ESMAC – Best Paper award 2011 – Runner UP

Single Event Multilevel Surgery in children with bilateral spastic cerebral palsy: A 5 year prospective cohort study

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A R T I C L E   I N F O

Article history:
Received 19 March 2012
Accepted 19 April 2012

Keywords:
Cerebral palsy
Orthopaedic surgery
Outcome

A B S T R A C T

Background: Single Event Multilevel Surgery (SEMLS) is considered the standard of care to improve gait and function in children with bilateral spastic cerebral palsy (BSCP). We have demonstrated in a randomized controlled trial (RCT) of SEMLS, that gait was improved at 12 months after surgery and gross motor function at 24 months after surgery. The question addressed in this study, was to determine if improvements in gait and function, would be maintained at 5 year follow-up.

Methods: Nineteen children with BSCP, GMFCS levels II (14 children) and III (5 children), mean age 9.7 years (range 7.7–12.2 years) participated in a prospective cohort study following participation in a RCT, with follow-up to 5 years. Outcome measures were Gait Profile Score (GPS), Gillette Gait Index (GGI), Gait Deviation Index (GDI), Gross Motor Function Measure (GMFM66) and Functional Mobility Scale (FMS).

Results: Eighteen children have completed follow-up, with interval analysis at 1, 2 and 5 years post SEMLS. One child was excluded because of neurological deterioration and his diagnosis was revised to Hereditary Spastic Paraparesis (HSP). GPS improved by 5.29 and GMFM66 by 3.3% at 5 years post SEMLS. Differences between outcome measures at 1 versus 5 years and 2 versus 5 years (except GMFM66) were not significant, indicating that improvements in gait and gross motor function were stable over time.

Conclusions: SEMLS results in clinically and statistically significant improvements in gait and function, in children with BSCP, which were maintained at 5 years after surgery.

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1. Introduction

Cerebral palsy (CP) is the result of a static encephalopathy or non-progressive lesion of the developing brain but the musculoskeletal deformities in growing children are often progressive [1]. Musculoskeletal deformities may impair both gait and gross motor function. Since the advent of instrumented gait analysis (IGA) emphasis has been placed on the correction of all fixed musculoskeletal deformities at one operative session, usually referred to as Single Event Multilevel Surgery (SEMLS) [2–5]. SEMLS is considered to be the standard of care to improve gait and function in children with CP [2,4–8]. SEMLS improves the likelihood of achieving sagittal plane balance [9] and reduces the need for repeated anaesthetics, reduces episodes of hospitalization and requires only one major period of rehabilitation [2,5].

The findings from our pilot randomized controlled trial (RCT) to evaluate the outcome of SEMLS in children with bilateral spastic CP (BSCP) showed that the timing of improvements following SEMLS were different for gait compared to gross motor function. Clinically and statistically significant improvements in gait were found at 12 months after SEMLS but functional improvements (GMFM66) were not found until 2 years after SEMLS [10]. The natural history in CP is for deterioration in gait and function with time, especially during the pubertal growth spurt [11]. Factors responsible for this decline may include progression of the musculoskeletal pathology as well as unfavourable changes in the ratio of body mass to strength [12,13]. The question to be addressed in this medium-term prospective cohort study was to determine if improvements in gait and function would be maintained through the pubertal growth spurt.

Systematic review [14] has shown that there are several well designed retrospective cohort studies which report an improvement in gait or function following SEMLS [3,4,6,7,15–19]. There are several prospective studies which also report improvements in gait [8,20–23]. The duration of follow-up in these studies ranged from 12 months [21–23], approximately 18–24 months [3,6,7,15,16,20], to approximately 4 year follow-up [8,17]. Only three studies...
reported follow-up of greater than 4 years [4,18,19], with only one reporting 10 year follow-up [18]. However, none of these longer term studies were prospective. Retrospective studies are more subject to bias because the composition of the cohort is not decided at the initiation of the study nor are the outcome measures defined and the testing intervals are usually not standardized. In contrast, a prospective cohort study permits the composition of a study cohort according to specified inclusion and exclusion criteria defined a priori. In addition, the outcome measures and testing intervals are standardized. There are ethical and practical problems with retaining children with CP in randomized controlled trials of more than 12 months duration because of the progressive nature of the musculoskeletal pathology and gait deterioration. Prospective cohort studies are probably the best design to investigate medium to long term changes in gait and functioning [24].

The aim of this study was to evaluate the outcome of SEMLS on gait, gross motor function and functional mobility 5 years post SEMLS.

2. Participants

2.1. Inclusion criteria

Children with a confirmed diagnosis of BSCP with registration on the Victorian state-wide CP register, GMFCS levels II and III and aged 6–12 years at the time of randomization in the RCT who required SEMLS were included. All children (n = 19) who had participated in the RCT phase of the study and who had IGA, on at least two occasions following SEMLS with one being at least 5 years post-surgery were eligible for the prospective phase of the study.

2.2. Exclusion criteria

Children with a diagnosis other than CP. For further details of inclusion and exclusion refer to the RCT phase of this study [10].

3. Sample size

This was a prospective cohort study of children in both the surgery and control groups of a RCT. The sample size was therefore determined by the considerations of sample size for the RCT [10].

4. Methods

This was a single centre, prospective cohort study, of children who had participated in a RCT of SEMLS, for a period of 12 months [10]. At the conclusion of the randomized phase of the trial, children who were randomized to the surgery group were followed up in the prospective cohort study. Children who were randomized to the control group proceeded to surgery, following the RCT protocol then continued their follow-up in the prospective cohort study. All children, regardless of group allocation, were followed for a minimum of 5 years with standardized outcome assessments at 1, 2 and 5 years post SEMLS. Each assessment included IGA and functional assessments including GMFCS, FMS and GMFM66. Children had elective removal of implants including blade plates between 12 and 18 months after SEMLS. Additional surgeries were scheduled either at the time of implant removal or at any time during the 5 year follow-up, according to clinical need and based on information from IGA.

The primary outcome measures were the Gait Profile Score (GPS), the Gillette Gait Index (GGI) and the Gait Deviation Index (GDI). The GPS and GGI are summary statistics of gait and are derived from gait kinematics (GPS) and kinematics plus selected temporospatial parameters (GGI). The GDI is a multivariate measure of overall gait pathology [25]. These measures are considered to be valid and reliable tools to describe gait dysfunction as a single variable and to assess change after intervention [10,18,25]. All three measures were included to allow comparison to previously published data. Functional measures namely the GMFM66 and FMS were also completed.

Ethical approval for this study was granted by the Ethics in Human Research Committee of the Royal Children's Hospital, Melbourne, Australia (reference number EHRC 23144). The trial design and reporting follow the CONSORT principles, as far as practically possible [26].

SEMLS was defined as at least one surgical procedure, performed on two different anatomic levels (hip, knee or ankle) on both sides of the body. The surgical prescription did not need to be symmetrical and was not uniform but individually tailored to the child's needs as determined by a comprehensive evaluation which included standardized physical examination, radiological evaluation and IGA. The multilevel surgical program included muscle tendon lengthening, tendon transfer, rotational osteotomy and stabilization of the hip and foot following published guidelines [5]. The basic principles were the identification and correction of all contractures and lever arm deformities, deemed to be interfering with dynamic gait function.

For the purpose of the prospective cohort study, children originally allocated to the control group proceeded to surgery within 4 weeks of the RCT 12 month assessment. The protocol for surgery for this group followed that of the surgical group of the RCT [10] and was carried out by the same surgical team.

Post-surgical review followed standard protocols [27] and the physical therapy protocol followed that of the RCT [10].

IGA was collected using a 50 Hz, 6 or 10 camera Vicon 370 system (Oxford Metrics, Oxford, UK). Reflective markers were applied to the bony landmarks using a standardized procedure [28]. Kinematic data was calculated using Plug-in Gait (Oxford Metrics, Oxford, UK). The Movement Analysis Profile (MAP), GPS, GGI and GDI were calculated for both legs on four individual gait cycles. The median GPS and mean GGI and GDI were calculated for each child using Gaitabase, a web interfaced repository for gait analysis data.

The GMFM66 and the FMS were conducted following the IGA using standard protocols. Assessments were conducted by senior gait laboratory physical therapists, experienced and trained in the use of all measures.

4.1. Statistical analysis

Analysis was carried out for the total cohort that is RCT surgical and control group combined. Linear regression with robust standard errors for comparison between 5 years and pre-surgery, 1 and 2 years post SEMLS were carried out for all outcome measures (except for FMS) using Stata 10.0 Statistical Data Analysis Program (Statacorp, TX, USA). Frequency data for change in FMS scores is reported.

5. Results

Of the 19 children with BSCP who participated in the RCT all have completed 1 and 2 years follow-up and 18 have completed 5 years follow-up. One child was excluded from this analysis as his diagnosis was revised from CP to Hereditary Spastic Paraparesis (HSP).

Fig. 1 shows the progress of children throughout the study from the start of the RCT until completion of the prospective phase of the study. Children's characteristics pre-surgery and 5 years post-surgery are summarized in Table 1. There was a mean increase in height of 29.7 cm and in weight of 25.1 kg during the 5-year study period.

Indications for surgery and surgical procedures performed are summarized in Table 2. The total number of procedures performed
was 142 with a mean of 8 procedures per child (standard deviation 3). Adverse events related to surgery were classified as mild if they resolved spontaneously, moderate if they resolved completely following simple treatment or severe if there were a permanent deficit. There were four mild adverse events related to poor postoperative pain management. In three children this was due to epidural malfunction and one child had difficulties with pain, excessive consumption of codeine, followed by constipation with emesis. Five children had moderate adverse events, three had pain over femoral osteotomy plates and two had foot pain following os calcis lengthening. Hardware related pain resolved following implant removal and the children with foot pain had spontaneous resolution by 6 months postoperatively. There were no severe adverse events.

There were 22 subsequent surgeries (Table 2). Soft tissue surgeries included additional muscle tendon lengthenings, deemed necessary because of recurrent or new contractures, related to continued growth. In addition, bilateral rectus femoris transfers were performed in a child who it was considered would have had problems coping with the rectus femoris rehabilitation protocol following SEMLS. Additional bony surgeries included one femoral derotation osteotomy in a 12 year old girl with a complex asymmetric gait pattern in the transverse plane. An additional four supramalleolar osteotomies of the tibia were performed for progressive lever arm deformity. External tibial torsion may increase during the adolescent growth spurt. Finally, minor residual knee flexion deformities were dealt with by growth plate surgery to the distal femur. In four knees this included distal femoral anterior physeal stapling and in two knees, the insertion of “8” plates to the anterior portion of the distal femoral physis [29]. There were bilateral medial malleolar screws inserted for ankle valgus in another child.

Results for comparison between 5 years post SEMLS and pre, 1 and 2 years post SEMLS assessments are shown in Table 3. At 5 years there was a highly significant 5.3% (95% confidence interval, 3.53, 7.04) improvement in the GPS which represents a 64% improvement compared to pre-surgery. Similar improvements were seen in the GDI, 40% (difference, 214, 95% confidence interval, 130, 299) and GDI, 22% (difference, –14, 95% confidence interval, –18.63, –9.34). A decrease in GPS and GDI and an increase in GDI represent an improvement towards normal gait. MAP and GPS for each assessment are displayed in Fig. 2.

These improvements were both clinically and statistically significant. The comparison between 5 years and 1 and 2 years showed no statistical or clinically important difference. However there was a small deterioration in all gait measures at 5 years when compared to 2 years.

The GMFM66 showed a significant improvement at 5 years of 3.29% when compared to pre-surgery. There was also a significant difference between 5 and 1 year but not between 5 and 2 years indicating that the improvements in motor function occurred between 1 and 2 years post SEMLS as previously reported [10].

FMS differences between 5 years and pre SEMLS measured on the ordinal scale are reported as the frequency of the same score, better score or worse score and are displayed in Fig. A1 (Appendix A). At 5 years functional mobility was better in nearly half of the children at 50 m and 500 m and no children were worse as rated by the FMS.

### 6. Discussion

Although the RCT is considered to be the gold standard in assessment of therapeutic interventions, there are significant ethical and practical limitations in this study design, for complex surgical interventions such as SEMLS. The ethical concerns include the fact that the natural history of gait is for deterioration, with growth and development [3,11,13] and many children presenting for SEMLS have general symptoms such as fatigue or specific symptoms such as foot pain. Practical objections to RCTs of SEMLS include the wishes of parents and the physical therapists of children with CP who may quite reasonably object to inclusion in a control group for more than 1 year. In a detailed review of the RCT phase, we concluded that randomization for a period of 12 months in selected patients was both ethical and practical. In our patient population, this could not be extended beyond 12 months, hence the current prospective trial. A prospective cohort study with a broad raft of standardized outcome measures, at regular intervals, may be a superior design to a short term RCT to investigate medium and long term outcomes of multilevel surgery in this population. Prospective cohort studies are vastly superior to retrospective cohort studies for a variety of reasons. These include
Table 2
Surgical indications and procedures performed as part of SEMLS children (36 lower limbs) and subsequent surgery.

<table>
<thead>
<tr>
<th>Soft tissue procedure</th>
<th>Indication</th>
<th>Sagittal plane kinematic</th>
<th>SEMLS Number (n = 18)</th>
<th>Subsequent Number (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoas over the brim (Psoas at the brim)</td>
<td>Hip FFD &gt; 10° Thomas Test</td>
<td>Pelvis “double bump” pattern</td>
<td>13 (6)</td>
<td></td>
</tr>
<tr>
<td>Adductor lengthening</td>
<td>Hip abduction &lt; 40°</td>
<td></td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Medial hamstring lengthening</td>
<td>Knee FFD 0–10°</td>
<td>Increased knee flexion at initial contact, terminal swing</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Medial hamstring lengthening plus semitendinosus</td>
<td>Knee FFD &gt; 10°</td>
<td>Increased knee flexion at initial contact, terminal swing</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>transfer to adductor tubercle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectus femoris transfer to semitendinosus</td>
<td>Positive Duncan Ely (prone rectus) Test</td>
<td>Decreased and/or late peak knee flexion in swing</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Gastrocnemius lengthening (Strayer)</td>
<td>Dorsiflexion &lt;0° under anaesthesia (fixed contracture)</td>
<td>Plantarflexion throughout stance phase</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Soleus lengthening</td>
<td>Dorsiflexion &lt;0° after gastrocnemius lengthening (intraoperatively)</td>
<td>Plantarflexion throughout stance phase</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Intramuscular lengthening tibialis posterior</td>
<td>Varus heel, adducted forefoot</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lengthening of peroneus brevis</td>
<td>Concomitant os calcis lengthening or subtalar fusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Split transfer of tibialis anterior</td>
<td>Flexible equinovarus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Bony procedure**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Transverse plane kinematic</th>
<th>SEMLS Number (n = 18)</th>
<th>Subsequent Number (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral derotation osteotomy</td>
<td>Hip rotation &gt; 10° internal through stance phase</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>Supramalleolar osteotomy of tibia (internal rotation)</td>
<td>Foot progression angle external through stance phase</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Os calcis lengthening</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Subtalar fusion</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Growth plate surgery</td>
<td>Knee FFD &lt; 10°</td>
<td>Increased knee flexion initial contact, mid stance, terminal swing</td>
<td>6</td>
</tr>
<tr>
<td>Growth plate surgery</td>
<td>Ankle valgus</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>142</td>
<td>22</td>
</tr>
</tbody>
</table>


Table 3
Mean (95%CI) for gait measures and GMFM66 pre, 1, 2 and 5 years post Single Event Multilevel Surgery (SEMLS) with linear regression of changes 5 years compared to pre, 1, 2 years post SEMLS.

<table>
<thead>
<tr>
<th>Measure mean (95%CI)</th>
<th>5 years post SEMLS (n = 17)</th>
<th>2 years post SEMLS (n = 18)</th>
<th>1 year post SEMLS (n = 18)</th>
<th>Pre SEMLS (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPS</td>
<td>9.6 (8.3, 10.9)</td>
<td>9.2 (8.1, 10.3)</td>
<td>9.9 (8.7, 11.2)</td>
<td>14.9 (12.9, 16.8)</td>
</tr>
<tr>
<td>Diff. 5 years (95%CI)</td>
<td>–0.38 (–1.44, 0.68)</td>
<td>0.32 (–0.99, 1.63)</td>
<td>3.52 (3.53, 7.04)</td>
<td></td>
</tr>
<tr>
<td>GGI</td>
<td>146 (103, 187)</td>
<td>135 (100, 170)</td>
<td>152 (111, 192)</td>
<td>360 (259, 460)</td>
</tr>
<tr>
<td>Diff. 5 years (95%CI)</td>
<td>–10.7 (–34.6, 13.3)</td>
<td>6.12 (–30.3, 42.5)</td>
<td>214.3 (130.0, 298.6)°</td>
<td></td>
</tr>
<tr>
<td>GDI</td>
<td>79.2 (74.4, 84.0)</td>
<td>80.8 (76.4, 85.3)</td>
<td>78.0 (73.7, 82.3)</td>
<td>65.2 (60.4, 69.9)</td>
</tr>
<tr>
<td>Diff. 5 years (95%CI)</td>
<td>1.67 (–2.54, 5.87)</td>
<td>–1.15 (–5.82, 3.52)</td>
<td>–13.98 (–18.63, –9.34)°</td>
<td></td>
</tr>
<tr>
<td>GMFM66</td>
<td>70.2 (63.8, 76.6)</td>
<td>71.0 (66.1, 75.8)</td>
<td>67.1 (62.3, 71.8)</td>
<td>66.9 (61.3, 72.6)</td>
</tr>
<tr>
<td>Diff. 5 years (95%CI)</td>
<td>0.78 (–2.31, 3.87)</td>
<td>–3.16 (–7.08, 0.76)</td>
<td>–3.29 (–6.17, –0.40)°</td>
<td></td>
</tr>
</tbody>
</table>

° p < 0.05.

avoidance of selection bias, the cohort being identified according to precise inclusion and exclusion criteria as for a RCT. In addition, the outcome measures are applied at standardized intervals and the likelihood of missing data and incomplete follow-up is dramatically reduced, in comparison to retrospective studies. The weakness of the prospective cohort study design is the lack of a control group. To some degree this is offset by reliance on objective outcome measures based on instrumented gait analysis, because they are objective and relatively immune to bias. The utilization of summary measures of gait is also important. The use of measures such as the GPS, GGI and GDI allow for an analysis of improvements and deteriorations across multiple gait parameters and reduces the risk of bias.

The extended follow-up, through the pubertal growth spurt, in a prospective cohort study raises problems of additional surgeries for recurrent contractures, new contractures and torsional deformities. In this study, the total number of procedures performed during the SEMLS was 142 and the total number of
follow-up surgeries was 22 (Table 2). Little has been written about the need for follow-up surgery in patients who have had SEMLS but it is widely recognized that “fine tuning” by additional surgeries is frequently required. It could be argued that this undermines the concept of Single Event Multilevel Surgery. However the principal concept behind SEMLS is to achieve sagittal plane balance, not necessarily to carry out all the procedures for the improvement of gait that will be required over the entire growth period, on one single day in the child’s life. The majority of the subsequent procedures listed required a much shorter hospitalization and a shorter and easier rehabilitation in comparison to the SEMLS. Whilst we concede that the description of patients as having been managed by Single Event Multilevel Surgery is not entirely accurate, the term still has some usefulness in emphasizing that the majority of procedures are performed on a single occasion.

In a systematic review of SEMLS [14], large improvements in gait were noted in the majority of studies reviewed. The systematic review also reported rather small changes in gross motor function. No studies, which included both summary statistics of gait and GMFM, showed a significant improvement in both. In this prospective phase, a small but clinically and statistically important improvement in gross motor function has been recorded. Changes in function as measured by the GMFM66 showed an improvement of 3.3% at 5 years compared to pre-surgery. When it is considered that the natural history of gross motor function in this age group is for deterioration, this finding becomes all the more important and clinically significant [30].

Three longitudinal gait studies have been published in which gait analysis has been repeated in children with CP, on two or more occasions without interval intervention [11–13]. All three studies confirm clinically and statistically significant deterioration in gait over intervals varying from 1 to 5 years with one study showing gait deterioration in children with previous orthopaedic surgery [13]. A small non significant deterioration was seen between 2 and 5 years and may be the expression of natural history in this population.

Maintaining functional mobility by reducing the level of support by assistive devices is an important goal of SEMLS. As measured by the FMS, at 5 years post SEMLS six children were showing improvement over 5 m, nine were showing improvement over 50 m and eight over 500 m and at this community distance only two children were using wheelchairs.

The strengths of this study were the relative homogeneity of the study population and the utilization of reliable outcome measures, in a prospective study design. Limitations were the small sample size and being from a single centre. In this small sample size it is not possible to relate baseline gait characteristics or outcomes to the number or type of surgical procedures and outcomes may not be generalizable.

7. Conclusion

SEMLS results in clinically and statistically significant improvements in gait and function, in children with bilateral spastic CP, which were maintained at 5 years after surgery.

Funding

The authors did not receive any external funding in support of this trial.

Disclosure Statement

The Authors do not have any actual or potential conflict of interests to declare in relation to the content of this manuscript.

Appendix A

![Image](147x612_to_458x739)

Fig. A1. Frequency of change in Functional Mobility Scale for 5, 50 and 500 metre distances at five years compared to pre-surgery.

References


