Carpal tunnel syndrome in lysosomal storage disorders: simple decompression or external neurolysis?
Kesavan Sri-Ram, Ashok Vellodi, Matthew Pitt and Deborah M. Eastwood

Thirty-two patients (61 limbs) with lysosomal storage disorders underwent surgery for ‘carpal tunnel syndrome’. Twenty-two limbs underwent a simple decompression whereas 39 limbs underwent additional neurolysis and tenosynovectomy. Data were incomplete for six patients (12 limbs). The mean age at operation for the decompression group (11 patients) was 10.5 years and for the neurolysis group (15 patients), 6.9 years. Overall, using a neurophysiological rating system, 39% of limbs demonstrated sensory improvement and 47% motor improvement with no significant difference between the groups. Only in the neurolysis group was a decline in motor conduction (2/29 limbs) or sensory conduction (four limbs) noted. Using neurophysiological criteria, no added benefit from external neurolysis was identified. J Pediatr Orthop B 00:000–000 © 2007 Lippincott Williams & Wilkins.

Introduction
Carpal tunnel syndrome (CTS) is uncommon in children but is seen frequently in lysosomal storage disorders such as the mucopolysaccharidosis (MPS) and mucolipidoses (ML), and is often associated with progressive disability [1–13]. These inherited storage disorders are associated with abnormal deposition of glycosaminoglycans within the tissues in MPS and with an abnormal lysosomal enzyme transport system in ML. Factors such as the deposition of glycosaminoglycans within the flexor retinaculum, synovial sheaths, flexor tendons and median nerve, as well as carpal bone dysplasia, are all thought to contribute to the development of CTS in these young patients.

Carpal tunnel decompression (CTD) forms the mainstay of treatment [14,15], but poor outcome and recurrence are frequent. The introduction of bone-marrow transplantation (BMT) has prolonged the survival of these patients and has increased the need for intervention for CTS. BMT alone has not been shown to improve the musculoskeletal manifestations of these conditions significantly; possibly as a result of poor penetration of the leucocyte-derived enzyme following the BMT [16–18].

The CTS in these children with lysosomal storage disorders differs from that seen in adults in that there are marked signs but few symptoms. Clinical evaluation is therefore difficult and, for diagnosis, reliance is placed on neurophysiological investigation. The pathological changes seen during CTD in these children include thickened flexor retinacula, masses of white tenosynovium engulfing the flexor tendons, and clear nerve constriction with marked epineurial thickening [14].

Our early experience with CTD in patients with lysosomal storage disorders was disappointing and was comparable with the results of decompression alone in patients with amyloidosis [19–21]. It was thought that concurrent median nerve neurolysis might improve outcome. The aim of this study was to assess the long-term neurophysiological outcome following CTD in patients with MPS and ML, and to evaluate the added benefit of external neurolysis over simple decompression.

Methods
Between 1991 and 2003, we performed carpal tunnel surgery on 32 patients with lysosomal storage disorders and neurophysiologically confirmed median nerve compromise. Bilateral surgery was carried out in 29 patients, and unilateral in three patients, producing 61 limbs in total. Twenty-one male and 11 female patients were present, with a mean age at surgery of 8.1 years. The age range was 2.1–15.3 years. A variety of different storage disorders were treated (Table 1).

Nerve conduction studies were performed using a Dantec Counterpoint (Minneapolis, Minnesota, USA), to record sensory action potentials to ring finger stimulation, with recording electrodes over both the median and ulnar nerves at the wrist. A double-peaked ring finger sensory action potential was considered diagnostic for CTS. In addition, a median motor study was recorded over
abductor pollicis brevis. Patients were classified preoperatively using an established system (Table 2) [14] based on published data [22,23].

The first 22 limbs underwent a simple CTD. The subsequent 39 limbs also underwent an external neurolysis and tenosynovectomy. This was on the basis of observations of a thickened epineurium at the time of the CTD and the identification of abnormal glycosaminoglycans deposition in biopsies of the epineurium. All procedures were performed under tourniquet control via an extended midpalmar skin incision. In all cases the flexor retinaculum was divided and a full exposure of the median nerve performed with or without exploration of the thenar branch as necessary. The thickened tenosynovium covering the flexor tendons was excised. In the ‘neurolysis’ group an external neurolysis of the median nerve was also performed. The wound was closed with nonabsorbable sutures and a dressing applied. Suture removal at 10 days was followed by physiotherapy-guided mobilization.

Routine postoperative follow-up included 6-monthly nerve conduction studies until a static neurophysiological picture emerged.

Statistical analysis was performed using Minitab release 13.32 (Minitab Inc., State College, Pennsylvania, USA) using the Student two sample $t$ and $\chi^2$ tests. Statistical significance was assumed at the level of $P < 0.05$.

### Results

Of the original 61 limbs in 32 patients investigated, 12 limbs in six patients were excluded from analysis owing to incomplete data leaving 49 limbs in 26 patients to form the basis of this study. Twenty limbs in 11 patients underwent simple CTD and 29 limbs in 15 patients underwent decompression with an additional neurolysis.

Most of the patients were from subgroups MPS I and MPS II (Table 1).

The simple decompression group was significantly older at operation than those who had neurolysis [10.5 years (range 4.0–15.3 years) versus 6.9 years (range 2.1–14.1 years) $P = 0.03$]. The mean duration of follow-up showed no significant difference being 3.4 years (range 0.3–11.0 years) and 3.0 years (range 0.1–6.8 years), respectively.

In most of the patients there was an improvement in the median sensory conduction velocity and a reduction in the distal motor latency. According to the classification system, however, the results were less promising (Table 3). No significant preferential improvement was observed in sensory or motor neurophysiology, and there appeared to be no relation between sensory and motor recovery in individual patients.

In the simple decompression group, 9/20 limbs showed sensory improvement, 11/20 showed no sensory improvement and there were no sensory declines. Ten of 20 showed motor improvement, 10/20 showed no motor improvement and there were no motor declines.

In the neurolysis group, 10/29 limbs showed sensory improvement, 15/29 showed no sensory improvement and in four limbs sensory decline was noted. Thirteen of 29 showed motor improvement, 14/29 showed no motor improvement and there were two limbs that showed a motor decline.

No statistical difference was shown when $\chi^2$ analysis was applied to tables comparing neurolysis and no neurolysis groups according to sensory improvement versus none or decline ($P = 0.46$), motor improvement versus none or decline ($P = 0.72$) and finally any improvement in either sensory or motor function.

### Table 1 Number of patients and types of lysosomal storage disease treated

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Male patients</th>
<th>Female patients</th>
<th>Total number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hurler (MPS IH)</td>
<td>7 (7)</td>
<td>5 (3)</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Hurler–Scheie (MPS IH/S)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Scheie (MPS IS)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Hunter (MPS II)</td>
<td>9 (5)</td>
<td>0 (0)</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Maroteaux–Lamy (MPS VI)</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Mucolipidosis III (ML III)</td>
<td>2 (2)</td>
<td>3 (3)</td>
<td>5 (5)</td>
</tr>
</tbody>
</table>

MPS, mucopolysaccharidoses; ML, mucolipidoses.

*Total number of patients. Figures in parentheses represent those with complete data.

### Table 2 Neurophysiological rating system [14]

<table>
<thead>
<tr>
<th>Sensory studies</th>
<th>Motor studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Normal median SAP</td>
<td>Normal distal motor latency</td>
</tr>
<tr>
<td>B Double peak SAP</td>
<td>Prolonged distal motor latency</td>
</tr>
<tr>
<td>C No recordable median SAP</td>
<td>No recordable motor response</td>
</tr>
</tbody>
</table>

SAP, sensory action potentials.

### Table 3 Improvement in motor and sensory neurophysiology following surgical treatment

<table>
<thead>
<tr>
<th>No neurolysis</th>
<th>Neurolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of limbs</td>
<td>20</td>
</tr>
<tr>
<td>Sensory improvement</td>
<td>9</td>
</tr>
<tr>
<td>No sensory improvement</td>
<td>11</td>
</tr>
<tr>
<td>Sensory decline</td>
<td>0</td>
</tr>
<tr>
<td>Motor improvement</td>
<td>10</td>
</tr>
<tr>
<td>No motor improvement</td>
<td>10</td>
</tr>
<tr>
<td>Motor decline</td>
<td>0</td>
</tr>
</tbody>
</table>
modality versus none or decline \( P = 0.44 \)). No adjustment for small numbers was needed.

Overall, according to the neurophysiological classification system, 39% of limbs showed evidence of sensory improvement and 47% showed evidence of motor improvement. No significant difference was observed, however, between the two methods of surgical management.

In the 16 limbs with the most severe CTS (i.e. ‘C3’), only two recovered fully (‘A1’) in terms of motor and sensory conduction. In 12 of the 16, however, there was a full motor recovery. Only the two limbs mentioned above recovered fully in terms of sensory conduction. Of these 16 severely affected limbs, five underwent neurolysis, and all five showed only motor improvement (to ‘C1’).

Within the disease subgroups, there were poor results with the single cases of both MPS IS and IH/S. No individual disease subgroup showed a particularly improved response compared with another.

Thirteen of the patients (23 limbs) had received a BMT, and thirteen (26 limbs) had not (Table 4). Overall, there was no significant difference in the neurophysiological response in those patients who had had a transplant (irrespective of type of operation) compared with those who had not \( (\chi^2 \text{ test}, P = 0.77) \). The small numbers did not allow accurate statistical analysis between the transplant and no transplant patients and the subgroups of simple decompression or neurolysis.

### Discussion
Survival and quality of life in MPS and ML is improving owing to a variety of factors, including BMT, enzyme-replacement therapy, gene therapy and better cardiorespiratory support. Surgical intervention for the associated musculoskeletal problems is increasing and it is becoming important to assess outcome carefully. CTS is common in these patients, but the outcome of surgery is not comparable to the results achieved in patients with CTS owing to other causes.

Previous experience with carpal tunnel surgery in these patients has been varied [1,4,5,7–13,15,24,25], and we report a similar mixed outcome.

The introduction of median nerve neurolysis was based primarily on observations of the pathology during the operative procedure and the histological findings but was supported by the comparable pathogenesis of CTS in haemodialysis patients, in whom amyloid deposition is found within the carpal tunnel during surgery [20]. Maurer et al. [26] had previously advised neurolysis in the management of CTS in patients with lysosomal storage disorders.

Despite this philosophy, this study has not demonstrated a benefit from neurolysis in addition to CTD in these patients. These findings are comparable with those reported following CTD in ‘normal’ adult CTS [27,28]. In such patients, the pathogenesis of the CTS is very different but neurolysis does not improve outcome, and in fact is often associated with a poorer outcome.

Nerve conduction studies are not usually relied upon for measuring outcome in ‘normal’ adults following CTD, but in the children in our study group they are an essential aspect of postoperative assessment, owing to the relative lack of symptoms and the difficulty in assessing symptom level in children who often have learning difficulties. Rather than compare absolute values from the nerve conduction studies we chose to classify our results in relation to known normative data. The categories for both motor and sensory studies were robust and changes between them could be relied upon to represent real change in the results.

Table 4 Neurophysiological improvement stratified with respect to BMT

<table>
<thead>
<tr>
<th>Total no of limbs</th>
<th>No neurolysis BMT</th>
<th>No neurolysis No BMT</th>
<th>Neurolysis BMT</th>
<th>Neurolysis No BMT</th>
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<tbody>
<tr>
<td>Sensory improve-</td>
<td>7</td>
<td>13</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>ment</td>
<td>3</td>
<td>6</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Sensory decline</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Motor improve-</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>ment</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Motor decline</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>4</td>
</tr>
</tbody>
</table>

**BMT, bone-marrow transplantation.**

The aim of this study was to see whether neurolysis impacts on the nerve conduction studies, rather than the function of the limb. It is acknowledged that the outcome following intervention is not only related to the surgery, but also perhaps to an aggressive postoperative physiotherapy regime [14]. Hand function in these patients is frequently affected by finger joint contracture and/or triggering of one or more digits. Intellectual difficulties may also affect function.

We accept that an improvement in neurophysiological outcome may not correlate with symptoms or function and indeed, a poor correlation between neurophysiological and functional outcome has been reported with studies [24,25] demonstrating clinical improvement, despite persistent neurophysiological abnormalities.
As with preoperative assessment, however, owing to a relative lack of symptoms and difficulty in eliciting physical signs, postoperative clinical evaluation remains difficult particularly if attempts are made to isolate improvement in hand function owing to improvement in median nerve function. Therefore, we chose not to assess outcome in terms of function.

BMT improves survival in MPS and ML. It was thought that this might impact on the results of this study but it appears not to have done. Other reports have suggested that BMT is not associated with improvement of the musculoskeletal complications of lysosomal storage disorders [16–18]. Guffon [17] found that eight out of nine patients with MPS IH still needed CTD despite BMT. Field [16] found that seven out of 11 MPS IH patients with BMT still needed CTD. We believe, however, that this is the first study that has looked at the outcome of CTD with respect to BMT.

The results of this study are difficult to interpret in view of the possible confounding factors such as BMT, age at surgery, and the possibility of other causes of poor hand function. Nevertheless, using a validated neurophysiological assessment method, there is no benefit in adding an external neurolysis to a routine median nerve decompression and flexor tenosynovectomy in this group of patients. Additionally, as declines in neurophysiological function were only seen in patients receiving neurolysis, we cannot recommend its use.

Acknowledgement
The authors thank Mr David Jones for allowing us to review his patients. There are no competing interests.

References
### Queries and Remarks

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