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The incidence of intensive care unit-acquired weakness syndromes: A systematic review

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Abstract

We conducted a literature review of the intensive care unit-acquired weakness syndromes (critical illness polyneuropathy, critical illness myopathy and critical illness neuromyopathy) with the primary objective of determining their incidence as a combined group. Studies were identified through MEDLINE, Embase, Cochrane Database and article reference list searches and were included if they evaluated the incidence of one or more of these conditions in an adult intensive care unit population. The incidence of an intensive care unit-acquired weakness syndrome in the included studies was 40% (1080/2686 patients, 95% confidence interval 38–42%). The intensive care unit populations included were heterogeneous though largely included patients receiving mechanical ventilation for seven or more days. Additional prespecified outcomes identified that the incidence of intensive care unit-acquired weakness varied with the diagnostic technique used, being lower with clinical (413/1276, 32%, 95% CI 30–35%) compared to electrophysiological techniques (749/1591, 47%, 95% CI 45–50%). Approximately a quarter of patients were not able to comply with clinical evaluation and this may be responsible for potential underreporting of this condition.

Keywords

Critical care, intensive care, epidemiology, muscle weakness, intensive care unit-acquired weakness

Introduction

Worldwide, the majority (70–80%) of patients admitted to an intensive care unit (ICU) now survive;[1–5] follow-up has identified multiple sequelae with generalised weakness in particular found to be a common and troublesome problem.[6–9] Whilst there has been major heterogeneity in terminology used to label this generalised weakness, a critical illness associated polyneuropathy, myopathy and neuromyopathy (where both neuropathy and myopathy coexist) have broadly been identified. These syndromes are now all included under the clinical diagnostic label of intensive care unit-acquired weakness (ICUAW).[10]

The development of an ICUAW syndrome may have important consequences on patient outcomes; prolonged ventilatory weaning,[11,12] increased ICU[12] and hospital length of stay,[13] increased hospital mortality,[14,15] increased 180-day mortality[16] and persistent disabling weakness with reduced quality of life out to one year from ICU discharge.[17–19] There may also be a number of potentially modifiable risk factors for ICUAW; prolonged ICU stay/bed rest,[20,21] hyperglycaemia/insulin therapy,[13,22–24] corticosteroids[20] and neuromuscular blockers.[14]

Unfortunately, there is marked heterogeneity across the studies of ICUAW. A systematic review by Stevens et al.[13] highlighted, for example, the heterogeneity in the diagnostic criteria used. This currently makes drawing firm conclusions regarding ICUAW difficult and may partly explain some of the inconsistent findings across the studies, such as an incidence varying from 9%[25] to 86%.[26]

With the increasing recognition that the ICU care we deliver needs to ensure the optimal functional outcome of patients, further study and a better understanding of ICUAW are important next steps. There have been a significant number of studies published[8,15,16,23,24,27–32] since the previous systematic

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review supporting updating the estimate of the incidence of ICUAW. In addition, with the marked variation in diagnostic criteria used across studies, further investigation of this heterogeneity may be useful in identifying trends, for example in incidence, within the diagnosis. This may then allow more homogenous groups and their outcomes to be identified for intervention and prognostication.

Unfortunately, the inconsistent reporting of the diagnostic criteria precludes its influence on incidence from being evaluated directly. However, part of the heterogeneity within the diagnostic criteria may relate to the varying diagnostic techniques used – clinical, neurophysiological or histological examination. The diagnostic techniques used across the studies are adequately reported and could be used to identify any variation in the incidence of ICUAW according to the diagnostic technique used.

The aims of this review are: (1) to determine the approximate incidence of all the ICUAW syndromes as a group, (2) to determine the incidence of the ICUAW syndromes categorised by diagnostic technique (clinical, electrophysiological and histological diagnoses) and (3) to determine the incidence of failure of completion of diagnostic assessment and the attributable causes (that are not a lack of study consent) categorised by diagnostic technique.

Methods

Data sources and searches

The online databases MEDLINE, Embase and the Cochrane databases were searched from the period 1977 until 1 July 2011 to identify studies to include in this review. The search terms used were: muscle weakness, paresis, polyneuropath(y)/(ies), muscle hypotonia, muscular disease(s), intensive care unit(s), intensive care, critical care, critical illness, respiration artificial, artificial ventilation. These terms were mapped to the appropriate subject headings and 'exploded'. The search was limited to studies published in English and those involving humans.

The title and abstract of all publications identified by the search strategy were screened, with the full text of all those describing an ICUAW syndrome reviewed. The reference list of each full text article reviewed was screened to identify additional relevant papers.

Study selection

Studies fulfilling the following eligibility criteria were included: (1) patients were admitted to an adult ICU, (2) patients were diagnosed with an ICUAW (critical illness polyneuropathy, critical illness myopathy or critical illness neuromyopathy), (3) sufficient data to calculate the incidence of an ICUAW was provided, (4) study patients were not potentially included in another study included in this review and (5) the full-length report was published. Patients with weakness attributed to a specific aetiology (e.g. spinal cord compression) were excluded.

Studies where the diagnostic criteria were either not consistent with a diagnosis of an ICUAW or were inadequate were excluded. Whilst there has recently been consensus diagnostic criteria published,[10] all studies included in this review recruited patients prior to this publication where diagnostic criteria were variable. The minimum criteria required for study inclusion were any of the following: (1) a new clinical diagnosis of generalised weakness determined by an objective clinical assessment tool (e.g. Medical Research Centre sum scores), (2) reduced compound motor and sensory nerve action potential amplitudes consistent with critical illness polyneuropathy, (3) normal sensory nerve action potential amplitudes with either of short duration, low amplitude motor potentials on electromyography (EMG) or low-amplitude motor potentials and nerve:muscle ratio >0.5 on direct muscle stimulation consistent with critical illness myopathy, (4) muscle histology consistent with critical illness myopathy or (5) a combination of neurophysiological abnormalities as given above consistent with critical illness neuromyopathy.

For the third question of this review addressing the incidence of failure to complete diagnostic testing, only papers presenting this information were included in this part of the analysis. The denominators abstracted from each paper for these calculations were the number of patients analysed in the study plus the number who were not included because of failure to complete the diagnostic evaluation.

Data extraction and quality assessment

A modified version of the validated Newcastle–Ottawa Scale (NOS)[33] with the addition of three further criteria suggested by Altman et al.[34] was used to appraise the observational studies. The NOS evaluates three domains; the selection of the study populations (range 0–4 points), the comparability of the study populations (range 0–2 points) and the assessment of the outcomes (range 0–3 points). The modified NOS we used had three additional assessments (objectivity of diagnostic criteria used (0–1 point), appropriateness of diagnostic criteria (0–1 point) and ability of diagnostic criteria to differentiate critical illness polyneuropathy (CIP), critical illness myopathy (CIM) and critical illness neuromyopathy (CINM) (range 0–2 points) within the outcome domain (range 0–7 points). The modified scale has a maximum score of 13 with a score of 0–4 being judged as a low-quality, 5–8 as medium-quality and 9–13 as a high-quality study. The modified NOS was agreed by the authors prior to commencing the review.

Randomised controlled trials (RCTs) were appraised according to the Cochrane Collaboration's assessment tool for risk of bias.[35] Each study was assessed by one of the authors for quality using these tools.

Data synthesis and analysis

Patient, illness, treatment and study design data were abstracted using a standardised data collection sheet and collated in Excel (Microsoft Corporation Redmond, WA, USA). Professional statistical advice was obtained and confidence interval (CI) analysis (95% CIs) on proportions using aggregated original study data was performed by one of the study authors using Confidence Interval Analysis Version 2.2.0 (University of Southampton, UK, 2000–2011).

Results

Study search and selection

The results of the literature search are shown in Figure 1; 33 studies including 2686 patients were evaluated in this review. The characteristics of the included studies are shown in Table 1. Of the 33 studies, 27 were prospective cohort studies, two were

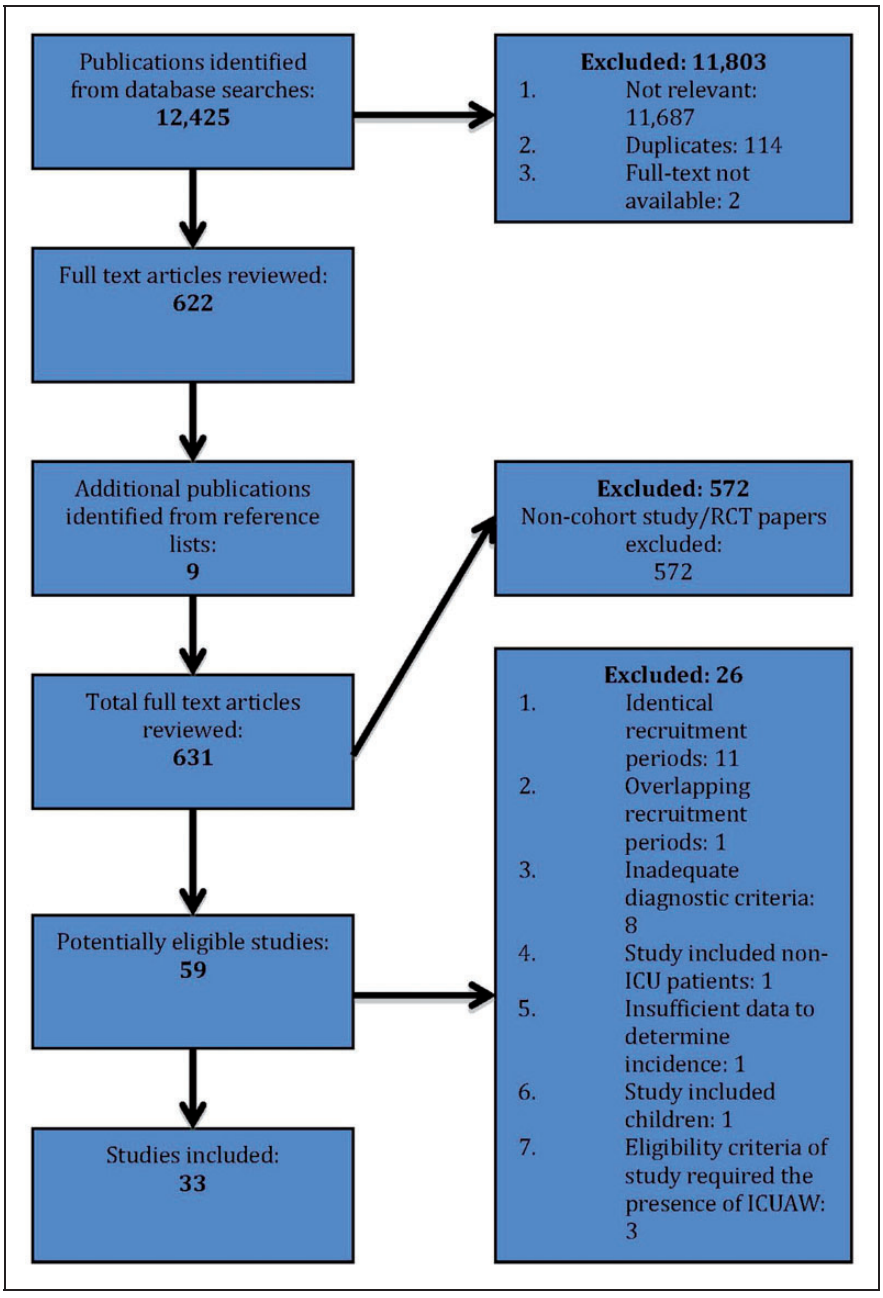

Figure 1. Literature search results.

Table 1. Study characteristics.

References	Study design, eligibility and study period	ICU population
Ahlbeck et al.[36]	Prospective cohort study Mechanical ventilation for three days Study period not stated	ICUs in a single University hospital in Sweden Mixture of medical, surgical, trauma and neurosurgical admission diagnoses Age (mean): 54 (range 21–79) years Males: 7 (70%)
Ali et al.[28]	Prospective cohort study Mechanical ventilation >5 days ICU admission between May 2005 and April 2007	Five medical ICUs in USA Range of medical admission diagnoses and comorbid conditions Age (mean): 58 (*SD* 16) years Males: 48%
Amaya-Villar et al.[43]	Prospective cohort study Acute exacerbation of chronic obstructive pulmonary disease (COPD) requiring mechanical ventilation for > 48 h and receiving ⩾240 mg methylprednisolone in the first 48 h ICU admission between 1997 and 2000	Single Spanish ICU Solely COPD patients evaluated Age (mean): ICUAW 62 (*SD* 9) years, no-ICUAW 66 (*SD* 7) years
Bednarik et al.[51]	Prospective cohort study ⩾2 organ failures and within 24 h of onset of critical illness Meeting study entry criteria between January 2000 and November 2002	One general and one neurological ICU in a single hospital in the Czech Republic Admission diagnoses provided incomplete; mixture of neurological and medical/surgical admission diagnoses in those provided Age (range): 22–81 years
Bercker et al.[37]	Retrospective cohort study Consecutive acute respiratory distress syndrome (ARDS) patients ICU admission between May 1998 and November 2001	Single tertiary ARDS ICU in Germany Solely ARDS patients Age (median): 37 (IQR 21–56) years
Berek et al.[38]	Prospective cohort study systemic inflammatory response syndrome (SIRS)/sepsis with multiorgan failure Study period: September 1992–August 1993	ICUs not described ICU admission diagnosis was predominately polytrauma with some additional general surgical diagnoses Age (median): 56 (range 23–77) years Males: 17/22 (77%)
Brunello et al.[16]	Prospective cohort study Mechanical ventilation ⩾48 h and ⩾2 SIRS criteria Study period: September 2005–May 2006	ICUs not described ICU admission diagnoses were predominately a mix of medical and surgical (general and cardiac) with a small number of trauma diagnoses Age (mean): 67 (*SD* 14) years Males: 28/39 (72%)
Campellone et al.[25]	Prospective cohort study Patients undergoing orthotopic liver transplant (OLTx) and either ventilated for >7 days or hospitalised >14 days Study period: August 1995–February 1996	Single ICU in USA Solely adult patients undergoing OLTx Age (mean): 53 (range 17–73) years
Coakley et al.[44]	Prospective cohort study ICU stay ⩾7 days and ⩾1 organ failing 11-month study period, time period not stated	Single ICU in UK Admission diagnoses a mixture of medical, surgical and trauma Age (range): 20–72 years Males: 15/23 (65%)
Coakley et al.[39]	Prospective cohort study ICU stay ⩾7 days 3-year study period, time period not stated	Single ICU in UK Admission diagnoses a mixture of medical, surgical (general and cardiac) and trauma Age (range): 27–84 years Males: 23/44 (52%)
De Jonghe et al.[20]	Prospective cohort study Mechanical ventilation for ⩾7 days Study period: began March 1999 for mean duration 8.6 months	Three medical and two surgical ICUs in four hospitals in France Admission diagnoses a mixture of medical, surgical and trauma Age (mean): 62 (*SD* 15) years Males: 69/95 (73%)

(continued)

Table 1. Continued.

References	Study design, eligibility and study period	ICU population
De Letter et al.[45]	Prospective cohort study Mechanical ventilation for ⩾4 days Study period: May 1994–July 1996	Single ICU in Holland Admission diagnoses not provided Age (median): 70 (range 15–85) years Males: 55/98 (56%)
Douglas et al.[40]	Prospective cohort study Mechanical ventilation for severe asthma 18-month study period, no further information provided	Single ICU in Australia Solely patients with asthma Age (mean): 39 (*SD* 17) years Male: 5/25 (20%)
Druschky et al.[41]	Prospective cohort study Mechanical ventilation for >4 days Study period: April 1997–December 1998	Single neurological ICU in Germany Admission diagnoses were either ischaemic stroke or intracerebral haemorrhage Age (mean): ICUAW 64 (*SD* 8) years, non-ICUAW 70 (*SD* 8) years Males: 18/28 (64%)
Garnacho-Montero et al.[14]	Prospective cohort study Sepsis with multiorgan failure and ventilated for >10 days Study period: November 1996–March 1999	Single mixed medical/surgical ICU in Spain Primary diagnoses were predominately abdominal and chest sepsis with small numbers of other sources of sepsis Age (mean): ICUAW 62 (*SD* 14) years, no ICUAW 62 (*SD* 12) years
Garnacho-Montero et al.[12]	Prospective cohort study Severe sepsis/septic shock requiring mechanical ventilation ⩾7 days Study period: July 1999–December 2002	Single mixed medical/surgical ICU in Spain Primary diagnoses were predominately abdominal and chest sepsis with small numbers of other sources of sepsis Age (mean): ICUAW 61 (*SD* 15) years, no ICUAW 62 (13) years Males: 39/64 (61%)
Hermans et al.[23]	Randomised controlled trial, preplanned subgroup analysis Eligibility not stated Study period: March 2002–May 2005	Single medical ICU in Belgium Preplanned subanalysis of intensive insulin therapy (IIT) vs. conventional insulin therapy (CIT) in those staying ⩾7 days Range of medical admission diagnoses Age (mean): CIT 64 (*SD* 16) years, IIT 61 (*SD* 15) years Males: 253/420 (60%)
Hough et al.[32]	Prospective cohort study Three days mechanical ventilation Study period: four months in 2006 and 2007	ICUs in a single hospital in USA. Mixture of surgical, medical and neurological admissions Age (mean): 49 (*SD* 15) years Males: 71%
Hund et al.[46]	Prospective cohort study Sepsis and prolonged mechanical ventilation Study period not stated	Single surgical ICU in Germany Mixture of general, cardiac, neurological and trauma surgical patients Age (median): 70 (range 16–80) years Males: 19/28 (68%)
Kesler et al.[29]	Retrospective cohort study Acute severe asthma requiring mechanical ventilation Study period: May 1983–May 1995 and May 1995–May 2004	Single medical ICU in USA Solely patients presenting with acute severe asthma Age (mean): Pre-1995 cohort 39 (*SD* 17) years, post-1995 cohort 38 (*SD* 13) years Males: Pre-1995 56%, post-1995 45%
Khan et al.[47]	Prospective cohort study Severe sepsis diagnosed within 72 h of ICU admission and 10 days of hospital admission and an ICU stay ⩾7 days Study period: April 2003–December 2004	Two medical ICUs in two hospitals in USA Approximately 50% chest source of sepsis, no further information provided Age (mean): ICUAW 53 (*SD* 16) years, no ICUAW 46 (*SD* 16) years Males: not stated

(continued)

Table 1. Continued.

References	Study design, eligibility and study period	ICU population
Latronico et al.[27]	Prospective cohort study ICU admission and a Simplified Acute Physiology II Score between 35 and 70 Study period: January 1998–March 2001	Nine ICUs in Italy Mixture of medical, surgical (general and neurological) and trauma admission diagnoses Age (median): 50 (range 18–85) years Males: 63/92 (69%)
Leijten et al.[48]	Prospective cohort study Mechanical ventilation >7 days Study period: July 1991–January 1993	Single mixed medical and surgical ICU in Holland Admission diagnoses were a mixture of surgical (general, thoracic and neurological), medical and trauma Age (mean): ICUAW 59 (*SD* 14) years, no ICUAW 55 (*SD* 17) years Males: 26/38 (68%)
Mohr et al.[49]	Prospective cohort study ICU patients with multiorgan failure 2-year study period, time period not stated	Single mixed surgical (general and neurological) and trauma ICU in Germany Primary diagnosis predominately trauma with smaller numbers of surgical (general and neurological) and medical diagnoses Age (median): no sepsis/no ICUAW 45 (range 16–69) years, sepsis/no ICUAW 52 (range 21–76) years, sepsis/ICUAW 48 (range 20–71) years Males: 19/33 (58%)
Nanas et al.[24]	Prospective cohort study ICU stay >10 days Study period: August 2005–September 2006	Single mixed medical and surgical ICU in Greece Mixture of medical, surgical and trauma admission diagnoses Age (mean): 54 (*SD* 19 years) Males: 127/185 (69%)
Routsi et al.[31]	Randomised controlled trial ICU patients with an admission Acute Physiology and Chronic Health Evaluation II score ⩾13 Study period: September 2007–June 2009	Single mixed medical and surgical ICU in Greece Randomised controlled trial of electrical muscle stimulation (EMS) to lower limbs versus usual care Mixture of medical, surgical and trauma admission diagnoses Age (mean): EMS group 55 (range 23–82) years, control 59 (range 19–84) years Males: EMS group 19/24 (79%), control 22/28 (79%)
Schweikert et al.[8]	Randomised controlled trial (RCT) Mechanical ventilation for <72 h and predicted to require a further 24+ h of mechanical ventilation Independent at baseline Study period: June 2005–October 2007	Two medical ICUs in USA RCT of early physical and occupational therapy versus usual care Mixture of medical admission diagnoses Age (median): intervention group 58 (IQR 36–69) years, control group 54 (IQR 47–66) years Males: 52/104 (50%)
Sharshar et al.[15]	Prospective cohort study Mechanical ventilation for ⩾7 days Study period: June 2003–June 2005	Two medical, one surgical and one mixed medical/surgical ICU in three hospitals in France Approximately 70% had a medical admission diagnosis Age (median): 65 (IQR 52–77) years Males: 75/115 (65%)
Tepper et al.[26]	Prospective cohort study Septic shock Study period: January 1995–August 1995	Single ICU in Holland Predominately chest and abdominal sources of sepsis with small numbers of other sources Age (mean): 57 (range 25–79) years Males: 18/25 (72%)

(continued)

Table 1. Continued.

References	Study design, eligibility and study period	ICU population
Thiele et al.[50]	Prospective cohort study Open heart surgery and mechanical ventilation >3–5 days Study period: June 1997–September 1998	Single cardiac surgical ICU in Germany Predominately bypass graft surgery with small numbers of valve surgery Age (mean): ICUAW group 66 (*SD* 5) years, non-ICUAW 68 (*SD* 7) years Males: 13/19 (68%)
Van den Berghe et al.[22]	Randomised controlled trial, preplanned subgroup analysis Adult patients in ICU for ⩾7 days Study period not stated	Single surgical ICU in Belgium RCT of conventional (CIT) vs. intensive insulin therapy (IIT) Mixture of cardiac, thoracic, general, vascular, neurological, trauma and transplant surgery admission diagnoses Age (mean): CIT 61 (*SD* 16) years, IIT 61 (*SD* 15) years Males: CIT 69%, IIT 67%
Weber-Carstens et al.[30]	Prospective cohort study Mechanically ventilated patients with a Simplified Acute Physiology II Score ⩾20 on three consecutive days within first seven days of ICU admission 18-month study period, time period not stated (dmCMAP: direct muscle compound motor action potential)	Single surgical ICU in Germany Mixture of trauma, pneumonia and abdominal sepsis as the predominate admission diagnoses Age (median): normal dmCMAP 42 (IQR 26–59) years, abnormal dmCMAP 53 (*SD* 40–61) years Males: 28/56 (50%) (only data provided)
Witt et al.[42]	Prospective cohort study Sepsis with multiple organ failure and ICU stay >5 days 14-month study period, time period not stated	Single hospital in Canada, single mixed ICU Mixture of medical, surgical (cardiac, general, vascular, gynaecological and thoracic) and trauma admission diagnoses Age (mean): 64 (range 21–78) years Males: 22/43 (51%)

Note: ICUAW, intensive care unit-acquired weakness; *SD*, standard deviation; IQR, inter-quartile range.

retrospective cohort studies and four were randomised controlled trials.

Quality of included studies

Eleven out of the 29 (38%)[25,28,29,32,36–42] observational studies were graded of low quality, 17 out of 29 (59%)[12,14–16,20,24,26,27,30,43–50] as medium and one (3%)[51] as high quality. There were four RCTs included; two studies were deemed of low risk,[22,23] one unclear risk[8] and one with high risk[31] of bias.

Incidence of ICUAW

The 33 studies included 2686 patients with 1080 (40%, 95% CI 38–42%) patients meeting the criteria for an ICUAW (see Table 2). The median incidence of an ICUAW across the studies was 47% (range 9–86%).

Incidence of ICUAW by diagnostic technique

Fifteen studies including 1276 patients made the diagnosis of an ICUAW using clinical examination, 20 studies including 1591 patients used electrophysiological examination to make the diagnosis and a single study of 23 patients used histological assessment (see Table 3). The incidence of ICUAW syndromes in the subgroups of patients separated by diagnostic technique is given in Table 3.

Failure of completion of diagnostic assessment

Fourteen studies including 1488 patients using clinical assessment and 17 studies including 742 patients using neurophysiological assessment provided data on failure of completion of diagnostic testing relating to the technique (see Table 4). The incidence of failure of completion of diagnostic assessment for an ICUAW syndrome is given in Table 4.

The reasons for failure to complete the clinical assessment were the combination of inadequate patient awakening and comprehension (377/381 [99%] patients), generalised pain (1/381 [0.2%] patients) and patient refusal to cooperate (3/381 [0.8%] patients). The reasons for failure to complete the electrophysiological assessment were inadequate patient compliance (11/17 [65%] patients) and technical problems (6/17 [35%] patients). The electrophysiological diagnostic criteria used across the studies were such that in only four of 17 (24%) studies

Table 2. Incidence of ICUAW.

References	No. of patients	No. with ICUAW	Proportion with ICUAW (%)	95% CI
Ahlbeck et al.[36]	10	5	50	24–76
Ali et al.[28]	136	35	26	19–34
Amaya-Villar et al.[43]	26	9	35	19–54
Bednarik et al.[51]	61	35	57	45–69
Bercker et al.[37]	45	27	60	46–73
Berek et al.[38]	22	18	82	62–93
Brunello et al.[16]	39	13	33	21–49
Campellone et al.[25]	77	7	9	5–18
Coakley et al.[44]	23	12	52	33–71
Coakley et al.[39]	44	37	84	71–92
De Jonghe et al.[20]	95	24	25	18–35
De Letter et al.[45]	98	32	33	24–42
Douglas et al.[40]	25	4	16	6–35
Druschky et al.[41]	28	16	57	39–74
Garnacho-Montero et al.[14]	73	50	69	57–78
Garnacho-Montero et al.[12]	64	34	53	41–65
Hermans et al.[23]	420	188	45	40–50
Hough et al.[32]	30	6	20	10–37
Hund et al.[46]	28	20	71	53–85
Kesler et al.[29]	170	30	18	13–24
Khan et al.[47]	20	10	50	30–70
Latronico et al.[27]	92	28	30	22–41
Leijten et al.[48]	38	18	47	33–63
Mohr et al.[49]	33	7	21	11–38
Nanas et al.[24]	185	44	24	18–30
Routsi et al.[31]	52	14	27	17–40
Schweikert et al.[8]	104	42	40	32–50
Sharshar et al.[15]	115	75	65	56–73
Tepper et al.[26]	22	19	86	67–95
Thiele et al.[50]	19	12	63	41–81
Van den Berghe et al.[22]	405	154	38	33–43
Weber-Carstens et al.[30]	44	25	57	42–70
Witt et al.[42]	43	30	70	55–81
Total	2686	1080	40	38–42

Note: ICUAW, intensive care unit-acquired weakness; CI, confidence interval.

was patient compliance actually required. In these studies, failure of diagnostic assessment because of inadequate compliance was 13% (11/83 patients).

Discussion

There are three main findings from this systematic review. First, the approximate incidence of the ICUAW syndromes as a group was 40% (95% CI 38–42%). Second, the incidence of the ICUAW syndromes when diagnosed clinically was significantly lower (32%, 95% CI 30–35%) than when diagnosed electrophysiologically (47%, 95% CI 45–50%). Finally, the incidence of failure of diagnostic assessment was significantly higher with a clinical diagnostic technique (26%, 95% CI 24–28%) compared to an electrophysiological technique (2%, 95% CI 1–4%).

There are two published systematic reviews in this area,[13,52] the most recent included studies up until 2006. This review adds approximately a further 1200 patients and 12 new studies to this work. The incidence of ICUAW in this review is lower than in those done previously (60%[52] and 46%[13]). The still sizeable incidence of ICUAW reflects the populations studied: those requiring mechanical ventilation beyond approximately seven days, patients with severe sepsis, multiple organ failure or conditions treated with relatively high doses of steroids.

This review is the first to evaluate the incidence of the ICUAW syndromes according to the diagnostic

Table 3. Incidence of ICUAW in subgroups according to diagnostic technique.

Technique	No. of patients	No. with ICUAW	Proportion with ICUAW	95% CI
Clinical diagnosis[8,15,16,20,24,25,28–32,37,40,45,51]	1276	413	32	30–35
Electrophysiological diagnosis[12,14,22,23,26,27,36–39,41–43,45–51]	1591	749	47	45–50
Histological diagnosis[44]	23	12	52	33–71

Note: ICUAW, intensive care unit-acquired weakness; CI, confidence interval.

Table 4. Incidence of failure of completion of diagnostic assessment according to diagnostic technique.

Technique	No. of patients	No. with failed diagnostic assessment	Proportion	95% CI
Clinical diagnosis failure[8,15,16,20,24,25,28,30–32,37,40,45,51]	1488	381	26	24–28
Electrophysiological diagnosis failure[12,14,26,27,36–39,41–43,45–47,49–51]	742	17	2	1–4

Note: CI, confidence interval.

technique. The significant difference in incidence found between the groups diagnosed with a clinical technique compared to an electrophysiological technique may be explained by the techniques themselves (a lack of concordance between clinical and electrophysiological findings[37,51]) and/or by other methodological differences; differing rates of successful completion of testing, variation in the frequency of assessments, the timing of the diagnosis and study population heterogeneity. We did not find a detectable difference in study quality between the clinical and electrophysiological technique groups to explain the difference.

This review found that there was a significant difference in the proportions of patients unable to complete clinical assessment (26%, 95% CI 24–28%) compared to electrophysiological assessment (2%, 95% CI 1–4%). The major cause of this was a lack of patient compliance with clinical assessment. Patients unable to comply with clinical assessment tend to have a higher mortality rate[15,16,20,28] and potentially have greater encephalopathy, both of which are associated with increased incidences of ICUAW.[14,20,23,42,51] The lower incidence of ICUAW in the group diagnosed on clinical assessment is likely to be explained in part by higher rates of incomplete testing.

The strengths of this review include the detailed literature search, the systematic evaluation of included studies with an objective assessment tool and the inclusion of studies utilising the full range of recognised diagnostic techniques. There are limitations to this review. This review was largely the work of a single reviewer with the risk of introducing bias both in the selection of studies to include and in the assessment of included studies. To minimise this risk, clear criteria were set for each domain on the study appraisal form which were used both to assess eligibility for the review and to appraise the quality of the study.

The tool we used to grade the evidence was a modification of the NOS[33] with additional criteria recommended by Altman.[34] The rating scale was modified after a pilot run because the NOS was felt not to adequately discriminate between the different qualities of studies. This is therefore a new tool that is unvalidated and may not have appropriately graded all of the studies. The modified scale did however provide an objective assessment tool that appeared to be appropriate for the majority of the studies.

Conclusion

This systematic review has provided a comprehensive update to those done previously and found that the ICUAW syndromes are common (40%) in the groups of ICU patients requiring more than approximately a week of mechanical ventilation. The incidence of ICUAW varies with the diagnostic technique used, being lower with clinical compared to electrophysiological techniques. Approximately a quarter of patients will not be able to comply with clinical evaluation and this may be responsible for underreporting of this condition. Further research is required to validate the 2009 consensus diagnostic criteria and to identify the optimal method and time point for identifying this problem to then allow interventions to be evaluated and introduced.

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