

The Research Fund: Final Report

Timing of Noninvasive Ventilation for Patients with Amyotrophic Lateral Sclerosis

Noah Lechtzin, MD, MHS, Department of Pulmonary and Critical Care, Johns Hopkins University, Baltimore, Maryland, nlechtz1@jhmi.edu

The Research Fund grant in 2005 from International Ventilator Users Network allowed our team to investigate the effects of noninvasive ventilation in patients with neuromuscular disease and with relatively preserved pulmonary function.

We conducted a retrospective cohort study of patients with amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease). Ninety-two patients were followed for a median of 3.5 years. We compared survival from time of diagnosis in subjects who started noninvasive positive pressure ventilation (NPPV) use when their forced vital capacity (FVC) was 65% of predicted (Early NPPV) with subjects who started NPPV when their FVC was \leq 65% of predicted (Standard NPPV).

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There were 25 patients in the Early group and 67 in the Standard group. The two groups were similar except for pulmonary function. Patients used bilevel positive pressure units with backup rates and a variety of full face and nasal masks. All patients used NPPV for four or more hours per day.

Survival was significantly improved in the Early NPPV group. The median time from ALS diagnosis to death was 2.7 years in the Early NPPV group compared to 1.8 years in the Standard NPPV group. The risk of death remained significantly lower in the Early group after adjustment for potential confounding factors, including time from symptom onset to diagnosis, age, gender, presence of a gastrostomy tube, and bulbar onset.

We concluded that survival from time of diagnosis was nearly one year longer in the Early group. Until more definitive data is available from randomized trials, our findings suggest that clinicians should test for respiratory muscle impairment with supine FVC, maximal inspiratory pressure

(MIP), sniff nasal pressure, and sniff transdiaphragmatic pressure, and encourage early use of NPPV.

Q & A with Dr. Lechtzin

Q: What impact will these results have for people with other neuromuscular conditions?

A: While ALS progresses more rapidly than many other neuromuscular conditions, there is no reason to think our findings are specific to ALS. If NPPV works by resting fatigued muscles, improving compliance of the lungs and chest wall, and preventing elevated CO₂ levels, it should be effective earlier in other conditions, such as muscular dystrophy.

Q: Can earlier use of NPPV benefit polio survivors? How would my physician and I decide when to start NPPV?

A: This is a challenging question. The time to start NPPV in ALS is better defined than in other neuromuscular conditions, but even in ALS it

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is not clear-cut. My feeling is that until more definitive information is available, this question should be approached clinically on an individual basis.

If patients have evidence of respiratory muscle impairment and are symptomatic, NPPV will likely be beneficial. I do not think there is any absolute value of FVC or other pulmonary function test that will determine if any individual with post-polio syndrome or another neuromuscular condition will benefit from NPPV. However, if they have shortness of breath (dyspnea), need to sleep sitting up (orthopnea), fatigue, hypersomnolence, or difficulty sleeping, NPPV may be beneficial.

Q: Is future research on early use of NPPV in ALS in the works?

A: We have a randomized crossover study ongoing at Johns Hopkins in which individuals with FVC above 60% are evaluated. There is also an ongoing multicenter study of early NPPV led by Ed J. Kasarskis, MD, PhD, at the University of Kentucky.

Q: Have you submitted the study results for publication?

A: We have submitted a manuscript to *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*. It is currently under review. ▲