Cerebral palsy (CP) causes physical disability in childhood and affects approximately 1 in 500 children. CP can be classified according to the following motor types: spastic, dyskinetic, ataxic, or mixed. Motor CP presents as increased muscle tone in spastic CP, abnormal movements or sustained postures in dyskinetic CP, abnormal balance and gait in ataxic CP, and features of both spastic and dyskinetic CP in mixed CP. About 80%–95% of children with CP have some spasticity as either the primary or mixed component of motor and functional

Comparison of intrathecal baclofen pump insertion and selective dorsal rhizotomy for nonambulatory children with predominantly spastic cerebral palsy

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OBJECTIVE In nonambulatory children with predominantly spastic cerebral palsy (CP), the authors compared care needs, symptom burden, and complications after surgical treatment with either intrathecal baclofen (ITB) pump insertion or selective dorsal rhizotomy (SDR). The patients were treated at two Canadian centers with variability in practice pertaining to these surgical options.

METHODS The authors performed a retrospective analysis of nonambulatory children with predominantly spastic quadriplegic or diplegic CP who underwent treatment with ITB or SDR. These two strategies were retrospectively assessed by comparing patient data from the two treatment groups for demographic characteristics, outcomes, and complications. A partial least-squares analysis was performed to identify patient phenotypes associated with outcomes.

RESULTS Thirty patients who underwent ITB and 30 patients who underwent SDR were included for analysis. Patients in the ITB group were older and had lower baseline functional status, with greater burdens of spasticity, dystonia, pain, deformity, bladder dysfunction, and epilepsy than patients in the SDR group. In addition, children who underwent SDR had lower Gross Motor Function Classification System (GMFCS) levels and were less likely to experience complications than those who underwent ITB. However, children treated with SDR had fewer improvements in pain than children treated with ITB. A single significant latent variable explaining 88% of the variance in the data was identified.

CONCLUSIONS Considerable baseline differences exist within this pediatric CP patient population. Factors specific to individual children must be taken into account when determining whether ITB or SDR is the appropriate treatment.

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KEYWORDS cerebral palsy; GMFCS; Gross Motor Function Classification System; nonambulatory; intrathecal baclofen; selective dorsal rhizotomy; SDR; spine
impairment. Many patients labeled as having spastic CP also have a smaller degree of dystonia; hence, clinical presentation is not necessarily dichotomous, but rather on a continuum. Spasticity in CP can result in contracture formation and occasionally pain, the latter of which is particularly seen in mixed or predominantly dyskinetic CP. Ultimately, these aspects lead to various degrees of functional limitation that adversely impact quality of life and increase caregiver burden. The Gross Motor Function Classification System (GMFCS) is a 5-level clinimetric index for assessment of GMF in nonambulatory children, who are classified as having the highest GMFCS levels, IV and V. Children who are nonambulatory have particularly high functional disability and caregiver needs.

Surgical strategies to address spasticity include selective dorsal rhizotomy (SDR) and intrathecal baclofen (ITB) pump insertion. Traditionally, ITB has been preferred in nonambulatory patients with severe generalized spasticity or mixed CP and has been shown to reduce spasticity in both upper and lower extremities as well as improve dystonia and its related pain. SDR, on the other hand, is most commonly offered to ambulatory children affected by spastic CP, with the primary goal of improving gait.

There is renewed interest regarding the indications for SDR for children who are nonambulatory, especially given recent technological advancements such as intraoperative neurophysiological monitoring and minimally invasive approaches. In a systematic review comparing ITB and SDR in nonambulatory children with CP, the authors found that both interventions improved spasticity and gross motor function, but meaningful clinical conclusions were precluded because there was significant heterogeneity in the literature with respect to reported outcome variables, patient selection methods, and surgical techniques.

The goal of the current study was to compare care needs, symptom burden, and complications of nonambulatory children with predominantly spastic diplegic or quadriplegic CP following surgical treatment with either ITB or SDR. Data were collected from two institutions with variability in practice pertaining to these two surgical options. At the Hospital for Sick Children (HSC) in Toronto, ITB is offered for nonambulatory children with CP in whom spasticity is adversely impacting their quality of life. At Sainte-Justine Hospital (SJH) in Montreal, SDR is preferred for these patients with predominantly spastic CP, and ITB is offered to those with primarily dystonic complaints, which were not the focus of this analysis. We sought to compare the effectiveness of these different treatment strategies. Differences in baseline patient characteristics, complications, and outcomes were gathered through a retrospective review of all surgical cases dating back over 30 years.

We present what is to our knowledge the largest retrospective cohort comparing SDR to ITB in the management of nonambulatory children with spastic CP. We hypothesized that while each surgical approach might offer unique symptom relief and have unique complication risks, each approach can effectively reduce spasticity and improve caregiver burden in nonambulatory patients with spastic CP. Ultimately, while various descriptive reports in the literature illustrate the outcomes of each treatment paradigm in a cohort of patients, this work is the largest to date to compare the two strategies in this patient population with challenging and complex care needs. We sought to highlight variability in practice, identify gaps in knowledge, and provide avenues for ongoing research in the surgical treatment of spasticity in children with CP who are nonambulatory.

Methods

Institutions

Data on patients with predominantly spastic diplegic or quadriplegic CP were retrospectively collected from HSC and SJH, two large quaternary care pediatric centers in Toronto and Montreal, respectively. The data from HSC spanned the period from 1991 to 2019 and encompassed all children with GMFCS levels IV and V who received ITB for spastic or mixed CP with the primary goal to improve caregiver burden. Clinical and functional reports from physicians and physiotherapists had to state that the main complaint was spasticity as opposed to dystonia; when any confusion arose, independent assessment by the physician involved was obtained for confirmation of the diagnosis. Again, a component of dystonia was acceptable as many patients with mixed CP or even with CJP designated as “spastic CP” have a component of dystonia; however, the clinical and functional reports had to clearly state that spasticity was a greater concern and a greater contributing factor to the quality of life than dystonia.

The procedures were performed by one of two surgeons. From 1983 to 2019, SJH had one surgeon who performed SDR in children with primarily spastic CP functioning at GMFCS levels IV and V. SDR was performed by exposing the cauda equina through multilevel laminoplasties. Patients who underwent SDR at this institution did not also undergo ITB during this assessment period. Instead, ITB was reserved for individuals with generalized dystonia or with dystonia as their main complaint if presenting with mixed CP (not included in this study). ITB at HSC was administered as a continuous infusion. The catheter tip was positioned in the high thoracic region in patients with spastic quadriplegia and the mid- to lower thoracic region in patients with spastic diplegia. Patient consent was not required for this retrospective study.

Participant Selection

Children were included if they had the following characteristics: 1) age younger than 19 years; 2) a diagnosis of predominantly spastic diplegic or quadriplegic CP with GMFCS level IV or V; 3) underwent either SDR or ITB, but not both treatments; and 4) had available postoperative data outlining functional outcomes. Clinical reports from both hospitals as well as rehabilitation centers were thoroughly reviewed with physician input in order to identify which motor subtypes were brought forward as the cause of significant complaints or issues addressed by the healthcare team. Spasticity was diagnosed and scored by a physician for all patients, including neurosurgeons and/or physiatrists with specialized training in CP. Again, patients with primarily spastic CP might endorse some dys-
tonia, and as such we inherently included patients with mixed spastic-dystonic presentations in which spasticity had to be the most significant complaint. However, we actively excluded patients with either generalized dystonia or dyskinetic or ataxic CP. We collected baseline demographic information (age at time of surgery, sex), and details surrounding early development, including gestational age, pregnancy, and existing comorbidities (epilepsy, dystonia, and spinal deformity requiring surgical correction).

Procedural Details
At HSC, nonambulatory children with primarily spastic CP were offered ITB, administered continuously. The mean dose of ITB was 803.3 µg/day at last follow-up. At SJH, patients were evaluated based on their history, physical examination, and imaging with physiatrists at multidisciplinary meetings to determine candidacy for SDR. The procedure entailed multilevel laminoplasties under neurophysiological guidance, but there was variability in how many rootlets were transected at each level. Most patients had greater than 50% of the dorsal rootlets transected from L2 to S1. No ventral rootlets were transected.

Predictors and Outcomes
Due to the limitations of retrospective chart reviews, granular data were extracted but coded coarsely and binarized. Subjective reports of preoperative pain and bladder dysfunction were documented on all patients. The degree of spasticity was objectively scored by specialized physicians with the Modified Ashworth score in both centers, with scores ranging from 0 to 4 for individual muscle groups. Each muscle group was graded at the preoperative assessment and a mean of the muscle group scores was generated for each patient.

Clinical and functional outcomes were garnered from follow-up assessments by the medical or rehabilitation teams. Time to last follow-up was recorded. Several outcome measures were collected, such as changes in spasticity in the upper and lower extremities, pain/discomfort (identified in reports from patients and caregivers depending on patient ability to communicate), presence of dystonia (if this was presented as a complaint by the patient or caregiver, or addressed by the healthcare team), presence of spinal deformity requiring surgical attention, range of motion on rehabilitation assessments, and bladder function (dysfunction was determined based on urology reports, patient and caregiver complaints, and objective measures such as urodynamics and postvoid residuals). Caregiver burden was collected from caregiver subjective reports; it was considered the primary outcome since children might have varied goals in specific symptom improvement, but the ultimate goal for surgical intervention was improvement in caregiver burden with improvement in patient spasticity. We elected to code these changes categorically as coarsely “same, better, or worse” to compare outcomes between institutions. Last, we collected data on postoperative complications and the nature of these complications; specific to ITB, we did not include routine pump exchanges as complications.

Comparative Analyses
First, we compared the two groups based on their baseline clinical and demographic outcome data using independent sample t-tests for continuous variables and chi-square analysis for categorical variables in IBM SPSS version 26.0 (IBM Corp.). Significance was denoted with a two-tailed p < 0.05.

Given the high degree of multicollinearity between the different variables, we performed a partial least-squares (PLS) regression in order to determine the association between the two surgical options and outcomes. PLS is a tool that can be leveraged to clarify multidimensional associations between predictors and outcomes. PLS may be used to decompose correlations between a set of variables and extract patterns of predictor contributions to the overall relationship with outcome.

First, data were separated into a predictor matrix (variable x, baseline variables, and treatment cohort—SDR vs ITB) and outcome matrix (variable y, pain, comfort, complications, and symptom reduction). Data centering was performed such that covariates with large absolute values did not dominate the analysis. To center continuous data, z-scores were generated from the sample distribution. Zero centering was performed for binary variables.

A heterogenous correlation matrix was calculated, allowing for both continuous and ordinal variables using the polycor library in the R statistical toolbox. A combination of Pearson, polyserial, and polychoric regression was utilized to determine pairwise associations between variables of different types. The covariance matrix was then decomposed using singular value decomposition, creating components that maximize the covariance between the predictors and outcomes. The effect size and amount of variance explained by each component may be derived by calculating the ratio of a single squared singular value to the sum of all squared singular values. The significance of each latent variable was determined using permutation testing (1000 iterations) with a threshold of p < 0.05, and significant contributions to each component were computed using bootstrap resampling (1000 iterations) with a threshold of |z| > 1.96.

Results
Baseline Clinical and Demographic Characteristics
Out of the 360 patients with data available in the retrospective registries, 30 patients from HSC underwent ITB and 30 patients from SJH underwent SDR; 151 patients were excluded for not meeting diagnostic requirements (dyskinetic or ataxic CP, or diagnoses other than CP), 24 patients were excluded for having more than one type of surgical intervention, and 125 patients were excluded for having incomplete data. The average age at the time of surgery was 9.1 ± 3.9 years, and 40 participants (66.7%) were male. Prematurity was prevalent, with an average gestational age of 32.1 weeks (range 25 to 41 weeks). Hypoxic-ischemic injury (n = 35, 58.3%) was the most common perinatal complication, followed by breech presentation (n = 2, 3.3%), twin-twin transfusion syndrome (n = 3, 5.0%), cytomegalovirus infection (n = 1, 1.7%), and neonatal encephalopathy (n = 1, 1.7%).
There was a greater representation of patients functioning at GMFCS level IV (60.0%) within the cohort. The baseline mean modified Ashworth score was 3.4 ± 0.5, which was an average of the scores for the upper extremity (elbow flexion, wrist flexion, and finger flexion) and baseline mean modified Ashworth score was 3.4 ± 0.5, which was an average of the scores for the upper extremity (elbow flexion, wrist flexion, and finger flexion) and lower extremity (hip adductors, hamstrings, quadriceps, gastrocnemius, and soleus muscles).

### Differences in Baseline Characteristics

While the groups were similar in representation of sex, gestational age, and time to last follow-up, they did differ significantly in several baseline clinical characteristics (Table 1). Patients within the ITB cohort had worse baseline functional status. This cohort included more patients with GMFCS level V \(x^2(2) = 13.6, p < 0.001\), with more severe burden of spasticity [Modified Ashworth score 3.53 vs 3.17, \(\text{t}(58) = 2.4, p = 0.018\)], dystonia \(x^2(2) = 29.4, p < 0.001\), epilepsy \(x^2(2) = 8.8, p = 0.003\), and pain/discomfort \(x^2(2) = 13.0, p < −0.001\]. Patients undergoing SDR were younger than the ITB cohort \(6.4 \text{ vs. } 11.7\) years, \(\text{t}(41) = 5.8, p < 0.001\) and had less bladder dysfunction preoperatively [83.3% vs 10.0%, \(x^2(2) = 32.4, p < 0.001\)].

### Univariate Analysis of Outcomes at Last Follow-Up

The average time to last follow-up was 18.7 ± 5.9 months for the 60 patients, with no significant difference between surgical intervention groups. The two interventions achieved similar changes in the proportion of children with improved spasticity in both the upper and lower limbs, with about 81.7% and 39.8% reporting improvement in the lower extremities and upper extremities, respectively; 13.4% and 60.2% reporting stable spasticity in the lower extremities and upper extremities, respectively; and 5% reporting postoperative worsening of lower-extremity spasticity (Table 2). There was also no statistical difference in caregiver burden between the two cohorts. The ITB cohort, however, reported greater improvements in postoperative pain \(x^2(2) = 33.7, p < 0.001\), bladder function \(x^2(2) = 5.5, p = 0.020\), and dystonia \(x^2(2) = 10.5, p = 0.005\).

There were significantly more complications in the ITB cohort than the SDR cohort \[46.7% vs 13.3%, \(x^2(2) = 7.9, p = 0.006\]. After ITB insertion, there were 7 postoperative infections (23.3%), 4 cerebrospinal fluid leaks requiring repair (13.3%), and 4 catheter disconnections (13.3%). The complications after SDR were not procedure related and included 1 case of antibiotic allergy (3.3%), 1 case of postoperative acute respiratory distress syndrome (3.3%), 1 case of laryngeal edema after extubation (3.3%), and 1 case of a new pressure sore (3.3%).
Multivariable Multidimensional Analysis and PLS Analysis of Outcomes

Following singular value decomposition, the PLS analysis yielded one significant latent variable (p < 0.001) that explained 88% of the variance between the presurgical variables (predictor) and outcome matrices. These contributions are depicted in Fig. 1 along with bootstrap ratios and 95% confidence intervals. Within this latent variable, a phenotype of patients undergoing SDR was characterized. These children tended to have less burden of spasticity, perform at a better GMFCS level, and have fewer baseline comorbidities such as spinal deformity. This latent variable was significantly associated with a set of correlated outcomes, including fewer complications, and less improvement in dystonia and pain.

Discussion

Traditionally, ITB is offered to manage increased tone in nonambulatory children with CP; however, there is an increasingly recognized role for SDR for this population. In the current report, we conducted a retrospective comparison of outcomes between two similar centers with differing preferred approaches for the surgical treatment of nonambulatory children with predominantly spastic quadriplegia. A PLS analysis modeled multidimensional associations between baseline and outcome variables. We report four main findings. First, there are significant phenotypic differences between the children undergoing SDR and ITB. Second, both ITB and SDR can effectively improve caregiver burden and spasticity. Third, ITB is associated with greater improvements in pain, bladder dysfunction, and dystonia, although children undergoing this therapy had significantly higher rates of both symptoms at baseline. Last, SDR is associated with fewer complications. The current report highlights opportunities for future multisite research to define the role of SDR and ITB for nonambulatory children with CP.

Phenotype Differences

One of the foremost findings of the current study is the presence of significant baseline clinical and demographic differences between children undergoing SDR and those undergoing ITB, even within this highly selected population. This result highlights the extensive heterogeneity within children with CP who are nonambulatory. We highlight our observation that children with CP who are nonambulatory are not a homogenous population group who might uniformly benefit from a singular treatment paradigm. Rather, individuals within this population present with unique combinations of clinical and functional complaints. A personalized management strategy would best address the heterogenous clinical and functional needs of this population.

Spasticity and Caregiver Burden

The patients in our study had significant caregiver burden with baseline poor functional status and severe spasticity. Traditionally, ITB has been employed for the nonambulatory cohort and SDR was reserved for ambulatory patients for improvement in gait (spastic diplegia) or improvement in care needs (spastic quadriplegia). However, we found that both ITB and SDR successfully addressed caregiver burden and spasticity in both the upper and lower extremities. The patient improvements in spasticity stem from different pathophysiological mechanisms. Baclofen infused in the lumbar region will penetrate the superficial layers of the spinal cord and impede the release of excitatory neurotransmitters for the lower extremities; similarly, baclofen can migrate up to the cervical region and exert the same function, thereby affecting the upper extremities. In SDR, the transection of dorsal lumbar rootlets is thought to cause an overall reduction in Ia sensory input to the spinal cord interneurons that not only affects the lumbar region, but also ascends up the spinal cord to the brainstem and cerebral cortex, thereby resulting in the widely observed “supra-segmental effects.”

Pain Control

Our study demonstrated that patients who underwent SDR were less likely to have improvements in dystonia and pain than those who underwent ITB. The lack of effect on dystonia is self-evident as SDR does not affect the pathological mechanisms that underlie dystonia.

The differential effects of SDR and ITB on pain and discomfort are more difficult to discern. ITB has been shown to decrease pain in CP, stroke, and spinal cord injury. This effect is thought to be mediated through its GABA-ergic activity and through reduction in muscle spasms. The limited study of the effect of SDR on pain is unclear and requires ongoing research. Summers and colleagues conducted a prospective observational study across 5 hospitals in England and followed ambulant children 1 year after SDR, finding that pain was one of several domains that improved after surgery. With a longer follow-up, Tedroff and colleagues assessed 18 children with CP after 15 to 20 years post-SDR and showed that reduction in spasticity was associated with reduction in pain as measured by the Brief Pain Inventory. Similarly, Park and colleagues also observed the sustained effects of pain improvement 20–30 years after SDR. Conversely,
Daunter et al. assessed 80 adults with CP after an average of 22 years post-SDR and compared them to those who did not undergo surgery and found that SDR did not have a significant effect on pain intensity or pain interference.31

Our findings were limited in that we did not have quantitative pain scores to objectively measure pain or discomfort and that these subjective reports were often provided by caregivers who may interpret pain differently than the patient. Nevertheless, these studies illustrate two important points: first, SDR does not confer a deleterious effect on pain and discomfort, and second, the burden of spasticity may not represent the sole contributor to the experience of pain. In fact, through our PLS analysis, we found considerably collinearity between pain and dystonia improvement; thus, the inability of SDR to improve dystonia may explain persistent pain in a subset of nonambulatory children with CP. A recent study by van de Pol and colleagues found that patients who did not have significant baseline dystonia had better pain control and fewer care needs after SDR, whereas those who had baseline dystonia with congenital causes for CP actually had worse pain and dystonia after SDR.32 Our cohort was primarily composed of patients with acquired CP from preterm birth, which might explain why there were very few patients whose dystonia and pain worsened after SDR. Ultimately, pain is a complex symptom that is modulated by physical as well as psychological stimuli that might evolve over time,33,34 and as such, the treatment of pain requires a multipronged treatment approach aimed at remediating the offending stimuli.

Complication Profile

Both ITB and SDR are associated with specific postoperative complications that need to be considered when managing patients with CP. Kolaski and Logan conducted a systematic review of adverse effects of ITB and found that it has a high complication incidence with severe morbidity due to issues of baclofen toxicity and hardware malfunctions.34 More recent studies corroborate this finding and reveal that the most common complications include wound infection, meningitis, catheter breakage or migration, and CSF leak.3,5,34 Our findings were in keeping with the literature, showing a high complication rate of almost 50% with predominance for surgery-related adverse events.

Tedroff and colleagues conducted a systematic review of long-term effects of SDR in children with CP33 and classified complications into short-term (<1 year post-operatively) and late (>1 year postoperatively). The most common short-term complications were gastrointestinal symptoms, sensory alterations, urinary tract infections, CSF leaks, and pulmonary issues. Late complications included mostly spinal deformities, bladder dysfunction, and refractory dystonia, although measurements were taken at various time points during skeletal maturity. Patients who underwent SDR in our study were followed for an average of 19.1 months (maximum 24 months); hence, we captured mostly early and some late complications, of which none reflected postoperative infections, which is in keeping with the aforementioned review. SDR and ITB thereby differ not only with regard to rate of complication, but also by type of complications; both of these factors need to be discussed with patients and their caregivers. Depending on their tolerance of adverse events, an individualistic patient-centered approach must be provided.

Study Limitations and Future Directions

While we gleaned important clinical lessons from our data, our study does have a few limitations worth noting. One limitation of this study is that only specific predictors and outcomes were collected retrospectively from two institutions, and as such, objective measures could not be obtained at each time point. Some variables such as dystonia were not reported using objective measures, but instead the variables were binarized or categorized to coarsely compare outcomes between institutions, and some encompassed both patient- and caregiver-endorsed subjective reports. Another limitation is the heterogeneity between cohorts due to different practices between hospitals and surgeons; direct comparisons of outcomes are confounded by the difference in baseline characteristics. We did make efforts to balance cohorts by enforcing strict inclusion and exclusion criteria focusing on children predominantly affected by spasticity; nevertheless, as highlighted in our findings, it was not possible to derive a homogenous population. Next, while we did attempt to include the latest follow-up information, we did not have adequate long-term follow-up data to determine if patients who underwent SDR at a young age eventually required ITB therapy in the future.

Prospective studies with long-term follow-up in this particular nonambulatory population are required to discern the optimal indications for each treatment. Ultimately, well-designed studies are needed to delineate long-term outcomes and inform individualized healthcare decisions for these patients.

Conclusions

Our study showed that both ITB and SDR may be considered as treatment options for nonambulatory patients with predominantly spastic CP as both treatment methods confer benefits in spasticity reduction and, importantly, relief for caregivers. Consideration needs to be paid to demographic and clinical imbalances at baseline assessment (such as age, functional level, comorbidities), primary complaints (baseline pain, presence of dystonia, bladder dysfunction), tolerance to possible complications, and caregiver’s ability for frequent follow-ups. Several patient factors, including distance from hospital, may inform pragmatic decision-making surrounding which treatment options are most reasonable.35 Furthermore, an institutional and societal burden of care must be considered in order to responsibly allocate resources; some studies indicate that SDR might be more cost-effective in the long run due to decreased complications, care needs, and hospitalizations.16 Finally, the needs of each patient are not static and evolve over time; as such, SDR and ITB should be targeted to these evolving needs and can be considered as adjuncts instead of alternatives.

References


Disclosures
Dr. Raskin reports receiving honoraria from Medtronic.

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Conception and design: Ibrahim, Mansur, Narayanan, Weil. Acquisition of data: Mansur, Lavigne, Phaneuf-Garand, Diabira, Venne. Analysis and interpretation of data: Ibrahim, Mansur, Lavigne, Phaneuf-Garand, Diabira, Venne. Drafting the article: Mansur, Morgan, Lavigne, Phaneuf-Garand, Diabira, Yan, Venne, Marois. Critically revising the article: Mansur, Morgan, Lavigne, Phaneuf-Garand, Diabira, Yan, Narayanan, Fehlings, Milo-Manson, Dalziel, Breitbart, Mercier, Venne, Marois, Weil, Raskin, Thomas. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ibrahim. Statistical analysis: Mansur, Morgan. Study supervision: Ibrahim.

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