

## CASE REPORT

# Phrenic pacing compared with mechanical ventilation

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**STUDY DESIGN:** Comparable case series.

**OBJECTIVES:** High-cervical spinal cord injury (SCI) may disrupt the ability to breathe sufficiently. To restore respiration a phrenic nerve pacer can be implanted. The aims of this study were to describe the use of phrenic nerve pacing in tetraplegics in Denmark and compare the users with a population of ventilator dependent tetraplegics.

**SETTING:** Clinics for Spinal Cord Injuries, and Respiratory Centre East, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark.

**METHODS:** Nine tetraplegic individuals who had implantation of a phrenic nerve pacer and 16 home mechanical ventilator dependent tetraplegics met the inclusion criteria. Data were retrieved from medical records and a structured follow-up interview with seven individuals from each group.

**RESULTS:** No significant differences were found when comparing age at injury, time since injury, length of hospitalization, incidence of pneumonia, number of pneumonia hospitalizations, number of tracheal suction, speech quality and activities of daily living or quality of life. On the Short Form Health Survey (SF36) mental health summary the median for both users of phrenic nerve pacing and users of mechanical ventilation was one s.d. above the mean of a standard population.

**CONCLUSIONS:** Nine people have had a phrenic nerve pacer implanted. They do not significantly differ from a group of home mechanical ventilator dependent tetraplegics on a number of performance measures, but both groups seem to have better quality of life than a standard population.

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## INTRODUCTION

Spinal cord injury (SCI) is one of the most devastating injuries a person can be the victim of. It renders the body sense- and motionless and incapacitates the autonomic nervous system including the loss of bladder, bowel and sexual function. The primary respiratory muscle is the diaphragm innervated by the phrenic nerve arising primarily from the C4 segment of the spinal cord. Any damage at or above C4 has the potential for destroying the link between the respiratory centers of the brain and the diaphragm. Thus, in the case of high-cervical SCI resulting in tetraplegia even the ability to breathe sufficiently may be disrupted.

By applying an electrical current to the phrenic nerve, it is possible to make the diaphragm contract, and thus create an inspiration. This has been known for centuries,<sup>1</sup> but the technology for making phrenic nerve pacing a viable alternative to mechanical positive pressure ventilation is only four decades old.<sup>2</sup> Reports of long-time use in tetraplegic patients came in 1976.<sup>3</sup>

Establishing phrenic nerve pacing consists of several steps:<sup>2-7</sup> at first the patient's phrenic nerve and diaphragm has to be tested to make sure that there is connection and sufficient contraction to secure adequate airflow. This is done by applying external current to the nerve transcutaneous on the neck, while measuring diaphragm contraction with fluoroscopy or ultrasound. If sufficient contractions are demonstrated, radio electrodes are surgically implanted bilaterally with the electrodes attached to the phrenic nerve (the exact design of the electrodes varies among different manufacturers), while radio receivers are placed subcutaneously on the chest or the abdomen. By attaching external antennas to the surface of the skin, an electrical impulse can be supplied to the nerve without the need for any transcutaneous wires.

The published physiological results have been positive,<sup>2,3,5,7</sup> and it seems that neither the phrenic nerve nor the diaphragm suffers any degradation due to the un-physiological electrical stimulation. The user experiences reported have also been positive<sup>4,5,7-11</sup> and are largely identical across countries.

The aim of this study is to describe the Danish population of tetraplegics with a phrenic nerve pacer implant and compare them to a group of respiratory impaired, mechanical ventilator dependent tetraplegics in order to elucidate possible differences imposed by the pacer.

## METHODS

### Design

In Denmark nine tetraplegic individuals have received a pacer through July 1988<sup>12</sup> until the currently last one operated in May 2012. Data regarding physical functioning, activity and participation and quality of life were not recorded methodically before the insertion of the pacer, and a before/after comparison is therefore not possible. Instead comparison was made with a group of tetraplegic patients who are mechanical ventilator dependent, but who for various reasons do not have phrenic nerve pacer. They either rely on constant mechanical ventilation or in a few cases they receive mechanical respiratory support only part-time of the day. The study design is a retrospective comparative study with a follow-up questionnaire.

### Participants

Participants are included in two groups with different inclusion criteria.

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Since one of the aims of this study was to get a comprehensive knowledge about the group of patients with a phrenic nerve pacer, and since this group had already been deemed eligible to get a pacer, several criteria like comorbidity, impaired mental health and so on had all been prerequisite. Thus, the inclusion criteria for the paced group were restricted to: tetraplegia with implanted phrenic nerve pacer, and 18 years or older.

The inclusion criteria for the control group were: tetraplegia who were active user of home mechanical ventilation constantly or some part of the day, and 18 years or older, with no mental disorders, and living in East Denmark.

As no interventions are made in this study approval by the Ethical Committee is not necessary, and all completing the study volunteered to the interview (see below).

#### Data retrieval

Data were obtained by retrieving the medical records at the Clinic for Spinal Cord Injuries and Respiratory Centre East, Rigshospitalet. In addition a structured interview with each of the participating patients was carried out over the phone or in a few cases during a home visit.

The two populations are described using the International Spinal Cord Injury Data Sets.<sup>13</sup> That is, registration of basic information like age, gender, date of injury and so on, according to the International SCI Core Data Set.<sup>14</sup>

Ability to speak with a normal voice has been cited as a benefit from getting a phrenic nerve pacer,<sup>4,11,15,16</sup> but speech quality has previously been only primitively assessed by Esclarin *et al.*<sup>11</sup> and more systematically by Hirschfeld *et al.*<sup>16</sup> In this study assessing speech quality was carried out at the end of each interview to make sure the impression of the patient's voice was, as thorough as possible. The evaluation followed the procedure described by Hirschfeld *et al.* placing the patient on a scale from 0 to 6 (0: no voice; 1: whispering, intermittently; 2: whispering; 3: low voice, intermittently; 4: low voice; 5: normal voice, intermittently; 6: normal voice).

A reduction of the number of respiratory infections is widely cited as a benefit of the phrenic pacer<sup>3-5,10,11,16</sup> but only systematically measured by Hirschfeld *et al.* Their approach was unfortunately not feasible due to insufficient data. Instead two questions from the International SCI Pulmonary Function Basic Data Set<sup>17</sup> were used: 'The number of episodes of pneumonia treated with antibiotics within the last year' and 'the number of episodes of pneumonia requiring hospitalization within the last year'.

Due to the experience in the Respiratory Centre, the participants were also asked to state the average number of daily tracheal suction, since this is experienced to correlate with respiratory infections.

Various questionnaires exist with regard to activity and participation,<sup>18,19</sup> but the Spinal Cord Independence Measure (SCIM)<sup>20</sup> is recommended by the International Spinal Cord Society (ISCOs) and chosen as the way to best assess these aspects of life. The scale goes from 0 to 100 with 100 being complete independence.

In addition the participants were asked about their occupation at the time of injury and at follow-up.

Regarding Quality of life measures recommendations from a review<sup>21</sup> and the consensus from experienced clinicians,<sup>22</sup> resulted in the use of three different questionnaires: The Short Form Health Survey (SF-36),<sup>23</sup> Satisfaction With Life Scale (SWLS)<sup>24</sup> and the International SCI Quality of Life Basic Data Set (ISCOs-QoL).<sup>22</sup> SF-36 was scored and summarized using normative data from the United States. This includes a linear T-score transformation making 50 the mean and 10 one s.d. Using American data makes international comparisons possible and normative data for the Danish population has a correlation to the American data of 0.991 for physical summary and 0.994 for mental summary.<sup>25</sup>

#### Statistics

Due to the small sample sizes, the statistics used is descriptive and follows recommendations from ISCoS.<sup>26</sup> Since there are no assumptions of normal distribution of the data, a Mann–Whitney test is applied when comparing two groups, and an approximate Kruskal–Wallis test is applied when comparing more than two groups. Threshold for significance is  $P < 0.05$ . Calculations and graphs have been made in Prism 6 for Mac OS X made by Graphpad Software Inc.

#### RESULTS

A total of nine patients have had a phrenic nerve pacer implant (manufactures: four Avery Biomedical Devices, USA and five Atrotech, Finland) in Denmark. Of those one was below 18 years of age at the time of the study and one had died, leaving seven eligible for inclusion. One used the pacer 8.5 h, that is, all time in wheelchair, while three used it 12–14 h, that is, all time out of bed, and the remaining three 16 h a day corresponding to all time awake. The recommendation from the Respiratory Centre is that no patient uses the pacer for >16 h per day to prevent any damage to the phrenic nerve. The pacers have been used from 1.5 to 25.4 years at the time of the study. All patients using pacer reported that it was very easy to make it work requiring a median of 3 min (range <1–5 min) for the helper to fit the antennas on the skin. On a scale where one is most possible trouble making it work, and seven is no problems at all, the median was six (range 5–7).

In Eastern Denmark 16 patients with tetraplegia and tracheostomy ventilation met the inclusion criteria. Some were not available for interview, and one was not interested in participating, thus leaving also seven patients eligible for interview from this group.

All patients in the study are staying in their own home and have a personal helper 24 h per day paid by the regional/municipality health care system.

#### Basic information

The group of individuals with phrenic nerve pacer was compared to the group of participating and not-participating group of individuals depending on mechanical ventilation regarding age at injury, days hospitalized initially after injury, and years since injury and no significant differences between the groups were found. In addition they were mainly men, and had no associated injuries and same frequency of spinal surgery at the time they contracted their tetraplegia (Table 1).

Neither were any significant differences found between the two participating groups regarding quality of speech, pneumonias within last year or hospitalizations for pneumonia within last year, or number of daily suction (Table 2).

After the SCI only one of the paced participants has completed an education. One on mechanical ventilation is completing his education and another is taking some occasional educational courses (Table 3).

Regarding Quality of life were no significant differences found between the two groups or to the US norm data (Table 4).

#### DISCUSSION

The central outcomes from this survey are a description of the use of phrenic nerve pacing in tetraplegic individuals in Denmark compared with a tetraplegic group depending on mechanical ventilation.

The study has several limitations. It is a cross-sectional study, thus leaving limited power for cause-effect reasoning. Those offered pacing were not a randomized sample of the tetraplegic population. The group that was offered and who accepted a pacer

**Table 1.** Basic information about the patients

	Participating phrenic pacer patients (n = 7)		Participating patients on mechanical ventilation (n = 7)		Non-responding patients on mechanical ventilation (n = 9)	
	Median	Range	Median	Range	Median	Range
Age at injury median (range)	26.7	(14.6–63.0)	34.4	(16.5–60.8)	49.5	(17.6–91.1)
Years since injury median (range)	14.3	(3.5–26.4)	10.1	(2.5–24.6)	2.2	(0.5–15.9)
Days hospitalized median (range)	291	(152–474)	331	(183–675)	298.5	(88–1158)
Gender – Male	6	85.7%	7	100%	8	88.9%
<i>Place of residence</i>						
Private	7	100%	7	100%	7	77.8%
Other	0	0%	0	0%	2	22.2%
<i>Associated injuries</i>						
Yes	0	0%	0	0%	0	0%
No	7	100%	7	100%	8	88.9%
Unknown	0	0%	0	0%	1	11.1%
<i>Spinal surgery</i>						
Yes	5	71.4%	5	71.4%	6	66.7%
No	2	28.6%	2	28.6%	2	22.2%
Unknown	0	0%	0	0%	1	11.1%

**Table 2.** Quality of speech, pneumonia and suction

	Participants using phrenic pacer (n = 7)		Participants using mechanical ventilation (n = 7)	
	Median	Range	Median	Range
Quality of speech	5	4–6	5	5–6
Number of pneumonias within last year	0	0–3	0	0–2
Hospitalizations for pneumonia within last year	0	0–2	0	0–1
Number of daily suction	3	0–12	1	0–5

**Table 3.** Spinal Cord Independence Measure at time of study and education/employment before and after spinal cord injury

	Participants using phrenic pacer (n = 7)		Participants using mechanical ventilation (n = 7)	
	Median	Range	Median	Range
Spinal Cord Independence Measure	9	8–9	8	5–14
	Before	After	Before	After
Under education, working > 10 h per Week	7	3	7	2
Working < 10 h per week, unable to work, retired	0	4	0	5

**Table 4.** Quality of life

	Participants using phrenic pacer (n = 7)		Participants using mechanical ventilation (n = 7)	
	Median	Range	Median	Range
Satisfaction With Life Scale	21	7–28	19	11–28
ISCIQoLBDS - General	7	0–9	7	3–9
ISCIQoLBDS - Physical	7	0–9	6	2–8
ISCIQoLBDS - Mental	7	5–10	8	2–10
SF36 Physical summary	35.4	12.9–37.6	23.6	14–37.6
SF36 Mental summary	62.3	51.1–71.2	61.4	27–71.4

SWLS: Satisfaction With Life Scale. Interpretation: 5–9 extremely dissatisfied, 10–14 dissatisfied, 15–19 slightly dissatisfied, 20 Neutral, 21–25 slightly satisfied, 26–30 satisfied, 31–35 extremely satisfied. ISCIQoLBDS: International Spinal Cord Injury Quality of Life Basic Data Set. Interpretation: 0 meaning completely dissatisfied, 10 meaning completely satisfied. SF36: Short Form (36) Health Survey. Normalized score, 50 is mean and 10 is one s.d.

operation may have had a lower degree of acceptance of mechanical ventilation than those not operated.

The group of ventilator treated patients included for interview was less than half of those meeting the inclusion criteria, making it possible that those not interviewed had less favorable life conditions. Even though there was no significant difference between the groups, the non-responding group was more recently injured. Previous studies<sup>27,28</sup> are suggesting that time since injury is a predictor for quality of life, but the relationship is not clear. Another limitation is data collection via interview since this prerequisites a rudimentary vocal function for participation in the study. Finally the number of participants is relatively small.

Having those limitations in mind, the following points are noteworthy:

#### Use of phrenic nerve pacing

In Denmark phrenic nerve pacing is recommended to be carried out part-time of the day only. At night the Danish patients are relying on a mechanical ventilator – and surveyed by their helper. This is similar to the use of pacing in most studied tetraplegic populations,<sup>5–7,29</sup> while Esclarin *et al.*<sup>11</sup> is the only group reporting 24 h pacing of their paced population. The reason that the patients should not use nocturnal electro-ventilation, is based

partly on the fact that tetraplegia is associated with a high incidence of obstructive sleep apnea,<sup>30,31</sup> and partly on the assumption that 6–8 h of rest per day of the phrenic nerve may reduce the risk of damaging the nerve. No users reported unwillingness to the use of pacer instead of mechanical ventilation, and all reported that the transition from mechanical ventilator to pacer required little time and was easy to get working.

#### Respiratory infection

The number of episodes with respiratory infections is similar and very low in both groups of participants in this survey. Hirschfeld *et al.*<sup>16</sup> found a significant reduction in the group of patients with a pacer, and their explanation is that the pacer makes suction unnecessary. In our survey the paced patients still needed suction, but had very few episodes of pneumonia. However, this was not different from the population dependent on mechanical ventilation.

#### Quality of speech

While other studies highlight the improvement of speech quality a pacer gives,<sup>9–11,16</sup> this was not seen in this survey. This is plausibly explained by the high level of speech quality in the group of Danish patients using mechanical ventilation, which really did not leave much room for improvement. In addition, the tool used for the assessment was rather crude and has not been standardized. Some patients did not feel that their level of speech quality was reflected very well in the scale. Their greatest difficulty is that they are not able to raise their voice in large crowds, but since the scale only went to 'normal voice' this difficulty was not reflected. Future studies of speech quality should have this in mind and a more sensitive formal tool for assessing speech quality should be developed.

#### Activity and participation

No previous study has systematically measured activity and participation in this group of patients, but one study<sup>16</sup> mentions an improvement in SCIM-score from 3 to 11 by the insertion of a pacer in a patient. Several studies mention greater mobility after implantation of a pacer.<sup>5,6,9,10</sup> These results are not found in the Danish population, but it seems that the patients dependent on mechanical ventilation scores better in Denmark than their counterparts abroad thus leaving little room for improvement from a pacer in a Danish context.

Previous studies<sup>4,7,15</sup> report that after getting a pacer it is possible to finish an education and get a job. This is also found in this study, but it seems that this is also true for the group of Danish mechanically ventilated patients.

#### Quality of life

Several studies are subjectively stating that quality of life improves after getting a pacer,<sup>7,11,16</sup> however only one previous study has measured this in a paced population,<sup>8</sup> using only the SWLS. They report a mean score of 18.5, which is very close to the median of 21 scored by the paced participants in our study.

The subjective advantage by getting a pacer did not show quantitatively in this survey—which has a different design comparing groups in a cross-sectional design. It could be that the tools for measuring quality of life are too crude for the subtle improvements a pacer gives.

One hopeful explanation is that quality of life in the group of patients depending on mechanical ventilation in Denmark is already high, and leaves little room for an improvement by a pacer. This is supported by the SF36 mental summary score where both the group with a pacer and the mechanically ventilated group have a median score slightly more than one s.d. above the

mean of a standard (not tetraplegic) US population. That patients suffering from such a severe chronic condition seem to have a better quality of life than a standard population may be surprising.<sup>32</sup> An explanation could be that they despite being exposed to an extreme physical and emotional trauma, followed by despair and misery, realize or even accept that their lives have changed dramatically. We have seen several patients going through this journey and ending up with a positive mind. They may among other things be grateful to the society that they have been supported and given the opportunity to stay alive.

#### CONCLUSION

In Denmark nine tetraplegic individuals have had an implantation of bilateral phrenic nerve pacer. One is dead and one was below 18 years of age, and was not included in the study. The remaining seven individuals are using pacing without problems, and very little difficulty while out of bed.

There were no significant differences between the seven included participants using pacer compared to seven ventilator dependent tetraplegic individuals using other means of mechanical ventilation with regards to the episodes of pneumonia, speech quality, activity and participation or quality of life. Previous literature gives a limited basis for comparison, but it is noteworthy that the mental health summaries for both Danish populations are one s.d. above a mean standard population.

#### COMPETING INTERESTS

The authors declare no conflict of interest.

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