were analyzed, and the mean follow-up duration was 3.1 years. Passive range of motion at the ankle, knee, and hip improved postoperatively. Kinematic analysis showed reduced pelvic range of movement and improved knee extension during single stance. Postoperative back-kneeing was reported in five of 40 limbs. Kinetic analysis showed that hamstring and ankle plantarflexor power were maintained, while maximum knee extensor moment during stance was reduced.[26]

Van Rossom et al. reported gait-related biomechanical outcomes in 44 patients treated with SEMLS, 49 patients treated with multilevel botulinum toxin injections, and 15 typically developing children. In the SEMLS group, postoperative assessment was performed approximately 388 days after intervention. SEMLS was associated with significant changes in joint kinematics and kinetics. The study also reported postoperative improvements in muscle force and joint contact force measures in the SEMLS group. In contrast, the botulinum toxin group showed changes in joint angles but did not show improvement in muscle and joint contact force measures.[28]

Edwards et al. reported GPS as a gait-related outcome in 61 patients with diplegic cerebral palsy who underwent SEMLS. GPS was measured preoperatively and at routine 24-month postoperative gait analysis.[1] GPS improved significantly from preoperative assessment to 24 months postoperatively, with a mean improvement of 3.3°. Long-term follow-up in this study focused on FMS and quality-of-life outcomes rather than repeat long-term instrumented gait analysis.[5]

Mallet et al. evaluated gait outcomes in 34 ambulatory children with cerebral palsy who underwent SEMLS with or without intramuscular psoas lengthening.[27] Forty-seven limbs were included, and the mean postoperative follow-up was 2.4 years. Both the IMPL and non-IMPL groups showed postoperative decreases in kinematic hip flexion and GGI. In the IMPL group, clinical hip flexion deformity, walking speed, and step length improved significantly. The improvement in kinematic hip extension was not significantly different between the IMPL and non-IMPL groups. Recurrent crouch gait was reported in three patients.[27]

Across the included studies, gait-related outcomes were most frequently reported using GPS, GDI, EVGS, GGI, three-dimensional gait analysis, and selected kinematic parameters. Reported postoperative changes included improvement in global gait indices, selected sagittal plane kinematics, ankle dorsiflexion, knee extension in stance, stride length, and walking velocity. Some studies also reported postoperative deterioration or residual abnormalities in selected gait components, including pelvic tilt, knee flexion during swing, reduced knee extensor moment, postoperative back-kneeing, and recurrent crouch gait.

Biomechanical and Procedure-Specific Outcomes

Biomechanical and procedure-specific outcomes were reported in four included studies. These studies evaluated musculoskeletal loading after SEMLS, aponeurotic calf muscle lengthening during SEMLS, conversion of biarticular to monoarticular muscles as part of multilevel surgery, and intramuscular psoas lengthening performed during SEMLS. The reported outcomes included joint kinematics, joint moments, muscle forces, joint contact forces, ankle dorsiflexion, knee hyperextension, hip flexion deformity, hip extension kinematics, and kinetic variables.

Van Rossom et al. evaluated biomechanical outcomes using musculoskeletal modelling in 44 patients who underwent SEMLS, 49 patients who received multilevel botulinum toxin injections, and 15 typically developing children.[28] Patients in the SEMLS group underwent postoperative assessment approximately 388 days after intervention. SEMLS was associated with significant changes in joint kinematics and kinetics. The SEMLS group also showed postoperative improvement in muscle force and joint contact force measures. In contrast, the botulinum toxin group showed changes in joint angles but did not show improvement in muscle force or joint contact force measures. Outcome variables included joint angles, joint moments, muscle forces, joint contact force magnitudes, and joint contact force orientations.[28]

Klotz et al. assessed aponeurotic calf muscle lengthening performed during SEMLS in 19 patients with bilateral spastic cerebral palsy and primary genu recurvatum.[25] A total of 26 limbs were analyzed, and the mean follow-up duration was 13.7 months. After surgery, ankle dorsiflexion during midstance improved significantly, and knee hyperextension during midstance was significantly reduced. The study reported a significant correlation between improvement in ankle dorsiflexion and reduction in knee hyperextension. Six limbs, corresponding to 23% of the analyzed limbs, were classified as nonresponders because postoperative knee hyperextension remained greater than one standard deviation from the age-matched reference group.[25]

Metaxiotis et al. evaluated conversion of biarticular to monoarticular muscles as a component of multilevel surgery in 20 ambulatory children with spastic diplegic cerebral palsy.[26] Forty limbs were analyzed, and the mean follow-up duration was 3.1 years. The operative approach included conversion of selected biarticular muscles, including semitendinosus and gastrocnemius, to monoarticular function, combined with other multilevel soft-tissue and bony procedures. Postoperatively, passive range of motion improved at the ankle, knee, and hip. Kinematic analysis showed reduced pelvic range of movement and improved knee extension during single stance. Postoperative back-kneeing was reported in five of 40 limbs. Kinetic analysis showed that hamstring and ankle plantarflexor power were maintained, while maximum knee extensor moment during stance was reduced.[26]

Mallet et al. compared outcomes after SEMLS with or without intramuscular psoas lengthening in 34 ambulatory children with cerebral palsy, comprising 47 analyzed limbs.[9] Fifteen limbs underwent intramuscular psoas lengthening, while 32 limbs did not. The mean postoperative follow-up duration was 2.4 years. Both groups showed postoperative decreases in kinematic hip flexion and Gillette Gait Index. In the intramuscular psoas lengthening group, clinical hip flexion deformity improved from 17° preoperatively to 2° postoperatively. Walking speed and step length also improved significantly in this group. However, the improvement in kinematic hip extension was not significantly different between the intramuscular psoas lengthening and non-intramuscular psoas lengthening groups. Recurrent crouch gait was reported in three patients.[27]

Across these studies, biomechanical and procedure-specific outcomes were assessed using heterogeneous methods. Van Rossom et al. focused on model-derived joint loading, muscle forces, and joint contact forces; Klotz et al. focused on ankle and knee sagittal plane mechanics in primary genu recurvatum; Metaxiotis et al. focused on gait analysis and kinetic outcomes after muscle conversion procedures; and Mallet et al. focused on hip flexion deformity and hip kinematics after intramuscular psoas lengthening. These studies reported postoperative changes in selected biomechanical or procedure-specific parameters, but the measured outcomes, surgical targets, and follow-up intervals differed across studies.

Additional Surgery and Long-Term Clinical Course

Additional orthopedic surgery or recurrent gait-related problems were reported in several included studies. The reporting of additional surgery varied across studies, with some studies providing detailed information on revision procedures, relapse, newly developed biomechanical problems, or recurrent deformity, while others did not report additional surgery as a primary outcome.

Visscher et al. reported additional treatment after SEMLS in a cohort of 13 children with bilateral spastic cerebral palsy followed for a mean of 11.1 years.[14] Overall, 8 of 13 participants required additional surgery during the 10-year follow-up period. The indications for additional surgery included relapse in three participants, newly developed biomechanical problems in two participants, both relapse and newly developed biomechanical problems in two participants, and other non-gait-related issues in one participant. Most additional surgeries occurred between the short-term and mid-term follow-up assessments, including five procedures for relapse and two for newly developed biomechanical problems. Two participants required surgery between the mid-term and long-term follow-up assessments because of newly developed biomechanical problems. After the long-term assessment, two additional operative interventions were reported, including one for a newly developed biomechanical problem and one for a fall-related femoral fracture. The study found no significant correlation between age at index surgery and the number of additional surgical interventions required.[14]

Terjesen et al. reported additional orthopedic procedures during follow-up after gait-analysis-based multilevel surgery in 34 ambulatory children with spastic diplegic cerebral palsy. Fourteen children required additional surgical procedures during follow-up. Additional surgery was more frequent among children who underwent the index operation at an earlier age. The study also reported that 17 children had undergone orthopedic surgery before the index operation, with 60 previous procedures recorded. Relapse of sagittal deformities occurred in 12 instances after previous surgery, requiring reoperation of six calf muscle lengthenings and six hamstring tenotomies; seven of these reoperations were performed during the index surgery, and five were performed later during follow-up. At the 5-year gait-analysis follow-up, clinical evaluation and gait analysis were used to propose additional surgery when indicated.[11]

Jones et al. reported additional surgical procedures in a long-term cohort of 26 patients with complete follow-up after multilevel surgery for diplegic cerebral palsy.[16] Eight patients had undergone surgical procedures before referral to the study institution. Following SEMLS at the institution, a second procedure was performed in 13 patients, corresponding to 50% of the cohort. Three patients underwent a third procedure, and one patient underwent a fourth procedure. Planned soft-tissue reconstruction within two months of bony reconstruction was performed in 12 of 13 patients who had a second procedure. Patients who underwent third and fourth procedures were categorized as revision cases. For patients who underwent additional procedures, 11 of 13 had video gait analysis after the final procedure.[16]

Mallet et al. reported recurrent crouch gait in a procedure-specific study evaluating intramuscular psoas lengthening during SEMLS.[27] Among 34 ambulatory children with cerebral palsy and 47 analyzed limbs, recurrent crouch gait was reported in three patients, corresponding to 8% of the cohort. The study did not primarily focus on revision surgery, but recurrent crouch gait was reported as part of the postoperative clinical course.[27]

Several other included studies reported postoperative follow-up beyond 12 months but did not provide detailed data on additional orthopedic surgery as a main outcome. Saraph et al. reported serial postoperative gait analyses at mean intervals of 1.0, 2.3, and 4.4 years after single-event multilevel gait improvement surgery, with changes in gait parameters across follow-up assessments, but additional orthopedic surgery was not reported as a main outcome.[6] de Freitas Guardini et al. reported that 116 of 258 patients in the SEMLS group had undergone previous orthopedic surgery before SEMLS, whereas 142 had not received previous surgical intervention, but postoperative additional surgery was not reported as a primary outcome.[15] Edwards et al. reported long-term functional mobility at a mean of 8 years after SEMLS and also reviewed surgical procedures performed as part of SEMLS, but additional postoperative surgery was not presented as a main long-term outcome.[5]

Across the included studies, additional surgery was most frequently reported in long-term cohort studies with follow-up of 5 years or longer. The reported frequency of additional surgery varied from 14 of 34 children in Terjesen et al., to 8 of 13 participants in Visscher et al., and 13 of 26 patients undergoing a second procedure after SEMLS in Jones et al.[15,16] Procedure-specific recurrence was reported by Mallet et al., in which recurrent crouch gait occurred in three patients.[27] Other studies either did not report additional surgery or reported previous surgery before the index SEMLS rather than postoperative revision procedures.

Patient-Centered Outcomes

Patient-centered outcomes were reported in three included studies. These outcomes included quality of life, patient-reported health status, parental satisfaction, and patient satisfaction. The instruments used across studies were heterogeneous and included the CP QOL Teen, the Short Form-36 questionnaire, and satisfaction ratings.

Edwards et al. assessed quality of life using an adapted online version of the CP QOL Teen self-reported questionnaire in patients who had previously undergone SEMLS.[5] Although FMS data were collected from all 61 patients, CP QOL Teen responses were available for 23 patients, corresponding to 38% of the cohort. The CP QOL Teen assessed five quality-of-life domains: general wellbeing and participation, communication and physical health, school wellbeing, social wellbeing, and feelings about function. The mean scores for these domains were reported overall and according to preoperative GMFCS group. No statistically significant differences were found between GMFCS grades I–II and GMFCS grade III for any of the five quality-of-life domains. The only statistically significant association between quality of life and functional mobility was between home FMS score and the "feelings about function" domain ($r = 0.55$; 95% CI 0.15 to 0.79; $p = 0.01$). There was no significant association between community FMS and "feelings about function" ($r = 0.22$; 95% CI -0.24 to 0.59; $p = 0.34$), and all other associations between quality-of-life domains and FMS scores at home, school or work, and community distances were non-significant.[5]

Jones et al. evaluated patient-reported health status using the SF-36 questionnaire at the most recent long-term follow-up in 26 patients with complete assessment after multilevel surgery.[16] The median follow-up duration was 18 years. The median SF-36 Physical Health Component Summary score was 43.0, with an interquartile range of 32.8 to 46.8. The median Mental Health Component Summary score was 55.3, with an interquartile range of 46.1 to 61.1. The reported median scores for the eight SF-36 domains were 27.5 for physical functioning, 75 for role physical, 62 for bodily pain, 75 for general health, 50 for vitality, 75 for social functioning, 100 for role emotional, and 74 for mental health. Internal consistency of the SF-36 domains was reported as acceptable, with Cronbach alpha values of 0.7 or higher for all eight items. The study also reported patient satisfaction as a secondary outcome, although the main numerical patient-centered results were presented through SF-36 scores and social situation data.[16]

Terjesen et al. assessed parental satisfaction after gait-analysis-based multilevel surgery in 34 ambulatory children and adolescents with spastic diplegic cerebral palsy. Parental satisfaction was obtained through telephone interviews performed 8 to 12 years postoperatively. Satisfaction was rated using a 10-point visual analog scale, where 0 indicated total dissatisfaction and 10 indicated complete satisfaction with the overall outcome of the index operation. Responses were obtained from the parents of all except one of the 33 children who were alive. The mean parental satisfaction score was 7.7, with a range from 2 to 10 points.[11]

Across the included studies, patient-centered outcomes were not reported uniformly. Quality of life was assessed in one study using CP QOL Teen, health-related quality of life was assessed in one study using SF-36, and parental satisfaction was assessed in one study using a 10-point satisfaction scale. The remaining included studies did not report patient-centered outcomes as primary or secondary endpoints.

DISCUSSION

Principal Findings

This systematic review synthesized evidence from 10 studies evaluating outcomes after SEMLS or related multilevel surgical procedures in ambulatory individuals with cerebral palsy. Using a follow-up threshold of more than 12 months, the included evidence showed that postoperative outcomes after SEMLS were multidimensional and could not be adequately characterized by a single gait or mobility measure.

The principal finding of this review is that SEMLS was generally associated with preservation or improvement of ambulatory function and gait-related outcomes beyond the early postoperative period. Functional mobility outcomes, when reported, demonstrated that many ambulatory patients maintained walking ability over time, although the level of independence differed across functional settings and baseline GMFCS levels. Gait-related outcomes also commonly showed improvement in global gait indices and selected kinematic parameters. However, these improvements were not uniform across all gait components, and several studies reported persistent or recurrent abnormalities in specific biomechanical or kinematic domains.

Another important finding is that functional mobility and laboratory-based gait outcomes did not always capture the same aspect of recovery. Some studies reported improvement in gait quality or kinematic parameters, whereas functional mobility outcomes were either not assessed or were reported using different instruments. Conversely, studies that focused on functional mobility demonstrated that walking capacity differed between household, school or work, and community distances. This distinction is important because gait improvement measured in a controlled laboratory environment may not fully reflect mobility performance in daily life.

The review also found that the long-term clinical course after SEMLS often included additional orthopedic procedures. Additional surgery was reported in several long-term cohorts, particularly among studies with follow-up extending over many years. This finding indicates that postoperative outcome after SEMLS should be understood as part of a longitudinal management pathway rather than as a single fixed endpoint. Nevertheless, the occurrence of additional surgery was reported inconsistently across studies, and not all studies distinguished between planned staged procedures, revision surgery, recurrence-related surgery, and surgery for newly developed biomechanical problems.

The included procedure-specific and biomechanical studies added further detail to the overall evidence base. These studies showed that individual components of multilevel surgery could produce measurable changes in targeted gait or biomechanical parameters. However, because SEMLS involves simultaneous correction at multiple anatomical levels, the contribution of any single procedure to the overall postoperative outcome was difficult to isolate. Therefore, procedure-specific findings were best interpreted as supportive evidence describing selected mechanisms or surgical targets within the broader multilevel approach.

Overall, the findings support a domain-specific interpretation of SEMLS outcomes. Functional mobility, gait quality, biomechanical correction, patient-centered outcomes, and additional surgery should be interpreted as related but distinct components of the long-term postoperative course.

Interpretation of Functional Mobility Outcomes

The functional mobility findings suggest that SEMLS may contribute to the preservation of ambulatory capacity beyond the early postoperative period, particularly in children who are ambulatory before surgery. Across the studies that reported FMS, FAQWS, or GMFCS, postoperative mobility was not limited to laboratory-based gait changes but extended to clinically meaningful walking ability in daily environments. This distinction is important because functional mobility reflects how patients walk in real-life contexts, including at home, at school or work, and in the community.

The available evidence also highlights that functional mobility after SEMLS is strongly influenced by baseline motor function. Patients classified as GMFCS levels I and II generally showed stable or favorable mobility outcomes, particularly for shorter distances. In contrast, patients classified as GMFCS level III had more variable functional outcomes and were more likely to require assistive devices or wheelchair use for longer distances. This pattern indicates that SEMLS may help maintain ambulation in GMFCS level III patients, but community-level independence remains more difficult to achieve and sustain in this subgroup.

Distance-specific assessment appears particularly important when interpreting functional mobility after SEMLS. Household mobility, school or work mobility, and community mobility represent different levels of physical demand. A child may retain independent or assisted walking at home while still requiring a wheelchair for longer community distances. Therefore, functional outcomes should not be interpreted as a single global construct.

The FMS-based studies show that walking ability after SEMLS may differ substantially depending on the distance being assessed.[1,3]

The stability of GMFCS level in long-term follow-up should also be interpreted carefully. GMFCS is useful for describing broad functional severity, but it may not be sensitive enough to detect smaller yet clinically relevant changes in walking independence, endurance, assistive device use, or participation-level mobility. In this context, the combination of GMFCS with distance-specific tools such as the FMS or functional walking scales such as the FAQWS provides a more complete description of postoperative functional status.[16]

An important limitation of the functional mobility evidence is that only a minority of the included studies reported functional mobility as a primary or major outcome. Most studies focused on gait analysis, kinematic indices, or procedure-specific biomechanical variables. As a result, the relationship between improved gait mechanics and real-world functional mobility remains incompletely defined. Improvements in gait parameters may not always translate directly into greater independence in daily mobility, especially in patients with more severe baseline impairment, reduced endurance, or higher environmental demands.

Overall, the functional mobility evidence indicates that SEMLS outcomes should be assessed not only by whether gait improves, but also by whether patients maintain or improve meaningful walking ability in daily life. Future studies should consistently include distance-specific mobility outcomes, assistive device use, wheelchair dependence, and participation-relevant walking measures to better define the long-term functional impact of SEMLS in ambulatory cerebral palsy.

Interpretation of Gait-Related Outcomes

The gait-related findings indicate that SEMLS can produce sustained improvements in overall gait quality beyond the early postoperative period, but these improvements should be interpreted with caution because gait outcomes were heterogeneous across studies and outcome measures. Global indices such as GPS, GDI, EVGS, GGI, and MAP provided useful summaries of postoperative gait deviation, but they did not always reflect the full complexity of joint-level or gait-cycle-specific changes. Several studies reported improvement in global gait scores while also documenting residual or worsened abnormalities in selected kinematic domains.

A key issue in interpreting gait-related outcomes is the distinction between global gait improvement and segment-specific gait correction. Global gait indices are valuable because they summarize complex three-dimensional gait data into clinically interpretable scores. However, they may obscure persistent abnormalities in specific components of gait, such as pelvic tilt, swing-phase knee flexion, recurrent crouch, or back-kneeing. This was particularly relevant in studies that combined global gait scores with more detailed kinematic or waveform-based analysis. Therefore, postoperative gait evaluation after SEMLS should not rely only on summary indices, but should also consider joint-specific and phase-specific changes.[14,26]

The longitudinal studies also show that gait outcomes after SEMLS are not necessarily static after the first postoperative assessment. Serial follow-up demonstrated that some parameters may continue to change over several years, and early postoperative improvements may be maintained, partially diminish, or evolve into different gait patterns. This has implications for how SEMLS outcomes are evaluated, because assessment at only one postoperative time point may provide an incomplete picture of the long-term gait trajectory. Studies with repeated gait analysis across multiple follow-up intervals are therefore particularly important for understanding whether gait correction is durable over time.[6,11,14]

The evidence also suggests that baseline functional severity and preoperative gait characteristics may influence gait-related outcomes. Studies that stratified results by GMFCS level or examined predictors found that children with less severe functional impairment tended to have greater improvements in global gait indices, whereas children with GMFCS level III or lower baseline gait velocity had more limited or more variable improvement. This pattern is consistent with the clinical expectation that gait correction is influenced not only by the surgical intervention, but also by underlying motor control, strength, endurance, and baseline walking capacity.[15]

Another important consideration is that gait-related improvement after SEMLS reflects the combined effect of multiple simultaneous procedures rather than the isolated effect of a single correction. SEMLS is intended to address deformities across multiple levels, including hip, knee, ankle, and foot segments. As a result, improvements in one segment may alter mechanics at another segment. For example, changes in hip motion may be influenced by knee extension, ankle position, or ground reaction force alignment rather than by a hip procedure alone. This makes causal interpretation of individual surgical components difficult, particularly in studies where several procedures were performed in the same operative episode.[25,27]

The procedure-specific studies help explain selected mechanisms of gait change, but their findings should be interpreted within the broader multilevel context. Calf muscle lengthening, conversion of biarticular to monoarticular muscles, and intramuscular psoas lengthening each targeted specific gait abnormalities, but the postoperative changes occurred within a surgical framework that included multiple concurrent corrections. These studies therefore add mechanistic detail, but they do not replace the need to evaluate SEMLS as a whole-limb, multilevel intervention.[25,26,27]

Overall, the gait-related evidence supports the view that SEMLS can improve gait quality in ambulatory cerebral palsy, but the interpretation of these outcomes requires a domain-specific approach. Global gait scores, segmental kinematics, spatiotemporal parameters, kinetic measures, and visual gait scores each describe different aspects of walking performance. The most informative assessment of SEMLS outcomes is therefore one that combines global gait indices with detailed kinematic interpretation and functional mobility outcomes, rather than relying on a single measure of gait improvement.

Biomechanical and Procedure-Specific Implications

The biomechanical and procedure-specific findings provide additional context for understanding how SEMLS may influence gait beyond visible kinematic correction. SEMLS is not a single anatomical intervention, but a coordinated multilevel approach intended to modify the interaction between joint alignment, muscle-tendon length, lever-arm function, and ground reaction force progression. Therefore, the biomechanical consequences of SEMLS should be interpreted as the combined result of multiple simultaneous corrections rather than the isolated effect of one surgical component.

The musculoskeletal modelling study included in this review adds an important mechanistic dimension to the evidence base. By evaluating muscle forces and joint contact forces, it extends the assessment of SEMLS beyond conventional gait indices and joint angles. This is relevant because improvement in kinematic appearance does not necessarily guarantee normalization of internal loading. The reported changes in muscle force and joint contact force measures after SEMLS suggest that multilevel correction may influence the mechanical environment of the lower limbs, not only the external walking pattern.[28]

The procedure-specific studies also demonstrate that targeted surgical components may affect selected gait abnormalities, but their effects are difficult to separate from the broader multilevel surgical context. For example, calf muscle lengthening was associated with changes in ankle dorsiflexion and knee hyperextension in patients with primary genu recurvatum, but this correction occurred as part of SEMLS rather than as an isolated procedure. Similarly, conversion of biarticular to monoarticular muscles was performed within a multilevel operative strategy that included other soft-tissue and bony procedures. These findings show that procedure-specific outcomes can describe local or segmental changes, but they should not be overinterpreted as independent estimates of the effect of a single procedure.[25,26]

The findings related to intramuscular psoas lengthening further illustrate the complexity of interpreting individual surgical procedures within SEMLS. Although hip flexion deformity and some gait parameters improved in the group undergoing psoas lengthening, the difference in kinematic hip extension improvement between groups was not significant. This suggests that changes in hip extension during gait may depend not only on hip flexor correction, but also on knee position, ankle mechanics, and overall sagittal plane alignment. In multilevel surgery, improvement at one joint may arise from correction at another joint or from changes in the relationship between adjacent segments.[27]

These findings have implications for outcome assessment. Procedure-specific studies are useful for understanding possible mechanisms of change, but they should be interpreted alongside whole-gait and functional outcomes. A technically successful correction of one deformity may not translate directly into improved global gait quality or functional mobility if other impairments remain. Conversely, improvement in a global gait index may occur because of several smaller changes across multiple segments rather than a large improvement in one targeted parameter.

The biomechanical evidence also highlights the need for outcome measures that extend beyond conventional observational or kinematic assessment. Joint moments, muscle force estimates, and joint contact forces may help characterize how SEMLS modifies lower-limb loading. However, these outcomes remain less frequently reported than GPS, GDI, EVGS, FMS, or FAQWS, and they require specialized modelling approaches that are not yet routine in most clinical outcome studies. As a result, biomechanical findings currently function as supportive evidence rather than the primary basis for evaluating long-term success after SEMLS.

Overall, the biomechanical and procedure-specific evidence supports a multilevel interpretation of SEMLS outcomes. The effect of SEMLS should be viewed as the result of interacting corrections across the hip, knee, ankle, and foot rather than as a sum of isolated procedures. Future studies should integrate procedure-specific reporting with global gait indices, functional mobility measures, and patient-centered outcomes to clarify how targeted biomechanical corrections contribute to meaningful long-term functional change.

Additional Surgery and Long-Term Course

The need for additional orthopedic surgery was an important feature of the long-term course after SEMLS. Across the included studies, additional procedures were reported most clearly in cohorts with longer follow-up. This pattern emphasizes that SEMLS should not necessarily be viewed as a single definitive intervention that completes orthopedic management in ambulatory cerebral palsy. Rather, for some patients, SEMLS appears to represent one major component within a longer continuum of musculoskeletal care.

Additional surgery after SEMLS should be interpreted carefully. Revision or subsequent procedures may reflect recurrent deformity, residual deformity, newly developed biomechanical problems, growth-related changes, or the evolving natural history of cerebral palsy. Therefore, the occurrence of additional surgery should not automatically be interpreted as failure of the index SEMLS. In several studies, patients maintained or improved functional mobility and gait-related outcomes despite the need for further procedures. This suggests that additional surgery may sometimes be part of maintaining or optimizing long-term ambulatory status rather than evidence of poor treatment response.[14,16]

The timing and classification of additional procedures are also important. Some procedures may be planned or staged, whereas others may represent revision surgery or treatment for recurrence. Without clear separation of these categories, it is difficult to determine whether subsequent procedures represent expected continuation of care, incomplete correction, relapse, or new pathology. This issue is particularly relevant in older cohorts, where surgical strategies and definitions of SEMLS may have differed from contemporary practice.[16]

Age at index surgery may also be relevant to the long-term course, although findings were not uniform across studies. One study reported that additional surgery was more frequent among children who underwent the index operation at a younger age, whereas another did not find a significant correlation between age at index surgery and the number of additional procedures. These differences may reflect variation in cohort characteristics, growth remaining at the time of surgery, surgical indications, follow-up duration, and definitions of additional surgery.[11,16]

The long-term course after SEMLS also highlights the importance of continued surveillance after the initial postoperative recovery period. Because gait and musculoskeletal alignment may continue to evolve over time, follow-up limited to the first postoperative year may not capture later recurrence, compensatory gait changes, deterioration in specific gait components, or the need for further intervention. This is consistent with the broader pattern observed in the included studies, where some outcomes remained stable while others changed across longer follow-up intervals.

Overall, additional surgery should be incorporated into the interpretation of SEMLS outcomes as a contextual long-term outcome rather than treated separately from function and gait. Reporting whether patients required further procedures, why those procedures were performed, and whether mobility or gait outcomes were preserved afterward would provide a more complete picture of postoperative trajectories. Future studies should distinguish planned staged procedures from unplanned revision surgery, report indications for subsequent procedures, and evaluate how additional surgery relates to long-term functional mobility, gait quality, and patient-centered outcomes.

Strengths and Limitations

This systematic review has several strengths. First, the review addressed a clinically relevant question by focusing on long-term functional mobility and gait-related outcomes after SEMLS in ambulatory individuals with cerebral palsy.[29] The review also used predefined eligibility criteria and included studies with postoperative follow-up exceeding 12 months, allowing the synthesis to extend beyond the early postoperative rehabilitation period.[30,31] In addition, the review considered multiple clinically relevant outcome domains, including functional mobility, gait quality, biomechanical outcomes, procedure-specific findings, additional surgery, and patient-centered outcomes.[32] This broad outcome structure allowed the evidence to be organized according to the multidimensional nature of SEMLS outcomes rather than relying on a single measure of postoperative success.[33-34]

Another strength is that the review included both overall SEMLS cohort studies and supportive evidence from biomechanical and procedure-specific studies. This approach provided a wider perspective on postoperative outcomes after multilevel surgery.[35] The overall cohort studies contributed information on functional mobility and global gait outcomes, whereas the procedure-specific and biomechanical studies provided additional detail on selected surgical targets and mechanistic outcomes. The use of the MINORS tool also allowed methodological quality to be assessed consistently across non-randomized studies, which represented the full body of included evidence.[36-37]

However, several limitations should be acknowledged. The most important limitation is the heterogeneity of the included studies. The studies differed in design, sample size, population characteristics, GMFCS distribution, cerebral palsy subtype, surgical composition, follow-up duration, and outcome measures. Some studies evaluated SEMLS as a whole, whereas others focused on individual procedures performed as part of multilevel surgery.[38] This heterogeneity limited direct comparison across studies and precluded quantitative meta-analysis.[39,40]

Second, the included studies were predominantly observational and non-randomized. Several were retrospective cohorts or case series, and many had small sample sizes. Comparator groups were absent in most studies, and when present, treatment allocation was not randomized.[41,42] These design characteristics increase the risk of selection bias, confounding, and incomplete adjustment for baseline differences. In addition, several studies included only patients with available postoperative gait analysis or long-term follow-up, which may have introduced follow-up bias.

Third, outcome reporting was inconsistent across studies. Functional mobility outcomes were reported in only a minority of studies, whereas most studies emphasized laboratory-based gait measures, kinematic parameters, or procedure-specific outcomes.[43,44] Patient-centered outcomes were also limited and were assessed using different instruments. As a result, the relationship between gait improvement, functional mobility, quality of life, and satisfaction could not be evaluated comprehensively across the full evidence base.[45]

Fourth, follow-up duration varied substantially. Although all included studies met the operational definition of long-term follow-up used in this review, defined as follow-up exceeding 12 months, some studies had follow-up close to the lower threshold, whereas others followed patients for many years or into adulthood.[46] This variation should be considered when comparing outcomes across studies, because gait, function, growth, recurrence, and the need for additional surgery may evolve over time.[47]

Fifth, the definition and reporting of SEMLS were not fully uniform. Some studies used contemporary definitions of SEMLS, while older studies used broader descriptions of multilevel gait improvement surgery or staged multilevel procedures that partially overlapped with SEMLS. The number and type of procedures performed also varied substantially among studies.[48] This made it difficult to isolate the effects of SEMLS as a standardized intervention. Sixth, several studies reported outcomes at the limb level, whereas others reported outcomes at the patient level. This distinction is important because limb-level analysis may overrepresent individuals with bilateral involvement and may not correspond directly to patient-level function or mobility. Differences between gait-laboratory outcomes and real-world functional outcomes further limited the ability to synthesize findings across domains.

Finally, this review was restricted to the articles provided in the predefined evidence set. No additional external studies were added during synthesis. This restriction ensured consistency with the predefined review scope, but it may limit the comprehensiveness of the available evidence compared with a broader systematic search that includes all potentially eligible published studies. Therefore, the conclusions of this review should be interpreted in relation to the included studies, their methodological limitations, and the heterogeneity of reported outcomes.

Implications for Clinical Practice and Future Research

The findings of this review have several implications for clinical practice. First, outcome evaluation after SEMLS should be multidimensional. Clinical assessment should not rely only on whether gait improves in the laboratory, because postoperative success may differ across gait quality, functional mobility, patient independence, and patient-centered outcomes. A patient may demonstrate improvement in global gait indices while still requiring assistive devices or wheelchair use for longer distances.[36,49] Therefore, postoperative assessment should include both instrumented gait analysis and real-world functional mobility measures.

Second, functional mobility should be assessed according to walking context and distance. Household ambulation, school or work mobility, and community ambulation represent different levels of functional demand. Distance-specific tools such as the FMS are particularly useful because they describe how patients move across daily environments rather than only whether they can walk under controlled testing conditions. This is especially relevant for patients with GMFCS level III, in whom household or short-distance walking may be preserved despite limitations in community mobility.[5,11]

Third, long-term follow-up remains important after SEMLS. Several studies showed that gait and functional outcomes may continue to evolve after the early postoperative period. Some patients may maintain early improvements, whereas others may develop recurrent deformity, residual gait abnormalities, or new biomechanical problems.[14-17] Follow-up limited to the first postoperative year may therefore miss clinically relevant changes in mobility, gait quality, or the need for further intervention.[6,20]

Fourth, clinicians should interpret SEMLS as part of longitudinal orthopedic management rather than as an isolated endpoint. The need for additional surgery was reported in several long-term cohorts, and subsequent procedures may reflect recurrence, growth-related changes, residual deformity, or newly developed biomechanical problems. This should be discussed with patients and families during preoperative consult. Expectations should include the possibility that further treatment may be required even when the index SEMLS produces meaningful improvement in gait or mobility.[14,16]

Fifth, baseline functional severity should be considered when counseling patients and families. Patients with GMFCS levels I and II may have different postoperative trajectories than those with GMFCS level III. Community-level independence may be more difficult to achieve or maintain in patients with greater preoperative motor impairment. Clinical decision-making should therefore incorporate GMFCS level, baseline gait pattern, walking speed, assistive device use, endurance, and family goals rather than relying only on surgical indication or gait-laboratory abnormalities.[15]

Future research should prioritize prospective, multicenter studies with standardized definitions of SEMLS, consistent eligibility criteria, and harmonized outcome measures.[45] Studies should report functional mobility, gait-related outcomes, patient-centered outcomes, and additional surgery using predefined time points. This would allow better comparison across cohorts and improve the ability to distinguish early postoperative effects from durable long-term outcomes.

Future studies should also report outcomes stratified by GMFCS level, age at surgery, baseline gait severity, and surgical composition. Such stratification is needed because SEMLS is not a single uniform procedure, and postoperative outcomes may vary according to patient characteristics and the combination of soft-tissue and bony procedures performed. Reporting the number and type of procedures, rehabilitation protocols, and previous surgeries would improve interpretability across studies.

Another research priority is the integration of gait-laboratory outcomes with real-world functional and patient-centered measures. Global gait indices, kinematic parameters, and biomechanical modeling provide valuable information about walking mechanics, but they should be linked with outcomes that matter to patients and families, including independence, participation, fatigue, quality of life, satisfaction, and community mobility.[46] Future studies should examine whether improvements in gait mechanics translate into meaningful changes in daily function.

Finally, future research should describe additional surgery in greater detail. Studies should distinguish planned staged procedures from unplanned revision surgery, recurrent deformity, residual deformity, and newly developed biomechanical problems.[50] They should also evaluate whether additional procedures are associated with maintenance, improvement, or deterioration of long-term mobility and gait outcomes. This would provide a more complete understanding of the long-term clinical pathway after SEMLS in ambulatory cerebral palsy.

CONCLUSION

In this systematic review, SEMLS and related multilevel surgical procedures were associated with favorable functional mobility and gait-related findings in ambulatory individuals with cerebral palsy at follow-up beyond 12 months. However, postoperative outcomes were heterogeneous and varied according to baseline functional level, walking distance, gait domain, surgical composition, and follow-up duration.

The findings highlight that SEMLS outcomes should be interpreted as multidimensional. Laboratory-based gait improvement, real-world functional mobility, biomechanical correction, patient-centered outcomes, and additional surgery represent distinct but related aspects of postoperative assessment. Additional orthopedic procedures were reported in several long-term cohorts, supporting the need to consider SEMLS within a broader longitudinal musculoskeletal management pathway.

Future studies should use standardized SEMLS definitions, consistent follow-up intervals, and combined reporting of gait analysis, functional mobility, patient-centered outcomes, and additional surgery to better characterize long-term postoperative trajectories in ambulatory children and adolescents with cerebral palsy.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to the conduct, authorship, or publication of this systematic review.

ETHICS CONSIDERATION

Ethical approval was not required for this study because it was a systematic review using data from previously published studies. No direct involvement of human participants, patient recruitment, biological sampling, or access to identifiable personal data was performed in this review. The review protocol was also still registered in the International Prospective Register of Systematic Reviews (PROSPERO).

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AUTHOR CONTRIBUTIONS

SF contributed to the study conception, literature search, screening process, data extraction, risk-of-bias assessment, data synthesis, and manuscript drafting. TWM contributed to study supervision, methodological guidance, interpretation of findings, and critical revision of the manuscript. DNU contributed to clinical interpretation, supervision, and critical review of the manuscript. AZ contributed to data interpretation, manuscript review, and intellectual content refinement. HY contributed to literature screening, data verification, manuscript editing, and final review. All authors read and approved the final version of the manuscript.

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