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Variation in definition of prolonged mechanical ventilation

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TITLE

Variation in definition of prolonged mechanical ventilation

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LR, BB, MS, DM conceived of the study idea and developed the study protocol. All authors have contributed to data collection, data analysis and report writing.

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The authors have no competing interests to declare.

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OUTLINE

Introduction

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ABSTRACT

Consistency of definitional criteria for terminology applied to describe patient cohorts receiving mechanical ventilation within intensive care unit and post-acute care settings is important for understanding prevalence, risk stratification, effectiveness of interventions, and projections for resource allocation. Our objective was to quantify application and definition of terms for prolonged mechanical ventilation. We conducted a scoping review of studies (all designs except single case study) reporting a study population (adult and paediatric) using the term prolonged mechanical ventilation or synonym. We screened 5331 references, reviewed 539 full text references and excluded 120. Of the 419 studies (representing 38 countries) meeting inclusion criteria, 297 (71%) reported data on a heterogeneous patient cohort, 66 (16%) studies included surgical patients only (46/66, 70% cardiac surgery). Other studies described chronic obstructive pulmonary disease (16, 4%), trauma (22, 5%), neuromuscular (17, 4%), and sepsis (1, 0.2%) cohorts. A total of 741 terms were used to refer to the 419 study cohorts. Most common terms were: prolonged mechanical ventilation (253, 60%), admission to specialized unit (107, 26%), and long-term mechanical ventilation (79, 19%). Some authors (282, 67%) defined their cohorts based on duration of mechanical ventilation with 154 (55%) using this as the sole criterion. We identified 37 different durations of ventilation ranging from 5 hours to 1 year with more than 21 days being the most common (28/282, 7%). For studies describing a surgical cohort, minimum ventilation duration required for inclusion was greater ≥ 24 hours for 20/66 (30%) studies. More than half (237, 57%) did not provide a reason/rationale for definitional criteria used, with only 28 (7%) studies referring to a consensus definition.

We conclude that substantial variation exists in the terminology and definitional criteria for cohorts of patients receiving prolonged mechanical ventilation. Standardization of terminology and definitional criteria is required for study data to be maximally informative.

ABSTRACT WORD COUNT: 300

KEY WORDS: prolonged mechanical ventilation; intensive care; chronic critical illness; long term mechanical ventilation; scoping review

INTRODUCTION

Better understanding of the relationship between the duration of mechanical ventilation and important patient outcomes such as weaning success and mortality may be useful to guide discussions of prognosis with patients and their families, facilitate clinical decision making, and to set goals of care ^{1,2}. Many studies have attempted to identify predictors of prolonged mechanical ventilation (PMV) ³⁻⁵ as well as development of mortality risk prediction models for patients requiring 21 ⁶ and 14 days of mechanical ventilation ⁷. Understanding predictors of PMV and outcomes of these patients may allow risk stratification enabling targeted and pre-emptive interventions designed to reduce risk. An understanding of projected PMV prevalence can be used to guide decisions related to resource allocation by organizations and healthcare systems.

Although a 2005 consensus conference led by the National Association for Medical Direction of Respiratory Care (NAMDRC) defined PMV as mechanical ventilation for 21 consecutive days or more, for at least 6 hours a day, of invasive (via endotracheal tube or tracheostomy) and/or non-invasive (facial/nasal interface) methods of delivery ⁸, variable definitions have been used by study authors. Furthermore, studies using different definitional criteria may be used to summarize prevalence and outcomes ⁹. For example a commonly cited administrative database study of the predicted prevalence of PMV in the United States (US) used a definition of ≥ 96 hours ¹⁰ as this corresponds to the ICD code 96.72 and therefore is easily identified within these databases. These authors refer to the study cohort as requiring prolonged acute mechanical ventilation (PAMV). Meanwhile, other US studies reporting prevalence and outcomes use other definitions to describe PMV ^{6,11}. Variable and inconsistent

definitions results in widely variable estimates of PMV prevalence, inconsistent identification of independent predictors for its occurrence, differences in estimates of treatment effects, and inaccurate estimation of patient outcomes to inform prognosis discussions and decisions to continue life sustaining therapy. Furthermore, variable and inconsistent reporting limits comparisons across studies and precludes pooling of data for meta-analyses ¹².

To answer the NAMDRG 2005 ⁸ call for further research to better understand which definitions of PMV are commonly used, to raise awareness related to definitional inconsistency among clinicians, researchers, and other key stakeholders, and to drive consensus for a standardized definition for PMV, we conducted a scoping review to quantify how PMV and its synonyms are defined in the literature.

REVIEW METHODS

We included studies that described the study population (adult and paediatric) using terms such as prolonged mechanical ventilation, prolonged ventilation, prolonged invasive ventilation, prolonged wean, or difficult to wean in the manuscript title or abstract or described a study population admitted to a specialized weaning facility, long term acute care (LTAC) hospital or respiratory unit and receiving mechanical ventilation. Search terms were developed in consultation with an experienced information specialist. We included all study designs including observational studies, randomized controlled trials, before and after studies, database studies, surveys, and qualitative studies. We excluded studies describing a long-term mechanical ventilation population defined as patients with minimal to zero expectation of weaning as we anticipated these patients would be receiving care in a long-term care facility

and thus not representative of patients receiving ventilation in an acute care setting. We also excluded studies describing patient cohorts receiving mechanical ventilation at home. We excluded single case reports, commentaries, editorials, reviews, and opinion papers, and for pragmatic reasons studies reported in languages other than English.

We searched the following electronic databases from 1980 to March 2013: Cochrane Central Register of Controlled Trials (CENTRAL), Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Latin American and Caribbean Health Sciences Literature (LILACS), and the Web of Science and Conference Proceedings.

Using a pre-designed screening tool, two authors (LR/MM) independently examined study titles and abstracts to identify eligible studies. Full text articles considered potentially relevant by either author were obtained and examined for eligibility. Disagreements were resolved through third author (DM) discussion. Two authors in pairs independently extracted study data using a standardized form, all data extraction was checked for accuracy by a third author (LR). We extracted data on the country(ies) where the study was performed, type of care venue, age range and diagnostic categories of patients, terms used to describe the cohort, definitional criteria for the terms used, and reasons provided for the definitional criteria used. We also extracted reported outcomes to examine types and variability in studies of this patient population. Data extractors were not blinded to study citations.

We generated summary tables reporting counts and proportions of study and cohort characteristics, terms used to describe the cohort, definitional criteria and study outcomes. Descriptive statistics were generated using SPSS Version 23 (Armonk, NY).

STUDY CHARACTERISTICS

We screened 5331 references and identified 539 references for full text review. We excluded 120 references for reasons shown in Figure 1. Of the 419 studies that met our inclusion criteria, 363 (86.6%) were conducted in a single care venue type (most commonly ICU), 30 (7.2%) in multiple care venue types, 18 (4.3%) were database studies and 9 (2.1%) were surveys (Table 1). Of the 419 studies, 366 (87.4%) included adults only, 41 (9.8%) paediatric only, 10 (2.4%) adults and paediatric, and 2 (0.5%) studies reported data on paediatric and neonates. Studies represented cohorts from 38 countries most commonly the US (187, 44%). Most (297, 70.9%) studies reported data on heterogeneous patient cohorts, 66 (15.8%) studies reported data on surgical patients only (46/66, 69.7% cardiac surgery). Other studies described patients with chronic obstructive pulmonary disease (COPD) (16, 3.8%); trauma including burns, spinal cord injury and acute brain injury (22, 5.3%); neuromuscular disorders (17, 4.1%); and sepsis (1, 0.2%) cohorts.

DEFINITIONS OF PROLONGED MECHANICAL VENTILATION

A total of 741 terms were used to refer to the 419 study cohorts. The most common terms used were: PMV (253, 60.4%), admission to a specialized unit (107, 25.5%), and long term mechanical ventilation (LTMV) (79, 18.9%); chronic critical illness (CCI) was a term used by 33

(4.5%) studies (Table 2). The proportion of studies using the terms PMV and LTMV were similar in adult only and paediatric only studies. No paediatric cohorts were defined using the term CCI and only 2 (2.8%) were defined based on unit admission criteria. Table 3 demonstrates that the top 5 terms, PMV, unit admission criteria, LTMV, tracheostomy and ventilator dependence remained consistent over time, although use of the terms LTMV and ventilator dependence decline after 2003 and 1999 respectively. Most studies (282/419, 67.3%) used the duration of mechanical ventilation as one of their definitional criteria with over half of these studies (154/282, 54.6%) using this as the only defining criterion. Of the 253 studies using the term PMV to describe their cohort, 182 (71.9%) included the duration of mechanical ventilation as a definitional criterion. In total, we identified 37 different durations of ventilation. This variability remained (range ≥ 72 hours to > 3 months) when including only multi-centre studies of >5 units, database, or survey studies. Of the 419 studies, 53 (12.6%) used ≥ 21 days to 1 month; 39 (15.4%) of those using the term PMV to describe the cohort (Table 3). The NAMDRRC recommended criterion of ≥ 21 days was used by only 12 (2.9%) studies; 7 after 2005 and 5 before. Use of ≥ 21 days to 1 month was most common in studies from Asia (18/60, 30%), in particular Taiwan (15/32, 46.9%) and least common in studies from the UK and Europe (6/121, 5%). For studies describing surgical cohorts, 20/66 (30.3%) required a minimum duration of ventilation of 24 hours or more for inclusion in the cohort with ≥ 15 days being the maximum duration used by a study for participant inclusion. Other commonly used definitional criteria for PMV cohorts were presence of a tracheostomy (81 studies, 19.4%), admission to a specialized unit (61 studies, 14.6%), and failure to wean (32 studies, 7.7%) (Table 5).

Rationales for cohort terms

Of the 419 studies, 237 (56.6%) gave no reason or rationale for the cohort term or the definitional criteria selected; 97 (23.2%) studies indicated it was specific to the admission criteria of the participating unit(s). Only 28 (6.7%) studies referred to a consensus definition despite 185 (44%) of included studies being published after the 2005 NAMDRC consensus definition. A further 27 (6.4%) referred to criteria associated with Diagnosis Related Groupings (DRG), International Classification of Diseases (ICD) or other local database coding. Eleven (2.6%) studies cited clinical relevance or because of local practices. Other rationales included use in previous studies (8, 1.9%), the median duration of ventilation of the study cohort (5, 1.2%), and as an indicator of transition from acute to chronic care (4, 0.9%) (2 studies reported miscellaneous reasons).

REPORTED OUTCOMES

There were 28 distinct outcomes reported by 5 or more studies. The most commonly reported study outcomes were length of stay (258, 61.6%), mortality (228, 54.4%), duration of mechanical ventilation (142, 33.9%) (Table 6). The rate of weaning and/or extubation success was a reported outcome in 119 (28.4%) studies and was variably defined as more than 6 hours (1, 0.8%), 24 hours (9, 7.6%), 48 hours (20, 16.8%), 72 hours (5, 4.2%), 5 days (1, 0.8%), 7 days (18, 15.1%), 14 days (1, 0.8%), or 28 days (1, 0.8%) of spontaneous breathing without mechanical ventilation. A further 26 (21.8%) studies considered successful weaning as spontaneous breathing without mechanical ventilation at unit or hospital discharge (31, 26.1% studies did not provide a definition). However, no study reported on the number of days or

hours between discontinuation and discharge. Only 8 (6.7%) studies commented on inclusion or exclusion of non-invasive ventilation after discontinuation of invasive support.

CRITIQUE

In this scoping review, we identified substantial variation in the application and definition of terms *a priori* hypothesized to describe mechanically ventilated patients no longer in the acute phase of mechanical ventilation. Duration of mechanical ventilation was a common defining criterion however there was lack of agreement across included studies as to the number of consecutive days (or hours) that patients should require mechanical ventilation to meet cohort inclusion criteria. More than half of the included studies did not provide a rationale for their chosen definitional criteria of cohort terms used; meaning the reasoning behind selection of these terms and their criteria was unclear. Inclusion of a large number of studies with heterogeneous study designs and study objectives resulted in identification of numerous reported study outcomes. Additionally, we identified variability in the criteria used to define weaning and/or extubation success, specifically the duration of monitoring subsequent to liberation from mechanical ventilation during which the patient did not require further invasive or noninvasive support.

Some of the identified heterogeneity in the duration of ventilation used as definitional criteria for patient cohorts may be due to characteristics of the study region. For example, use of ≥ 21 days was most common in Asian countries, particularly Taiwan where this criterion is used to step patients down to a lower level of care¹³. Twenty-one days is also used as a trigger

for transfer to an LTAC in the US ¹⁴, however only 17 LTAC studies from 187 US studies were identified in this review. The duration of mechanical ventilation used as a defining criterion was also influenced by inclusion of surgical only versus a mixed study population. The longest duration used in studies of surgical patients was ≥ 15 days compared to a maximum of over one year in heterogeneous cohorts. Furthermore, inclusion of studies using various data sources (direct observation versus administrative databases) may have generated heterogeneity. Data collection from administrative database requires use of codes, such as the International Classification of Disease code 96.72 indicative of ≥ 96 hours of mechanical ventilation, to identify a patient population whereas prospective studies can use any criteria considered appropriate by the investigator team.

There is little doubt that there is a distinct cohort of relatively low volume, high cost, and poor outcome patients requiring mechanical ventilation for longer than the average ICU patient ¹⁵⁻¹⁹. In 1989, Wagner and colleagues identified 6% of a cohort of nearly 4,000 ICU patients were ventilated for seven days or more and consumed 37% of ICU costs ²⁰ suggesting this is not necessarily a new phenomenon solely due to advances in technology or worsening population comorbidity. However, our data suggest we are far from understanding if study cohorts are referring to similar patient phenotypes within or across studies or from establishing consensus on how to define this cohort. Using terms such as chronic or persistent critical illness, several studies have documented a syndrome of persistent organ dysfunction characterized by profound weakness and extreme symptom burden ²¹. Such terms may have merit when trying to distinguish patient cohorts within the spectrum of critically illness; however, whilst also suffering from lack of consensus, some authors believe this term

encompasses patients without concomitant prolonged need for mechanical ventilation. Conversely, patients such as those with established neuromuscular disease may require prolonged to indefinite mechanical ventilation and not meet other definitional requirements of CCI ²².

Lack of consistency as to the number of consecutive days (or hours for surgical patients) used as definitional criteria suggest this may be a rather arbitrary marker and may not be the best criterion to identify transition from acute to PMV and concomitant review of goals of care. Indeed, using Delphi methods and a 38 member expert panel to establish the criteria that should define the transition from acute to PMV, our group recently identified that the number of consecutive days of mechanical ventilation was one of six (out of 20) defining criteria that did not gain consensus ²³. Preferred criteria were: patient stability from a physiological perspective; repeated unsuccessful attempts at weaning; and the patient's wishes to remain ventilated. These criteria reflect transition from the acute phase of critical illness and an estimation of weaning difficulty as reflected in the simple, difficult, and prolonged weaning classifications proposed in 2007 ²⁴. These weaning classifications may be more useful than terms such as PMV not only because they incorporate an element of weaning difficulty but also because they provide an objective marker that weaning attempts have been commenced. What is missing from these classifications warranting further consideration is when to classify a patient as unweanable.

We found that definition of the time period in which determination of weaning and/or extubation success occurred was highly variable, ranging from 6 hours to 28 days. The NAMDRRC definition suggests PMV patients should only be considered successfully weaned when able to

maintain spontaneous breathing without invasive or non-invasive ventilatory support for a minimum of seven days⁸. Rationales for monitoring over seven days for the need to re-establish mechanical ventilation included the potential for slower recovery of the respiratory system and the likelihood of more chronic comorbidities in this patient population. Additionally, some authors have suggested that the need for reestablishment of mechanical ventilation after three days is most likely due to a new or unrelated process²⁵. However, from a patient and healthcare system provider perspective, no further requirement for mechanical ventilation enabling discharge from the admitting unit is a more useful definition of weaning and/or extubation success as it demonstrates recovery and the ability to transition to a lower acuity and therefore lower cost care location.

Few studies included in this scoping review commented on the inclusion of non-invasive ventilation after discontinuation of invasive support when defining weaning success. The role of non-invasive ventilation is an important element for consideration for this definition²⁴, particularly in view of increased utilization in recent years²⁶. A Cochrane systematic review found use of non-invasive ventilation as a weaning strategy to enable extubation for patients with the potential to wean, but not yet able to tolerate mechanical ventilation discontinuation, demonstrated decreased weaning failure, mortality, ventilator associated pneumonia, ventilation duration, and ICU length of stay compared to weaning strategies that did not include non-invasive ventilation²⁷. Failure to consider the use of non-invasive ventilation after extubation when pooling data from studies that do or do not use an early extubation to non-invasive ventilation approach will produce inaccurate estimates of weaning success.

We identified 39 distinct study outcomes reported by three or more included studies with length of stay, mortality, and mechanical ventilation duration described by over one third of studies. Previously, our group has identified substantial variation in the selection and definition of outcomes among trials of interventions hypothesized to influence mechanical ventilation duration²⁸. Initiatives such as the Core Outcome Measures in Effectiveness Trials (COMET) group aim to facilitate development and application of agreed standardized sets of outcomes, referred to as core outcome sets²⁹. Numerous critical care professional societies have called for standardization in the reporting of study endpoints and a standard set of outcome measures with several core outcome set development projects related to critical care underway³⁰. However such initiatives are relatively recent. Our data can be used to inform such a project to inform studies of patients experiencing PMV. Without strategies to gain consensus, known variation in the selection and measurement of outcomes of studies recruiting mechanically ventilated patients combined with variation in patient cohort definitions as identified in this scoping review will continue to drive inconsistency and limit interpretation of study findings.

Classification of homogeneous cohorts of mechanically ventilated patients experiencing critical illness using clear definitional criteria is important. Prognostication, care goal setting, implementation of effective therapies, or conversely conversations around limitation of therapy may be limited due to a failure or delay in recognizing patient transition from acute to PMV²³,³¹. Additionally, clear definitions are required for successful conduct of further research, including enrolment of patients with a similar phenotype into clinical trials, epidemiological studies, and meta-analyses^{32,33}. Our data suggest further consensus work is required to classify

these cohorts considering defining features in addition to the duration of mechanical ventilation. Such consensus work is likely to result in a set of terms as opposed to a single term to describe the patient spectrum.

Strengths and Limitations

To our knowledge this is the first scoping review to use rigorous and *a priori* developed methods to systematically quantify cohort terms and their definitional criteria hypothesized to describe patients no longer in the acute phase of mechanical ventilation. Our scoping review has the following limitations. First, our search only extends to March 2013 and therefore may not reflect terms and definitions in most recent publications. However, we included over 400 studies and did not detect a demonstrable shift in terms used and their definitions over time, particularly after publication of the 2005 NAMDRG definition⁸. We therefore believe expanding the search to 2016 would not substantially influence our results and conclusions. Second, for pragmatic reasons we limited our inclusion criteria to studies published in English meaning our findings may not reflect the use of cohort terms in studies published in other languages.

SUMMARY

We identified substantial variation exists in the terminology and definitional criteria for cohorts of patients receiving mechanical ventilation as well as reported study outcomes. Few studies provided a rationale for selection of cohort terms and their definitional criteria making it difficult to draw conclusions as to the reasons for this substantial variation. Standardization of terminology and definitional criteria is required for study data to be maximally informative for clinical decision making and future research.

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FIGURE 1 LEGEND

Prisma diagram of scoping review search.