Functional recovery after critical illness
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CHAPTER 2

CRITICAL ILLNESS POLYNEUROPATHY: A SUMMARY OF THE LITERATURE ON REHABILITATION OUTCOME

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APPENDIX

UPDATE MAY 2009

CRITICAL ILLNESS POLYNEUROPATHY AND MYOPATHY: AN UPDATE OF THE LITERATURE ON FUNCTIONAL OUTCOME

M. van der Schaaf, A. Beelen and F. Nollet (not published)
ABSTRACT

Purpose
To evaluate the available literature on outcome of critical illness polyneuropathy (CIP) and to identify rehabilitation problems.

Methods of study selection
A literature search in electronic databases. Primary articles on outcome in CIP using the classification of ICIDH or Quality of Life were enrolled in this study. Because of the types of study design, the lack of information regarding validity and the variability, a quantitative analysis was not possible. Instead, the overall results were evaluated in a qualitative approach.

Results
In the literature minimal attention was given to the rehabilitation aspects and long-term outcome of patients with CIP. Outcome measures were mainly used on the level of impairments and in lesser extent on the level of disabilities. One year after the onset of CIP, muscle weakness and decreased sensory function were frequently observed. Reported functional disabilities were dependency in Activities of Daily Living (ADL) and walking disabilities.

Conclusion
The specific course and long-term outcome of CIP remains unclear. Research on the course and long-term functional outcome in CIP is necessary in order to identify rehabilitation problems and to formulate treatment strategies specifically directed towards the outcome of CIP.
Introduction

In recent years, the neuromuscular syndrome, Critical Illness Polyneuropathy (CIP) has been diagnosed with increasing frequency in Intensive Care Units (ICU). CIP is a predominantly distal axonal degeneration of motor and sensory fibres. Since its first description in 1983 by Bolton et al.1 various percentages are reported about the incidence of CIP. In prospective studies incidence values range from 47% in patients who had been on the respirator for more than seven days and who developed multiple organ dysfunction syndrome (MODS)2 to 73% for ICU patients with MODS and sepsis.3,4 Because of major developments in intensive care medicine which prevented or delayed death of critically ill patients, this polyneuropathy now exists. The nature of the clinical features of CIP are predominantly motor, leading to muscle weakness or paralysis.5 Sensory impairment is often difficult to determine because of the state of the patients in the ICU.6 CIP is associated with rehabilitation problems, although it improves in all survivors, all authors agree on a 50% chance of complete recovery depending on the severity of the initial symptoms.1,3,5,7,8 Despite agreement on the extent of recovery, a clear and uniform description of outcome measures used to assess recovery, is missing in the literature. Based on the fact that most investigations are performed from a critical care, neurologic, or electrophysiologic background, one may expect outcome measurements at the level of pathology and to lesser extent at levels of disability and handicap.

Since Bolton’s study2 much pathophysiological research has been conducted which has increased knowledge about aetiology, diagnosis and clinical characteristics. Yet, for optimal rehabilitation treatment, more insight in the nature of the disease, the course and its sequelae is necessary. The aim of this study is to review the available literature on long-term functional outcome in CIP in terms of the classification of the ICIDH,9 impairments, disabilities, handicaps and Quality of Life, in order to identify rehabilitation related problems.

Materials and methods

We performed a literature search using the following computerized databases: Medline, EMBASE, Current Contents and Cinahl, using the text words ‘critical illness polyneuropathy’ in combination with ‘outcome’, or ‘rehabilitation’, or ‘physical therapy’, or ‘physiotherapy’, or ‘prognosis’, or ‘recovery’, or ‘course’. Articles published in English, Dutch or German from 1983 to
September 1999 were enrolled in this study. Any additional relevant articles from the reference lists were identified and retrieved. All studies were collected without consideration of research design. Subsequently the following inclusion criteria were applied to the full manuscripts by two of the authors (MvdS and AB) independently. The manuscripts had to be primary articles, all studies had to enroll patients diagnosed as CIP (confirmed by EMG), and outcome measures used in these studies had to be in terms of impairment, disability or handicap as defined by the World Health Organization or Quality of Life. We abstracted the data concerning number of subjects, study design, patients characteristics (diagnosis at admission in the ICU, age, gender), duration of follow-up, therapeutic interventions and outcome measures. We also extracted information reflecting the validity for each study, including: definition of the sample of patients, moment of inclusion point in the disease, follow-up, outcome criteria, description of the clinical examination and description of the electrophysiological examination according to the guidelines by Oxman et al. Because the types of study design, the lack of information regarding validity and the variability, a quantitative analysis was not possible. Instead we have evaluated the overall results in a qualitative approach.

Results
The literature search on the textword CIP in combination with ‘outcome’, ‘rehabilitation’, ‘physical therapy’, ‘physiotherapy’, ‘prognosis’, ‘recovery’, or ‘course’ yielded 34 articles. Nine reports fitted the inclusion criteria. Two studies had been conducted prospectively and seven were collections of case histories. The validity of the papers was moderate to poor. In some studies, important information such as case selection, measuring point in the course of the disease, rehabilitation interventions or description of the clinical examination was not available. Furthermore, most outcome measures used in the included studies were considered to be less relevant for rehabilitation medicine. In a prospective study by Leijten et al., 12 patients with CIP underwent serial neurological examination up to one year after discharge. Four weeks after discharge eight patients had not reached a rehabilitation end point which was defined as strength greater than grade 4/5 in all muscles, according to the scoring system of the Medical Research Council, and the ability to walk for more than 50 metres without aid or ataxia. The authors report improvements in motor, sensory and ADL functioning in all patients after 1 year, yet severe residual functional handicap due to polyneuropathy was found in five patients. Berek et al., prospectively examined 15 patients clinically with CIP three
months after discharge from the ICU. Improvement was found in all patients, though a moderate motor weakness was observed in two, a mild weakness in four and no motor weakness in nine patients. In their report, the authors did not describe the outcome measures being used with regard to motor strength. Sensory loss described as decreased pain and temperature sense was found in five patients and loss of vibration sense was found in four patients. In eight patients there was no sensory loss. Position sense was measured but not impaired in any of the patients. Reflexes were normal in eight patients and reduced or absent in seven patients.

In seven reports of case histories, 1,7,12-16 21 patients with CIP were described. At 6 months after admission in the ICU, impairments were: severe or moderate muscle weakness of limbs (legs more than arms), paresis of ankle dorsiflexors, absent two-point discrimination, decreased position sense and pain and temperature sensation distally, absent or reduced tendon reflexes, joint contractures and ossification.

Reported disabilities were impaired walking, dependency in activities of daily living and use of different walking aids or wheelchair. No outcome measures on handicap or Quality of Life were used in the different case reports.

Discussion

In the recent medical and critical care literature, the aetiology and pathology of CIP has been discussed extensively but the course and functional outcome of CIP has scarcely been the object of investigation. Our literature search yielded mainly case studies. Combining and interpreting the results from case studies is difficult with regard to patient selection, information about prognostic factors, final outcome measures, follow-up duration and rehabilitation intervention. Only two prospective studies on outcome in impairments and disability were found. Due to differences in follow-up duration (one year versus three months) and endpoints (disability versus impairments) we were not able to combine the results. In our opinion, a duration of follow-up of 3 months is relatively short in order to be able to draw conclusions regarding rehabilitation treatment goals. Although duration of follow-up in the study of Leijten et al. 5 was sufficient, it gave little qualitative information about disabilities that still exist after one year. All reported residual deficits were mainly on the level of impairments. To a lesser extent, deficits on the level of disability, handicap or Quality of Life have been reported, this might be due to the fact that outcome measures on these levels have not been used. Muscle weakness and decreased sensory function are frequently observed impairments one year after the onset of CIP.
Reported functional disabilities are mainly dependency in ADL and walking disabilities. The duration of rehabilitation for patients with CIP is prolonged compared to other critically ill patients, often including clinical rehabilitation for at least a few months. None of the prospective studies and case studies describe the contents of the rehabilitation treatment. In this respect, it is remarkable that in many publications early physiotherapy is recommended as it leads to favourable outcomes, without any evidence or suggestions for one specific treatment.\textsuperscript{5,7,11,14,15} Despite our literature research it remains unclear what the course and long-term outcome of CIP is.

In our experience the burden of patients with CIP on our department of rehabilitation is extensive. The length of stay of patients with CIP in the ICU is prolonged due to muscle weakness and weaning problems. In some cases muscle weakness is extreme leading to a quadriplegia which impedes mobilisation. In our hospital, patients who are weaned from the ventilator are transferred to a general ward. At discharge from the ICU all CIP patients are completely dependent for ADL. Without any other medical complications most patients with CIP are discharged from hospital between 4 and 16 weeks after ICU discharge. A majority of these patients is admitted to a clinical rehabilitation centre or is referred for a temporary stay in a nursing home with rehabilitation facilities. Based on the literature and our own experiences we do know that patients with CIP receive rehabilitation treatment for a long period which may last one year or more. It is not known however, to what extent recovery may take place spontaneously. To us it remains unclear what CIP attributes to the prolonged rehabilitation period because long-term outcome may be determined not only by CIP but also by many other factors like initial illness and comorbidity. In our opinion, research on long-term outcome of CIP is necessary in order to describe rehabilitation problems and to develop a treatment specifically directed towards the outcome of CIP. Therefore in the Academic Medical Center we have started with a prospective longitudinal pilot study on the course of CIP with clinical outcome measures in terms of impairments, disabilities, handicaps and quality of life.

References


APPENDIX CHAPTER 2

CRITICAL ILLNESS POLYNEUROPATHY (CIP) AND MYOPATHY (CIM):
AN UPDATE OF THE LITERATURE ON FUNCTIONAL OUTCOME (SEPTEMBER 1999-MAY 2009)

M. van der Schaaf, A. Beelen, and F. Nollet

Not published
Background

Critical illness polyneuropathy (CIP) and myopathy (CIM) are major complications of severe critical illness. CIP/ CIM prolongs weaning from mechanical ventilation and delays physical recovery since both limb and respiratory muscles can be affected.1

In 2000 our literature review, summarizing the available literature on functional outcome in patients with CIP, was published in Disability and Rehabilitation.2 By then, studies on functional outcome of patients with CIP, classified according to the International Classification of Functioning (ICF3) in impairments of body functions, activity limitations, and participation restrictions, were scarce and the validity of the studies were moderate to poor. Recent studies have advocated the use of the term critical illness polyneuromyopathy (CINM), which will be used throughout this review, indicating a primary axonal degeneration of motor and sensory fibers causing muscle weakness and sensory disturbances, as a complication of critical illness. Apart from difficulties in differentiating CIP and CIM, they frequently co-occur and the clinical relevance of differentiating between neuropathy and myopathy is still under debate.1,4

The aim of this update is to provide an overview of the literature on long-term functional outcome in patients with CINM in terms of the ICF classification and quality of life (QoL), published between September 1999 and May 2009.

Methods

For this update we reviewed the available literature published after 1999 in Medline (PubMed), using the text words ‘critical illness polyneuropathy’ or ‘critical illness myopathy’ and ‘rehabilitation [MeSH]’, ‘physical therapy [MeSH]’, or ‘physical therapy modalities [MeSH]’, or ‘quality of life [MeSH]’, or ‘recovery of function [MeSH]’, or ‘convalescence [MeSH]’, or ‘functional status’, or ‘activities of daily living’.

Articles published in English, Dutch or German between September 1999 and May 2009 were enrolled in this study. Any additional relevant articles from the reference lists were identified and retrieved. All studies were collected without consideration of research design. Subsequently the following inclusion criteria were applied to the abstracts or full manuscripts by the author (MvdS). The manuscripts had to be primary articles, all studies had to enrol adult patients with an electrophysiological diagnosis of CINM, for whom a follow-up after hospital discharge was reported on outcomes according to the ICF or QoL. Data were abstracted concerning study design, number of
subjects, patients characteristics (diagnosis at admission in the ICU, age, length of stay in the ICU, duration of follow-up, and outcome measures and with respect to regarding body functions, activities, participation and QoL. Finally, the results of the studies were evaluated in a qualitative approach.

Results

The sensitive search yielded 393 articles. Seven articles met the inclusion criteria and reported on outcomes after hospital discharge in terms of the ICF in patients diagnosed with CINM.5-11 All studies were collections of case reports and case series, including the follow-up data of 80 patients with CINM. In some case reports, important information such as length of stay in the intensive care, measuring point after the critical illness, or description of the clinical examination was not available. A wide variety of ICU admission diagnoses were reported, including medical, elective surgery, and acute surgery or trauma. Duration of follow-up after discharge from the ICU varied from 3 to 57 months.

Impairments in muscle strength were reported in 6 studies5-8,10,11, and sensory functions in 4 studies.5,6,10,11 Restrictions in activities were reported in 5 studies (walking ability [3 studies7,8,10], dexterity [1 study10], activities of daily living; ADL; assessed with the modified Rankin Scale [1 study9], Barthel index [2 studies10,6], Sickness Impact Profile [SIP68; 1 study10]). One study reported on restrictions in participation (measured with the impact on participation questionnaire; IPA) and two studies reported on the quality of life (Short-health form 36; SF-3610, Niemie questionnaire11) in patients with CIP.

The study characteristics and findings with respect to impairments in body functions, limitations in activities, restrictions in participation and QoL of the 6 included studies are presented in Table 2.1.

Conclusions

In the past 10 years, reported impairments in body functions (i.e. decreased muscle strength with lower limbs more affected than upper limbs, and sensory deficits), and restrictions activities (i.e. ADL and walking) were in concordance with the findings of our previous literature review.2 One study reported data on rehabilitation relevant outcomes which had not previously been described, such as limitations in hand function (assessed with the Jebsen hand function test), restrictions in physical activities (assessed with the SIP68 questionnaire), participation (assessed with the IPA questionnaire) and QoL (assessed with the SF-36).10

Appendix: Critical illness polyneuropathy
There is a large variation in the course and in the extent of functional recovery in patients with CINM, varying from complete functional recovery within 3 months, to persistent tetraplegia with severe disability and functional dependency after more than one year. Due to the variation in duration of follow-up and in outcome measures used in the different studies on functional outcome, a quantitative combination of study results, and the identification of prognostic factors for functional recovery is not possible. With this, the identification of patients at risk for a poor functional outcome is not possible.

This update of the literature on functional outcomes in patients with CINM, confirms our previous findings that attention should be paid to the high prevalence of long-term impairments in body functions, limitations in activities, restrictions in activities and reduced QoL in patients with CINM.
<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>No. of pts.</th>
<th>Age (years)</th>
<th>ICU LOS (days)</th>
<th>Follow-up after ICU (months)</th>
<th>ICF outcome measure (measurement instrument)</th>
<th>Results:</th>
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<td>- body functions</td>
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<td>- quality of life</td>
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Latronico N. et al. (1999)\(^8\)

<table>
<thead>
<tr>
<th>N = 2</th>
<th>33-72</th>
<th>13-36</th>
<th>5-6</th>
<th>- strength (not reported)</th>
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<td>- ambulation (not reported)</td>
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</table>

Normal arm/reduced leg strength: 1 pt
Strength not reported: 1 pt
Walking independently: 1 pt
Walking with assistance: 1 pt

Sèze, de M. et al. (2000)\(^5\)

<table>
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<tr>
<th>N = 19</th>
<th>Mean 56</th>
<th>Not reported (range 15-74)</th>
<th>3-24</th>
<th>- muscle strength (MRC)</th>
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<td>- sensory function (not reported)</td>
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<td>- functional recovery (not reported)</td>
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Incomplete functional recovery: 4 pts at 24 months:
Tetraparesis: 2
- MRC UL5, LL2, NSF
- MRC UL 5p 3d, LL 4p 3d, SL d
Tetraplegia: 2
- MRC UL 2p 0d, LL 2p 0d d SL
- MRC UL 2p 0d, LL 1p 0d, SL d

Complete functional recovery: 11 pts
- within 3 months: 4 pts
- within 6 months: 4 pts
- within 12 months: 3 pts
### Table 2.1 Continued

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>N</th>
<th>Age (range)</th>
<th>Score</th>
<th>Mean (range)</th>
<th>Measure</th>
<th>Details</th>
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<tr>
<td>Nagaratham N. et al. (2001)</td>
<td>2</td>
<td>67-76</td>
<td>Not reported</td>
<td>5</td>
<td>Disability (Modified Rankin Scale; MRS)</td>
<td>Slight disability (MRS grade 2): 2 pts after 5 months Full recovery after 15 months: 1 pt</td>
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<td>Fletcher SN. et al. (2003)</td>
<td>22</td>
<td>Median 62 (range 45-78)</td>
<td>Median 41 (range 30-104)</td>
<td>12-57 (median 43)</td>
<td>Muscle strength (MRC) ADL (Barthel Index)</td>
<td>Motor weakness (MRC &lt; 4): 4 pts Sensory deficits: 8 pts Combined motor weakness and sensory deficits: 3 pts Bilateral peroneal nerve palsy with foot drop: 2 pts Bilateral upper limb weakness: 3 pts ADL: independent; Barthel index: median 100 (range 55-100)</td>
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<td>Study</td>
<td>N</td>
<td>Median/Range</td>
<td>6-12</td>
<td>6 months (n=8)</td>
<td>12 months (n=5)</td>
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<td>Schaaf, van der M. et al. (2004)&lt;sup&gt;10&lt;/sup&gt;</td>
<td>N=8</td>
<td>Median 67 IQR 39</td>
<td>6 months (n=8)</td>
<td>MRC (median) UL LE 4-5</td>
<td>12 months (n=5)</td>
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<td>Mean 32-78 (IQR 10-90)</td>
<td>6-12</td>
<td>SL foot: 4 pts</td>
<td>Complete functional recovery: 1 pt</td>
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<td>Hand function within normal range: 8 pts</td>
<td>Incomplete functional recovery: 4 pts</td>
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<td>ADL: dependent for washing, bathing, dressing: 3 pts</td>
<td>Independent in self-care and basic ADL: 5 pts</td>
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<td>Limitations in mobility: stairs: 4 pts, walking outdoors: 5 pts</td>
<td>Limitations in mobility/ambulation: 4 pts</td>
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<td>Participation restrictions: 8 pts</td>
<td>Restrictions in participation: 3 pts</td>
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<td>Reduced QoL</td>
<td>Reduced QoL: 2 pts</td>
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<td>Guarneri B. et al. (2008)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>N=14</td>
<td>Mean 45 (SD 15)</td>
<td>3-12</td>
<td>3 months</td>
<td>Complete recovery: 4 pts</td>
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<td>Mean 24 (SD 13)</td>
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<td>Tetraparesis: 3 pts</td>
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<td>Tetraplegia: 3 pts</td>
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<td>Complete recovery:</td>
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<td>Complete recovery:</td>
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No. of pts: number of patients; ICU LOS length of stay in the intensive care unit; ICF international classification of functioning; MRC medical research council; UL upper limb; LL Lower limb; p proximal; d distal; NSF normal sensory finding; SL sensory loss. ADL: activities of daily living; SIP = Sickness Impact Profile-physical dimension; IPA = Impact on Participation and Autonomy; SF-36: Medical Outcomes Study 36 Item Short form
References


