# Survival of Veterans With Sleep Apnea: Continuous Positive Airway Pressure Versus Surgery

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# Survival of veterans with sleep apnea: Continuous positive airway pressure versus surgery

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***OBJECTIVES:*** **Continuous positive airway pressure (CPAP) improves sleep apnea survival. We tested whether CPAP is associated with better survival than uvulopalatopharyngoplasty (UPPP).**

***STUDY DESIGN AND METHODS:*** **This retrospective cohort database study included all sleep apnea patients treated with CPAP or UPPP in Veteran Affairs facilities from October 1997 through September 2001. Treatment groups were compared with Cox regression, adjusting for age, gender, race, year treatment was initiated, and comorbidity. Sleep apnea severity and CPAP use data were not available.**

***RESULTS:*** **By September 2002, 1339 (7.1%) of 18,754 CPAP patients and 71 (3.4%) of 2,072 UPPP patients were dead ($P < 0.001$). After adjustment, CPAP patients had 31% (95% confidence interval, 3% to 67%, $P = 0.03$) higher probability of being dead at any time, relative to UPPP patients.**

***CONCLUSIONS:*** **UPPP confers a survival advantage over CPAP, after adjustment for age, gender, race, year of treatment, and comorbidity. However, we were unable to adjust for sleep apnea severity or CPAP use. Surgical treatment should be considered in sleep apnea patients who use CPAP inadequately.** (Otolaryngol Head Neck Surg 2004;130: 659-65.)

Untreated obstructive sleep apnea (OSA) appears to decrease long-term survival.[1-3] Untreated OSA also is associated with cardiovascular disease,[4-7] a likely mechanism for reducing survival.[8] Treatment for sleep apnea appears to reduce these complications of sleep apnea.[1-4,9,10]

Provision of continuous positive airway pressure (CPAP) is the first-line treatment for sleep apnea because it is the most efficacious treatment, besides tracheostomy, for reducing the physiologic abnormalities measured on polysomnography. The CPAP device is worn over the nose during sleep, and it pneumatically stents open the upper airway. However, for CPAP to be effective, patients must be adherent to its use. The effectiveness of CPAP is unknown because adherence to lifelong treatment is unclear. Short-term adherence to CPAP ranges from 40% to 80% of patients who use the device at least 20 hours per week.[11,12]

The most common surgical treatment for OSA is uvulopalatopharyngoplasty (UPPP), often combined with other procedures.[13] Surgery effectiveness is estimated at 40% to 80% based on the success rate of significantly reducing the physiologic abnormalities measured on polysomngraphy.[14] Patient adherence is moot for surgically treated patients, but the duration of treatment effect is not well established.

Survival rates of CPAP and UPPP patients were compared in 3 published studies, each based on a single-site cohort with limited or no adjustment

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for comorbidity.[1,3,15] One study[1] reported greater survival in CPAP patients compared with UPPP patients, whereas the other 2 studies[3,15] found no significant difference. A larger cohort study may help discern the long-term survival rates of each treatment. A recent 7-year cohort study found that UPPP was at least as effective in reducing cardiovascular disease as CPAP, because CPAP adherence was poor.[4] Incompletely treated patients had a much higher risk of subsequent cardiovascular disease seven years later.

The primary aim of this study was to test the hypothesis that providing a CPAP device was not associated with better survival than UPPP (with or without other sleep apnea operations) in sleep apnea patients, adjusting for important confounding variables. A secondary aim was to evaluate the importance of adjustment for age, gender, race, and comorbidity.

## METHODS

### Study Design

This study is a retrospective cohort study of all sleep apnea patients treated with either CPAP or UPPP at Veterans Affairs (VA) medical facilities from October 1997 through September 2001 (defined as fiscal years 1998 to 2001). It compares the survival rates of each treatment. The study and waiver of informed consent were approved by the University of Washington human subjects review committee.

### Study Population

Subjects included all veterans treated for sleep apnea with CPAP or UPPP at any VA facility, for whom complete outpatient and inpatient administrative records were available (see Data Sources). The cohort was identified with diagnosis and procedure codes in the Outpatient Care and Patient Treatment Files (see Data Sources). Typically, a small group of sleep apnea patients are referred for UPPP (or other surgical treatment) and only after CPAP fails. Thus we included all UPPP patients in the surgical group, even if they had been previously prescribed CPAP.

The cohort included patients treated in fiscal years 1998 to 2001. We required outpatient and inpatient comorbidity data for 1 year before treatment, and these data were available only since fiscal year 1997. Thus the cohort started from the beginning of fiscal year 1998. We required at least 1 year of survival data, which were available up to the end of fiscal year 2002 at the time of this study. Therefore the cohort included patients up through the end of fiscal year 2001.

### Data Sources and Collection

The Outpatient Care File is an administrative database of all ambulatory encounters and ancillary services provided at VA medical centers nationwide. All ambulatory procedures in fiscal years 1990 to 2001 are recorded with Current Procedure Terminology (CPT) codes. All outpatient CPAP prescriptions (CPT 94660) and outpatient UPPP operations (CPT 42145) were identified. Since fiscal year 1997, the Outpatient Care File has listed all ambulatory encounter diagnoses, recorded with *International Classification of Diseases (ICD-9)* codes. We extracted all diagnoses to confirm an OSA diagnosis and to enable comorbidity adjustment (see Outcome and Covariate Variables).

The Patient Treatment File is an administrative database of all inpatient discharges at VA medical centers nationwide. It is managed in a fashion analogous to the Outpatient Care File. We used data from several files within the Patient Treatment File. The Main File includes demographic data, principal diagnosis, up to 9 additional diagnoses (*ICD* diagnosis codes), and vital status since 1970. The Procedure File includes all inpatient procedures not performed in an operating room since 1988. All inpatient CPAP prescriptions were identified by the *ICD-9* procedure code for CPAP (93.90) *and ICD-9* diagnosis codes for sleep apnea (780.51, 780.53, or 780.57) to minimize misclassification of non-OSA CPAP (ventilator) patients into our cohort. The Surgery File includes all inpatient operations since 1984. All inpatient UPPP surgeries were identified by *ICD-9* procedure codes for UPPP (27.1, 27.69, 27.72, or 27.79) and *ICD-9* diagnosis codes for sleep apnea (as earlier).

To ascertain subsequent vital status, we also used the Beneficiary Identification and Records Locator System Death File database.[16] Death notices are issued from multiple sources, including survivor benefit applications, the Social Security

**TABLE 1.** Cohort description

| Variable | Entire cohort (N = 20,826) | CPAP (n = 18,754) | UPPP (n = 2,072) | CPAP versus UPPP *P* value |
|---|---|---|---|---|
| Age at treatment (yr) | 57 ± 12 | 57 ± 12 | 51 ± 11 | <0.001 |
| Gender (% male) | 98 | 98 | 97 | 0.02 |
| Race (% white) | 82 | 82 | 82 | 0.56 |
| Comorbidity Index | 2.0 ± 3.0 | 2.0 ± 3.1 | 1.1 ± 2.0 | <0.001 |
| Survival (yr) | 2.75 ± 1.20 | 2.75 ± 1.21 | 2.81 ± 1.17 | 0.03 |
| No. dead (%) | 1,410 (6.8%) | 1,339 (7.1%) | 71 (3.4%) | <0.001 |

*CPAP*, Continuous positive airway pressure; *UPPP*, uvulopalatopharyngoplasty.

Administration, and others. Outcome data (date of death) were extracted.

## Outcome and Covariate Variables

The primary outcome is death. Deaths were identified from the Patient Treatment File and the Benefits Identification and Records Locator System Death File in fiscal years 1998 to 2002, 1 year beyond the treatment period. Survival time was calculated as the time between treatment (CPAP provision or UPPP operation) and death or study conclusion (end of fiscal year 2002, September 30, 2002), whichever came first.

Covariates include age at the time of treatment, gender, race, date of treatment, and comorbidity. Demographic variables and date of treatment were identified from the VA databases. Race was categorized as white, not white, or unknown. Sleep testing data were not available in the databases, so adjustment was not made for sleep apnea severity. CPAP adherence data were not available, so no adjustment was made for use of CPAP provided.

The comorbidity covariate was based on the Deyo modification[17] of the Charlson Comorbidity Index.[18] The Charlson Comorbidity Index is a weighted score of 19 specific comorbid conditions, extracted from medical records, that predicts mortality. The Deyo modification extracts and weights the same conditions from administrative databases using the corresponding *ICD-9* codes. Deyo showed that extraction of data from the year before the exposure of interest was as predictive as longer periods of comorbidity extraction.[17]

The Deyo-modified Charlson Comorbidity Index was created for each subject from all outpatient diagnoses in the year preceding CPAP provision or UPPP operation. When outpatient comorbidity data were missing, a Deyo-modified Charlson Comorbidity Index was created from the Patient Treatment File. Only 60 (0.3%) of 20,826 of study subjects lacked comorbidity data between the 2 sources.

## Statistical Analyses

Continuous data are presented as mean ± SD. Bivariate comparisons between CPAP and UPPP patients were carried out with the Student *t* test and $\chi^2$ test. Survival between CPAP and UPPP patients was compared with the log rank statistic. Cox proportional hazard regression was used to compare unadjusted and adjusted hazard ratios in the 2 treatment groups. Adjustments were made for age, gender, race, year of initial treatment, and comorbidity. The proportional hazards assumption was tested (and verified) on each covariate and globally on scaled and unscaled Schoenfield residuals, respectively, for each regression model. Odds ratios and hazard ratios are presented with 95% confidence intervals. $P < 0.05$ was considered statistically significant.

# RESULTS

UPPP patients made up approximately 10% of the cohort. There were significant differences in the characteristics between CPAP and UPPP patients (Table 1). The CPAP patients were older and had more comorbidity than UPPP patients. UPPP patients underwent a variety of other concurrent procedures (Table 2).

A greater proportion of CPAP patients died during the study period, and UPPP patients survived almost 22 days longer, on average, than CPAP patients (Table 1). Throughout the study period the UPPP survival appears to be better than the CPAP survival (Fig 1). These curves are not

**TABLE 2.** Common concurrent procedures with uvulopalatopharyngoplasty (UPPP)

| Procedure | No. (%) |
|---|---|
| UPPP | 2,072 (100) |
| Tonsillectomy* | 781 (38) |
| Septoplasty | 720 (35) |
| Turbinate procedure | 499 (24) |
| Tracheotomy | 39 (2) |
| Tongue procedure | 32 (2) |

*Tonsillectomy is often considered part of UPPP and is not always coded separately.

adjusted for confounding variables like age and comorbidity.

After adjustment for several known confounders of mortality, CPAP patients had a 31% greater probability of being dead at any time during the study period compared with UPPP patients (Table 3). Age, gender, and comorbidity all have a significant independent impact on survival. A later treatment date decreases the chances of dying during the study period, simply due to reduced opportunity to die. Reported race was not associated with survival, but "unknown" race was associated with a significantly increased survival (data not shown).

## DISCUSSION

These results suggest that UPPP (sometimes with concurrent surgery) provides greater long-term survival than provision of CPAP. The survival advantage persists even after adjusting for age, gender, race, date of treatment, and comorbidity.

This study has unique features. The large sample size expands on previous single-site survival studies that had cohorts of less than 500 patients.[1,3,15] The large sample size allows for adjustment for confounding variables while maintaining statistical power. OSA is a chronic disorder and mortality is a distant outcome. To accurately measure mortality, an adequate sample is necessary. The study sample draws from a broad geographic distribution throughout the United States. It includes a broad array of practice styles, diagnostic protocols, CPAP management protocols, surgeons, perioperative protocols, hospitals, and demographics. This heterogeneity of the population strengthens the generalizability of the findings.

Most important, this study adjusts for several important confounding variables. The CPAP and UPPP patients, on average, were quite different. The CPAP patients tended to be older and sicker. A direct comparison on the survival of these groups may be biased because these confounding variables bias against CPAP survival. Our data convey the importance of adjustment. Without adjustment, UPPP patients had greater than double the survival relative to CPAP. With adjustment, UPPP patients experienced a survival benefit approximately 30% greater than CPAP patients.

It is critical to adjust for comorbidity because it is related to treatment choice and has an important impact on survival. In the sleep apnea literature, the most rigorous comorbidity adjustments have simply included a tally of several cardiovascular and other miscellaneous diseases. Here, we used the Deyo modification of the Charlson Comorbidity Index, which has been validated to prognosticate mortality.[17,18] This index provides state-of-the-art adjustment for this complex, but important, confounding variable.

This study has several important limitations. Administrative data are known to have errors in coding that may result in misclassification of patients. The observational cohort study design has inherent limitations associated with uncontrolled conditions. Known and unknown confounding variables that we are unable to control may have affected the outcome. For example, we did not have data on OSA severity, which may affect treatment choice and outcome. However, more severe OSA is presumably related to mortality in part by causing other comorbid conditions, like cardiovascular disease. Thus, our comorbidity adjustment may have accounted for some of the possible effect of disparate OSA severity between treatment groups. There may be other unknown variables that confounded our results.

Complete comorbidity data were limited to fiscal years 1997 through 2001, thus restricting our cohort to patients treated in fiscal years 1998 through 2001. An earlier cohort would provide longer-term outcomes. To test the robustness of our findings, we also performed an analysis of patients with treatment dating back to 1991. Un-

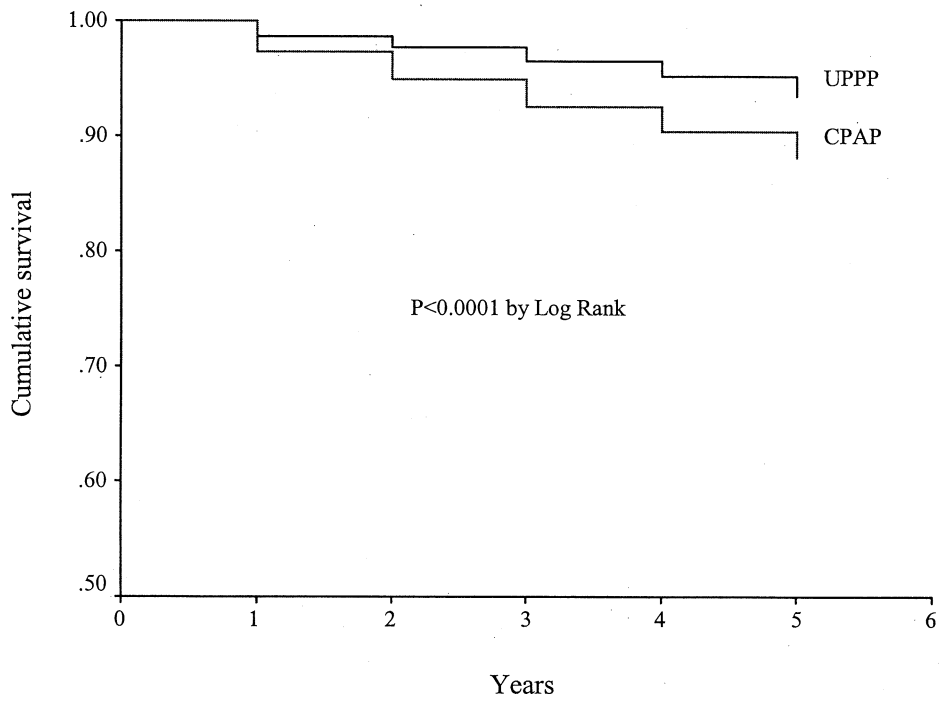


**Fig 1.** Survival curves for uvulopalatopharyngoplasty (UPPP) and continuous positive airway pressure (CPAP). Proportion of UPPP and CPAP patients alive in the time (years) after treatment (UPPP operation or provision of CPAP device). UPPP patients had significantly better survival than CPAP patients.

**TABLE 3.** Mortality hazard (Cox regression)

| Variable | Reference group | Unadjusted HR (95% CI) | Adjusted* HR (95% CI) | *P* value (adjusted model) |
|---|---|---|---|---|
| Therapy (CPAP) | UPPP | 2.11 (1.66-2.68) | 1.31 (1.03-1.67) | 0.03 |
| Age at treatment (yr) | One year prior | 1.07 (1.07-1.08) | 1.06 (1.06-1.07) | <0.001 |
| Sex (male) | Female | 2.76 (1.52-4.99) | 1.82 (1.01-3.30) | 0.048 |
| Race (white) | Nonwhite | 1.16 (1.00-1.35) | 0.98 (0.84-1.13) | 0.77 |
| Date of treatment (yr) | One year prior | 0.93 (0.88-0.98) | 0.92 (0.87-0.97) | 0.001 |
| Comorbidity Index | One less index score | 1.11 (1.10-1.12) | 1.09 (1.08-1.10) | <0.001 |

*UPPP*, Uvulopalatopharyngoplasty; *CPAP*, continuous positive airway pressure; *HR*, hazard ratio, the hazard of being dead at any time relative to the reference group; *CI*, confidence interval.
*Adjusted for age at treatment, sex, race, date treatment initiated, and comorbidity.

adjusted analyses of this fuller cohort shows an *identical* unadjusted hazard ratio (data not shown). However, adjustment for partial comorbidity data available only from inpatient records was inconsistent. Results depended on how we defined comorbidity, which affected the proportion of patients excluded due to missing data. Some analyses showed superior survival for UPPP patients, and other analyses showed equivalent survival for UPPP and CPAP patients. In no analysis did CPAP show superior survival (data not shown).

Our population sample included only veterans treated at VA medical facilities. Results in veterans may not generalize to the entire US adult population. We did adjust for some of the known characteristics (eg, gender and comorbidity) of VA populations that may confound the relationship between treatment choice and outcome.

It should be noted that we did not have data to document physiologic improvement after surgical treatment. UPPP rarely provides complete normalization of polysomnography parameters,[14] and therefore some may believe it does not have a role in the treatment of OSA. The results from this study demonstrate that the physiologic improvement of OSA, even without cure, is valuable. The lack of physiologic cure of OSA should not be grounds for deciding against surgical treatment, as this surgery appears to improve survival. Other studies suggest surgical therapies also improve reaction time, quality of life, and motor vehicle crash risk while not providing physiologic cures.[19,20]

Special note should be made of the fact that we did not know patients' adherence to CPAP therapy. This study shows that UPPP is superior to the provision of CPAP, but we cannot (and should not) conclude that UPPP is superior to the *use* of CPAP. It is likely that there was a large proportion of CPAP patients who did not use the device and thus were untreated. It is also likely, based on previous studies, that CPAP use improves survival.[1,3,10,15]

Thus the results from our study strongly suggest, at the very least, that OSA patients who do not use CPAP should be evaluated for surgical therapy. Even those who use CPAP, but inadequately, should be evaluated for surgical therapy. This conclusion is consistent with a recent 7-year prospective cohort study that showed that inadequate CPAP use (defined as objective CPAP use $\leq$50% of estimated sleep time) resulted in much greater incidence of cardiovascular disease compared with adequate CPAP use or with adequate improvement on steep study following UPPP.[4] In that cohort, only 36% of CPAP patients had adequate use, whereas 50% of UPPP patients had adequate improvement on sleep study 1 to 2 years after UPPP.

Unfortunately, the minimum CPAP use that is adequate is currently unknown. Emerging data suggest that there is monotonic improvement in outcome with use (eg, 8 hours per night is better than 7 hours per night, and 7 hours is better than 6 hours).[21,22] The previous standard of 4 hours per night over 70% of days (20 hours per week)[11,12] is clearly inadequate, as it provides treatment during only 36% of the expected 56 hours of sleep time per week. It is important for clinicians to try to identify inadequate CPAP users to offer other treatment to improve OSA patients' ultimate outcome. OSA is a disorder best managed with a multidisciplinary approach.

## CONCLUSIONS

Surgical therapy for sleep apnea provides better survival than provision of CPAP therapy to all comers. We are unable to draw conclusions about the relative benefit of UPPP compared with patients' adherent to CPAP therapy. OSA patients who do not use CPAP (or who use it inadequately), however, should be evaluated for surgical therapy. Although surgical therapy may not completely correct the physiologic abnormalities of OSA, it appears to improve the long-term clinically important outcome of survival.

### REFERENCES

1. He J, Kryger MH, Zorick FJ, et al. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest 1988;94:9-14.
2. Partinen M, Jamieson A, Guilleminault C. Long-term outcome for obstructive sleep apnea syndrome patients. Mortality. Chest 1988;94:1200-4.
3. Marti S, Sampol G, Munoz X, et al. Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J 2002;20:1511-8.
4. Peker Y, Hedner J, Norum J, et al. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. Am J Respir Crit Care Med 2002;166:159-65.
5. Young T, Peppard P. Sleep-disordered breathing and cardiovascular disease: epidemiologic evidence for a relationship. Sleep 2000;23:S122-6.
6. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
7. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283:1829-36.
8. Lavie P, Herer P, Peled R, et al. Mortality in sleep apnea patients: a multivariate analysis of risk factors. Sleep 1995;18:149-57.
9. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165:1217-39.
10. Veale D, Chailleux E, Hoorelbeke-Ramon A, et al. Mortality of sleep apnoea patients treated by nasal continuous positive airway pressure registered in the Antadir Observatory. Association Nationale pour le Traitement a Domicile de l'Insuffisance Respiratoire Chronique. Eur Respir J 2000;15:326-31.
11. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993;147: 887-95.

12. Pepin JL, Krieger J, Rodenstein D, et al. Effective compliance during the first 3 months of continuous positive airway pressure. A European prospective study of 121 patients. Am J Respir Crit Care Med 1999;160:1124-9.
13. Kezirian EJ, Weaver EM, Yueh B, et al. Incidence of serious complications after uvulopalatopharyngoplasty. Laryngoscope 2004;114:450-3.
14. Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 1996;19:156-77.
15. Keenan SP, Burt H, Ryan CF, et al. Long-term survival of patients with obstructive sleep apnea treated by uvulopalatopharyngoplasty or nasal CPAP. Chest 1994;105:155-9.
16. Cowper DC, Kubal JD, Maynard C, et al. A primer and comparative review of major US mortality databases. Ann Epidemiol 2002;12:462-8.
17. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613-9.
18. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40:373-83.
19. Woodson BT, Steward D, Weaver EM. A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 2003;128:848-61.
20. Haraldsson PO, Carenfelt C, Lysdahl M, et al. Does uvulopalatopharyngoplasty inhibit automobile accidents? Laryngoscope 1995;105:657-61.
21. Meslier N, Lebrun T, Grillier-Lanoir V, et al. A French survey of 3,225 patients treated with CPAP for obstructive sleep apnoea: benefits, tolerance, compliance and quality of life. Eur Respir J 1998;12:185-92.
22. Blondet MC, Perez J, Rodriguez W. Continuous positive airway pressure and obstructive sleep apnea in an Hispanic population. Sleep Breath 2001;5:109-14.