Tracheostomy in motor neuron disease

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Abstract

Tracheostomy-associated ventilation for the respiratory insufficiency caused by amyotrophic lateral sclerosis (motor neuron disease, MND) is a complex issue with practical, ethical and economic dimensions. This article considers the current prevalence of tracheostomy in MND, the evidence for its benefit in terms of both survival and quality of life, and the practicalities of implementation. The decision to request invasive ventilatory support is among the most challenging for those living with MND. Neurologists should be prepared to discuss this option in an open and objective way, and we suggest a framework for discussion, including the issue of withdrawal of therapy.

Introduction

Motor neuron disease (MND), synonymous with amyotrophic lateral sclerosis (ALS), is a severely life-shortening neurodegenerative disorder in which a complex series of genetic and environmental factors result in progressive loss of motor neurons from the spinal cord, brainstem and motor cortex (1). There is clinical, histopathological and genetic overlap with behavioural variant frontotemporal dementia (FTD). The majority of MND cases appear to be sporadic, but genetic variants account for up to 15% of cases, the commonest of which is a hexanucleotide expansion in *C9orf72*, associated with nearly 10% of all ALS and 15% of all FTD (2).

The essential clinical feature of MND is progressive loss of skeletal muscle strength, with death, usually due to ventilatory insufficiency, a median of 30 months from symptom onset. The pathway for those living with a diagnosis of MND involves multiple difficult decisions which have to be considered in the context of relentless loss of limb and bulbar function, where intervention to prolong life does not stop or slow the decline in physical independence (3). Invasive and permanent ventilatory support is one such intervention. This review considers the current use of tracheostomy ventilation (TV), the evidence for benefit in MND, the practicalities of its implementation and withdrawal, and offers a framework for professionals to help individuals living with MND to make an informed decision on its application to their care.

The cause of death in MND

In counselling those living with MND, a frequent issue which arises and acts to reinforce the motivation to undergo tracheostomy is the perception of the mode of death as sudden and unpleasant. Due to the diversity of care in the palliative phase of MND, and the overwhelming wish of most individuals to die at home, it is difficult to objectively establish the cause of death in most cases, and there are very few systematic and unbiased studies in population-based cohorts. It is generally assumed that the majority of those with MND die of respiratory failure, with or without superadded respiratory infection. However, it is the common experience of MND specialists that a proportion of people who, based on disability scales such as the ALS Functional Rating Score (ALSFRS) and forced vital capacity (FVC) measures would normally be predicted to live for a period of months, in fact die unexpectedly and abruptly.

A French study of 302 individuals (estimated to be 70% of all deaths expected from MND in the study population, so with caveats) found that 77% died of respiratory complications of MND (the majority were recorded as 'terminal respiratory failure', with some cases coded as bronchopneumonia) (4). A smaller proportion of deaths were recorded as due to pulmonary embolism, cardiac dysrhythmia, head injury or suicide (2% or less in each case), with less than 1% due to medical conditions considered to be unrelated to MND. In 13% of cases the cause of death was undetermined. Typical ALSFRS scores at death were 15-17 (range of 9-28), which means that most were in a profound state of disability at the time of death. Studies from Italy and Germany report similar data, but with the additional information that

6-12% died suddenly (5, 6). A *post mortem* study in 100 individuals may contain biases, as these were people admitted to hospital care having undergone a precipitous decline (7). This may explain the finding of a significant rate of pulmonary embolism (6%, mostly affecting spinal-onset individuals with lower limb paralysis), as a likely contributor to the cause of death, and also a significant incidence (10%) of clinically relevant heart failure as a terminal event. Other factors which are plausible triggers of sudden unexpected death, but for which there is currently no clear evidence, might include cardiac dysrhythmia, or loss of brainstem respiratory reflex control (eg; from neuronal loss in the pre-Botzinger nucleus) (8, 9). It should be noted that asphyxiation through 'choking', a very common focus of anxiety for those living with MND, was exceptionally rare in these studies.

An important question is whether more intensive supportive treatment, NIV and enteral feeding, as well as tracheostomy, might change the mode of death in MND. Longer term studies will be needed to definitively provide an answer, but a recent *post mortem* study indicated that in those using NIV, bronchopneumonia was significantly more frequent compared to the non-NIV group (10).

Prevalence of tracheostomy in MND

There are marked geographical differences in the prevalence of TV, even between countries of similar economic standing with near-identical diagnostic criteria and general disease management for MND. A review by Takei highlights some of this variation, albeit with the source articles not primarily focusing on prevalence of ventilatory support (**Table 1**, summarised from (11)). It has been highlighted that the neurologist's preference, caregivers attitudes and presence or absence of advanced planning may influence a patient's choice to have a tracheostomy (12), and it is possible that this varies even between states of the US or Countries within Europe. Models of care funding may contribute to this variation, but additional factors are likely to be relevant, for example in Japan where concern has been raised about the fear of legal action in shaping physician behaviour around end of life care (13). The increasing use of non-invasive ventilation (NIV) in Europe has been driven by guidelines which emphasise the importance of maintaining the individual's ability to communicate, and their autonomy, for example the NICE Quality Standard on motor neurone disease (14) and European guidelines (EFNS guidelines (15). From the financial perspective, in Japan, the cost of TV is fully covered by the government and medical insurance, and universal long-term care insurance was introduced in 2000 (16). In contrast, securing funding for the additional care to provide for the more complex needs of an individual on TV is a significant source of delayed discharge in the UK NHS model, and other countries where funding is not readily available.

It is perhaps not surprising that in countries where TV is much less common than in Japan, the majority of tracheostomies are inserted as an emergency, for example 30/ 38 (79%) in one survey from four UK centres, with 76% of these being related to

acute illness requiring intubation (unpublished abstract (17)). Of those undergoing elective tracheostomy two thirds were male, three quarters wanted to live as long as possible or were struggling with continuous use of the NIV interface, and all lived with a partner or parent.

Patterns of ventilatory support provided to those with respiratory insufficiency due to MND in Japan have changed with time (**Figure**).

In a Japanese series, the proportion of those living with MND undergoing TV has not changed substantially (28% and 33% respectively) but, whereas in the early years NIV use was infrequent (5%), it has become increasingly common over time (one third overall, with half of these going on to receive TV in due course) (16). As a consequence, fewer individuals received no ventilation at all (two thirds versus one third respectively). This change in practice has been attributed to publication of studies demonstrating the efficacy of NIV in terms of survival (18), and quality of life (18, 19), in association with its increasing availability and tolerability.

It has consistently been shown that transition to TV from NIV is much commoner in men than women (16, 20, 21). For example, in one cohort of 20, the ratio was 17 males:3 female in those transitioning, versus 19:20 in those simply continuing with NIV (16). This difference may reflect a greater willingness of men to undergo invasive life-prolonging treatments. The presence of a caregiving spouse or partner may make the individual living with MND who is considering a tracheostomy more willing to accept this invasive procedure. Those who are married were more than twice as likely to proceed to a tracheostomy and to have a longer survival after the

procedure (22, 23), although marital status is itself an independent predictor of survival in MND in multivariate analyses.

Differences in the clinical pattern of disease between men and women may also be relevant, with men being over-represented in younger-onset, lower motor neuron-predominant MND, which has an intrinsically slower progression and better prognosis (24, 25), and often earlier respiratory muscle involvement. The probability of transitioning to TV reduces the longer individuals have been on NIV (16). Those who have used NIV for a longer period may have more successfully accommodated to ventilatory support, and therefore the issue of invasive ventilation loses its immediacy. Although, they may have accumulated greater physical limitation, and therefore be reticent about escalating treatment, it is also likely that individuals who can tolerate long term NIV also have different disease characteristics, though this is difficult to prove with small and highly selective studies. There is also a trend for those transitioning to TV to be slightly younger (65 versus 68) (16).

Evidence of benefit of tracheostomy in MND

In order to make an informed decision about TV the potential risks and benefits have to be considered. There is no high-quality evidence to support the challenging discussions that take place when people living with MND raise the issue. It is important for healthcare practitioners to approach the conversation in an objective and value-free manner. Existing evidence can form part of the discussion as long as the limitations are acknowledged, including the impossibility of inferring direct causation about survival and quality of life in the absence of a controlled trial, and the considerable biases inherent in retrospective cohorts and anecdotal reports. Cases described of those who intended to have TV but then opted not to and went on to have prolonged survival with NIV alone of 5 years, underline the uncertainty about choosing TV on the basis of an effect in increasing survival (26). Accepting these limitations, a number of reports indicate survival in MND with TV of up to 74 months (23, 26-33), with a number indicating individuals with TV had better survival than those receiving NIV alone. The decision to have elective TV and indeed survival were influenced by the age of the individual, presence of a spouse, and the presence of enteral feeding. Interesting observations include the absence of a survival benefit in the older population (over 60 years). If one accepts that TV affects survival, potential mechanisms in addition to the obvious effect of replacing the work of breathing using pressure support, include improving gas exchange, lung compliance and secretion management. TV aftercare typically requires the availability 24 hours a day of highly trained personnel, whether in a managed care facility or at home. The increased level of specialist care may in itself play a major role in the reported survival benefit. Median survival after tracheostomy in an Italian 10-year study was 253 days (one quarter survived 3 years, and 10% survived 5 years)

with lower mortality in those followed at MND specialized multidisciplinary centres (23).

Personality type may be a strong driver for survival, and it is often those with a desire to live at any cost, with an energetic drive to exert control of all aspects of MND that have elective TV (34). However, the lack of systematic data on outcomes in TV, make it difficult to draw any firm conclusions, particularly since much of the data that exists relates to those who have undergone unplanned TV in respiratory crisis (35). Furthermore, those living with MND frequently change their mind about interventions or defer decisions. A major factor which appears to colour the attitude of physicians to TV in MND is the perception that it will have a negative effect on quality of life, particularly if an individual loses the ability to communicate and has profound physical impairments. Predictably, there is no high-quality evidence to draw upon, and such studies as exist are by definition carried out retrospectively in the highly selected group in whom TV has been carried out and are unlikely to be generalizable. In a small German study quality of life was assessed using questionnaires in those with TV (n=21) and their carers (n=20) (36). Approximately 80% of those with TV indicated they would choose ventilation again and would advise others to do the same. Similar findings were seen in two Italian cohorts (28, 37). A common theme in these studies was the identification of high levels of stress and burden on the carers, with 30% of the TV caregivers rating their own overall quality of life lower than that of their loved one.

Finally, a key area for future study is the effect on efficacy of TV (as well as NIV) of the balance of clinical upper versus lower motor neuron involvement in the individual living with MND. Anecdotally, those with lower motor neuron-

predominant phenotypes, those with respiratory-onset to symptoms and those with slowly-progressive disease may benefit most from TV, but this issue needs to be objectively delineated.

Logistics of tracheostomy in MND

Disease progression and transition to TV is accompanied by an increase in dependence on mechanical ventilation to prevent rapid death from respiratory failure. Individuals living with MND are dependent not only on the ventilator but a team of carers, formal and informal, who work closely with expert clinical and technological professionals to ensure that the risks attached to ventilator malfunction, power failure, mucus plugging, tube displacement, etc. are managed in a timely and appropriate way to prevent permanent harm.

In Europe, recent studies show between 62% and 86% (17, 37) of those who had tracheostomy ventilation in MND were discharged to their own home. Twenty-four-hour ventilation in a domiciliary setting can be associated with significant carer burden, depression and burnout (28, 37). Therefore, those living with MND and their families require appropriate information to enable informed decision-making related to the final destination. Engagement of all stakeholders necessitates frequent multidisciplinary meetings with the individual living with MND or their relative present throughout the hospital stay, particularly during the planning stages of, and directly before, discharge.

In the UK the majority of care at home for those with TV in MND is undertaken by trained carers rather than registered nurses (mean 22 versus 2 hours respectively (17)). The situation in Europe is similar. In the USA those with TV must have care provided by more expensive licensed practical nurses or registered nurses. Placement in a formal care setting does not always mitigate the risk, with a number

of serious incidents involving ventilator-dependent individuals being reported over the past decade (38, 39).

Wherever the final destination or professional level of the primary carer, risk can only be managed through the provision of an appropriate team of formal care givers who are trained to a suitable level of competence to provide safe and effective care at home. Such packages are costly and can be extremely difficult to arrange and maintain. A 1:1 24-hour care package in the UK costs in the region of £180-200k per annum. In the USA a 16.5-hour package provided by licensed practical or registered nurses for those with tracheostomy has been costed at $270k (40).

Accessing funds via local continuing health care funding panels in the UK and insurance companies in other countries, together with recruitment and training of carers and safe discharge preparation can all be fraught with logistical difficulties and delays. Mean length of stay in the UK is 18 weeks post-emergency tracheostomy for MND (17). In some cases, funding can be authorised within a few weeks and in the case of elective procedures could be sanctioned before admission. In one Spanish centre the mean time to discharge from the respiratory care unit was just 27 days (29). Prolonged hospital stays lead to increasing burdens and frustrations for those living with MND, families and the institution. These are exacerbated by the lack of control that the individual and professionals have in expediting discharge.

Financing the care package, however, does not mean that discharge is imminent. In the UK, a shortage of health care workers and the need for the necessary pre-employment checks causes delays sometimes of many weeks in recruitment to care agencies or, if using a personal care budget, directly to the care team. Once

appointed the 8 or so carers required to provide 24-hour care, 7 days per week need to be trained to safely manage the ventilator-dependent individual, provide tracheostomy care, along with effective and safe augmented cough technique. In addition, there are other training and equipment needs which can hamper discharge. Enteral feeding, positioning and manual handling all need to be addressed to effectively manage risk upon discharge. At times recruited carers are tracheostomy, ventilation and even MND naïve and drop out can be high; others require many hours of working with the individual in hospital to achieve the required level of competence and confidence to provide safe management without supervision in their own home.

Uncuffed TV tubes mean the individual remains at considerable risk of developing aspiration and bronchopneumonia. The ability to provide adequate suction mitigates this to some extent but nonetheless, a significant proportion of those with uncuffed TV will succumb to the development of aspiration bronchopneumonia and are at risk of sudden death from respiratory or cardiac strain and insufficiency. The majority (80%) of MND TV individuals receive a cuffed tube (UK audit by JP - unpublished). While the use of a subglottic tube might allow safer deflation the purposes of speaking, many living with MND have severe dysarthria at this stage anyway. An initially cuffed tracheostomy tube is usual in those admitted with acute respiratory failure. In that setting, some individuals diagnosed with MND may be able to be weaned completely or moved to NIV, but this is less likely in those with significant bulbar dysfunction.

Withdrawal of tracheostomy in MND

It is profoundly important that clinicians discuss with individuals their wishes concerning future care as their MND progresses, especially in anticipation of the loss of the ability to communicate. For those with planned TV this should be a facet of the informed consent discussions. Advance care planning is not a single event and individuals will value their views and thoughts about the future being revisited as a standard part of their care as their situation evolves (41, 42). Individual preferences may change over time and discussion enables a more considered view concerning assisted ventilation and resuscitation to be developed. It is very important that those living with MND and their families are aware that there is a choice about treatment and that they may change their mind.

In most, but not all, countries it is entirely legal for an individual to ask that their TV be stopped. The UK General Medical Council has clarified for doctors that such a request by an individual with capacity must be honoured in exactly the same way as it is for PEG and NIV. The MND Association provides excellent information about TV and considerations of choice in future care. Some may wish to document their wishes in relation to withdrawal of ventilatory support by completing paperwork that is of legal standing such as an Advance Decision to Refuse Treatment (ADRT) or appoint an attorney to make decisions on their behalf should they lose the ability to communicate their wishes (or mental capacity). All discussions should be documented and shared across the professionals and services caring for the individual living with MND. These discussions may usefully be formalised in an advance statement of wishes and noted in treatment escalation plans such as the ReSPECT template recently introduced in England. These discussions need to

consider the possibility of sudden, unexpected respiratory events so that attending staff aware of management decisions. The Association for Palliative Medicine of Great Britain and Ireland (APM) have developed clinical guidance to support best practice in withdrawing assisted ventilation (**Table 2**).

The withdrawal of assisted ventilation may lead rapidly to breathlessness and distress and effective management of these expected symptoms is a professional responsibility described in UK case law (e.g. R v Adams 1957, Crim LR 365; House of Lords debate re: Annie Lindsell, Hansard HL 721-724, Nov 20 1997), and is similar to the anticipatory and ongoing symptom management required for painful procedures and operations. This is a challenging area of practice for many clinicians, as it is rare and often raises practical and ethical concerns (43, 44). Involvement of palliative care is crucial. Preparation of the person living with MND, the family and the professional team is a key part of a safe and successful outcome. All parties need assurance about the ethics and legality. Professionals especially and occasionally family members can be concerned that this is assisted suicide or euthanasia. This has been discussed in the context of an ADRT for discontinuation of ventilation for an individual living with MND when they became unable to communicate (45).

The process may take several hours, and the team needs to plan adequately for this and prepare the family with information that, although the individual will probably die within 15 minutes after the ventilation has been withdrawn, some have more respiratory reserve than anticipated and live longer (several days in exceptional circumstances). Symptoms require an individualised approach, with titration of a combination of an opioid and benzodiazepine (and occasionally additional drugs) to an adequate level of sedation before the TV is removed. The effectiveness of the

symptom management should be assessed and adjusted by trial removal of the ventilation or reduced ventilation settings before complete removal. Both the subcutaneous and the intravenous routes for drug administration have proved effective. Although the former may require more time for the required level of sedation to be reached it will be more aligned to the practices of palliative and end of life care and may be more feasible especially in the home and care home situations.

Single centre case series in a Danish home ventilation service and German neurology service have been published (46, 47). There is less experience of withdrawal of TV in MND in the UK since it is much less commonly used but the body of experience is systematically being documented through prospective evaluation (48). Most of the expertise in undertaking the withdrawal in the UK is vested in home ventilation nursing and palliative medicine and, whilst neurologists may have a key role in discussing initiation of ventilation support, they will seldom have a role in its discontinuation.

Supporting decision-making

A balanced discussion of risks versus benefits for any intervention between medical practitioner and the individual with illness is an axiom of optimal healthcare. Being proactive with regard to discussing TV in MND is a significant evolution from the reactive approach which is common practice currently. It is critical to understand the expectations of those considering TV, which may be based on unrealistic ideas about how the disease progresses. Furthermore, introducing ethically-charged concepts such as the best use of limited healthcare resources or consideration of the carer and family burden of TV (49), is likely to be uncomfortable for both parties, though undoubtedly relevant to debate at a societal level.

MND has significant clinical and pathological overlap with FTD. Although the prevalence of overt dementia with loss of capacity in MND is estimated to be <15%, uncertainty remains about the natural history of cognitive and behavioural decline. In initial studies, those without significant cognitive impairment at baseline did not appear to develop this during the period of follow-up (50). However, the natural attrition in longitudinal MND studies is known to enrich for more 'benign' and slowly-progressive phenotypes. Analysis using clinical staging systems based on motor decline does suggest a greater burden of extramotor involvement over time (51), with obvious potential impact for those contemplating long-term TV. The limited number of autopsy studies in individuals with TV in MND over several years reveal significant clinical heterogeneity, in which there may be very profound cerebral (frontal) atrophy over less than a decade on TV, presumably with associated dementia (52), versus cases with preserved communication and sparse if any TDP-43 cortical pathology after a total disease duration of more than 30 years (53). The

assessment of cognitive function becomes important in the optimal management and maintenance of autonomy of those with long-term TV in MND, and this is challenging for those unable to write or speak. Although the use of eye-tracking for cognitive function testing has potential (54), the resistance of oculomotor function in MND is only relative compared to limb and bulbar musculature, and the use of brain-computer interfaces is the next frontier (55).

When discussing TV with patients it is important to acknowledge the lack of evidence in this area. There is no simple equation for harm or benefit from TV in terms of survival and quality of life, and more research needs to be done to be certain which (if not all) clinical phenotypes benefit. A lay summary of the evidence, limited though it is, would be a good starting point. This could be followed by a description of the practicalities of living with TV. Open questions might then help to facilitate an individual living with MND to explore all of the issues in TV (**Table 3**).

Closing remarks

For a condition like MND, in which respiratory failure is the key feature defining the survival in the majority of individuals, openness to discussion about TV should be considered part of routine multidisciplinary care. The use of NIV offers a clear quality of life and survival benefit for many individuals living with MND with symptomatic respiratory insufficiency, but TV is a more nuanced issue in which aspects of the long-term natural history of the condition are not currently clearly predictable. Identifying unrealistic expectations is important, but also acknowledging practical issues which include the availability of resources for healthcare delivery. Making the experiences of individuals living with MND, who have made a firm decision either way in respect of TV, more widely available to those still in the decision-making process might be a valuable resource.

Table 1

Summary data on prevalence of NIV and TV in MND (derived from (11))

	Japan	US	Europe (UK, Italy, Denmark & Sweden)
NIV use, range (%)	7 - 46	19 - 87	3 – 44
TV use, range (%)	29 - 38	4	1 - 31

Table 2

Useful resources on institution and withdrawal of TV in MND

Body	Title	URL
General Medical Council	Treatment and Care towards the End of Life: Good Practice in Decision Making	www.gmc-uk.org/guidance/ethical_guidance/end_of_life_care.asp
Motor Neurone Disease Association	Ventilation for Motor Neurone Disease	https://www.mndassociation.org/wp-content/uploads/2015/07/08b-ventilation-for-motor-neurone-disease.pdf
	Withdrawal of ventilation with MND	https://www.mndassociation.org/wp-content/uploads/08C-Withdrawal-of-ventilation-with-MND.pdf
ReSPECT	Recommended Summary Plan for Emergency Care and Treatment	https://www.respectprocess.org.uk
Association for Palliative Medicine of Great Britain and Ireland	Withdrawal of assisted ventilation at the request of a patient with motor neurone disease	https://apmonline.org/committee-pages/apm-professional-guidelines/

Table 3

Questions to consider in a broad discussion about TV in MND

Core questions	Issues to explore within
What benefits do you expect and hope from having TV?	How long they hope to live for; Are the survival expectations (or those of long-term therapy development) realistic?
When do you think the best time for TV would be?	Value of planning ahead of critical respiratory failure to avoid crisis intervention
Have you thought about any of practical aspects of TV and how things would work at home?	Equipment size and complexity; Need for regular home visits; Tube blockage, infection etc.
How do you feel about the issue of increasing physical dependence?	Increasing external or family care input requirements; Bladder and bowel management; Potential prolonged hospitalisation
How does your partner or close family feel about TV?	Has there been an open discussion? What do they think the impact on them might be?
What are your thoughts on communicating your wishes in the long-term?	The impact on speech of both disease and TV; Loss of limb movements; Loss of eye movements
How do you feel about the possibility of developing cognitive (thinking and planning) problems with longer-term MND?	Acknowledging uncertainty about this in current literature; Understanding current difficulty in assessing these functions in advanced disease, and inherent loss of insight
Are there circumstances in which you would want TV to be withdrawn?	Making a detailed Advance Directive; Understanding the management of symptoms after withdrawal of TV; Expectations of timing of death after TV withdrawal realistic or too rigid?

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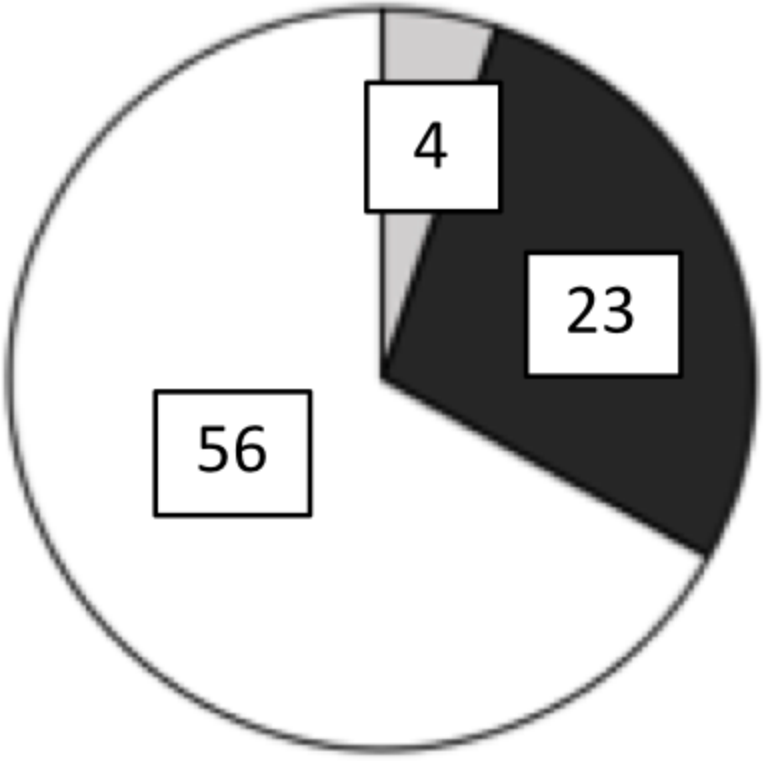
Figure legend

Number of individuals in a Japanese series with respiratory insufficiency secondary to MND receiving ventilatory support pre-2000 (left panel) and post-2000 (right panel) by modality. NIV alone (grey), NIV transitioning to tracheostomy ventilation (grey-black hashed) and primary tracheostomy ventilation (black), or no ventilatory support (white). Date derived from (16).

1990 – 1999 (n = 83)



2000 – 2015 (n = 114)