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Comparison of the effect of weight change, simulated computational continuous positive airway pressure treatment and positional therapy on severity of sleep apnea

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Abstract

Weight loss, continuous positive airway pressure (CPAP) and positional therapy (PT) are important treatments in obstructive sleep apnea (OSA). Although all of these reduce the apnea–hypopnea index (AHI) effectively, the benefits of these treatments have not been thoroughly investigated in a patient-specific manner. Therefore, clinicians do not have objective means to choose an optimal treatment for each patient. We aim to provide clinicians the possibility for treatment optimization in a patient-specific manner by introducing a computational simulation approach. The effect of actual weight change, computationally simulated CPAP treatment and PT and their combinations on the AHI were compared in 54 OSA patients divided into three equally sized groups (weight loss > 7%, weight loss 0%–7%, and weight gain) after a 5-year follow-up with lifestyle intervention. Weight loss reduced the AHI by 43.5% ($p < .05$) and 18%, simulated CPAP treatment with 3.3-hr adherence by 42.4% ($p < .05$) and 35.5% ($p < .05$), and simulated PT by 13.5% ($p < .05$) and 30.7% ($p < .05$) in > 7% and 0%–7% weight loss groups, respectively. Simulated CPAP treatment and PT were able to compensate for the increase in the AHI caused by weight gain. A developed simulation approach could help clinicians to estimate treatment success in advance in order to prescribe the most optimal patient-specific treatment to reduce OSA-related health risks.

KEYWORDS

AHI, CPAP treatment, obstructive sleep apnea, positional therapy, simulation, weight loss

1 | INTRODUCTION

Obstructive sleep apnea (OSA) is a complex medical problem with a high prevalence and severe health consequences. Total (apnea) and partial (hypopnea) breathing cessations during sleep can cause daytime fatigue and are linked to increased risk of cardiovascular morbidity and mortality (Marin, Carrizo, Vicente, & Agusti, 2005; Somers et al., 2008). The severity of OSA is estimated by the average number of breathing cessation events per hour of sleep (i.e., the apnea–hypopnea-index [AHI]) (American Academy of Sleep Medicine Task Force 1999). There are several different modalities available to manage OSA and the related health risks. Lifestyle intervention (aimed at weight loss), continuous positive airway pressure (CPAP) treatment, and positional therapy (PT) are important options for OSA management. These methods, however, do not take into account the patients' individual needs and are often similarly prescribed to all patients despite the differences in characteristics of OSA.

As OSA is related to obesity, one of the main options for reducing the symptoms, besides reducing the number of breathing cessations, is weight loss (Young, Skatrud, & Peppard, 2004). Weight change not only affects the AHI (Newman et al., 2005) but also modulates the severity of individual breathing cessation events (Kulkas et al., 2013, 2014, 2015; Leppanen, Kulkas, Mervaala, & Töyräs, 2019). Although weight loss has been shown to reduce the AHI and provide other health benefits, the clinical implementation of sustainable weight loss in overweight patients is a challenging task (Joosten, Hamilton, & Naughton, 2017; Sacks et al., 2009).

CPAP treatment is considered to be one of the most important methods for OSA treatment (Bakker, Weaver, Parthasarathy, & Aloia, 2019). With optimal use of a CPAP device, breathing cessation events can be significantly reduced. However, the efficiency of CPAP treatment is often compromised by the limited adherence (Bakker et al., 2019; McEvoy, Antic, & Heeley, 2016). The nightly CPAP adherence has been shown to be relatively low, ranging from 3.3 to 5.1-hr per night, leaving residual breathing cessation events during the treatment (Cistulli et al., 2019; McEvoy et al., 2016). The adherence level needed to reduce the AHI to a normal level (i.e. <5 events/hr) is often, however, much higher, depending on the severity of OSA (Kulkas et al., 2018).

More than 50% of OSA patients have the positional form of the disorder (i.e. there are twice the number of events in the supine posture compared to non-supine postures) (Omobomi & Quan, 2018). The prevalence of positional OSA is highest in mild OSA and decreases as OSA severity increases (Mador et al., 2005). OSA is typically more severe in the supine position compared to non-supine positions and in addition to the AHI, the severity of individual breathing cessation events is higher in the supine position compared to a non-supine position (Leppänen et al., 2016; Oksenberg, Khamaysi, Silverberg, & Tarasiuk, 2000). Therefore, positional therapy, where a supine sleeping position is avoided, may be used effectively to reduce the AHI and the severity of individual breathing cessation events (Omobomi & Quan, 2018).

To satisfactorily treat OSA and effectively reduce the related health risk, it has been suggested that individualized treatment plans should be applied in the clinical management of the patients. Therefore, novel clinical tools are needed to estimate the efficiency of different treatment modalities and their combinations in individual patients in advance. The aim of this study is to evaluate and compare the effectiveness of different treatment modalities and their combinations on the AHI using a computational simulation approach. It was hypothesized that different treatment modalities are not equal in reducing the AHI and therefore patient-specific tools are needed to estimate the treatment success and to guide clinicians. To achieve this aim, 54 patients who underwent weight loss intervention (Tuomilehto et al., 2009) were analysed at baseline and after a 5-year follow-up. In this study, the effects of simulated CPAP treatment, simulated positional therapy, actual weight change and their combinations on the AHI in individual patients were evaluated and compared. This is the first study to address a computational simulation approach in individual OSA patients to compare the effects of weight loss, simulated CPAP treatment and simulated positional therapy and to provide novel tools for clinicians to estimate treatment success.

2 | METHODS

Eighty-two patients meeting the inclusion criteria (age ≥ 18 yr, body mass index (BMI), 26-45 kg/m^2; AHI ≥ 5 events/hr) were recruited into this study involving lifestyle intervention to reduce weight. Details of the study protocol can be found from previous reports (Kulkas et al., 2015; Tuomilehto et al., 2009). The Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland, gave approval for data collection (127/2004 and 1034/2019) and the patients gave their informed consent to participate in the lifestyle intervention. Home ambulatory polygraphy recordings were performed at baseline and after a 5-year follow-up with an Embletta Gold device (Embla). The recording montage consisted of nasal pressure, blood oxygen saturation, respiratory movements of the abdomen and thorax, snoring and body position. The data were analysed with Remlogic 3.2 software (Embla) and manually corrected based on the visual inspection of the signals. American Academy of Sleep Medicine (AASM) 2007 rules were applied in the respiratory event scoring (Rule 4A for hypopnea scoring) (Iber, Ancoli-Israel, Chesson, & Quan, 2007). For oxygen desaturations ≥4% was used as the threshold to score a desaturation event based on the AASM rules (Iber et al., 2007).

During the 5-year follow-up period 28 patients dropped out or were excluded from the analysis due to partially failed polygraphy recording. Thus, a total of 54 patients were included in the analysis. The 54 patients were further divided into three equally sized subclasses based on their weight change during the follow-up period. Based on the histograms the limits for weight change for the equally

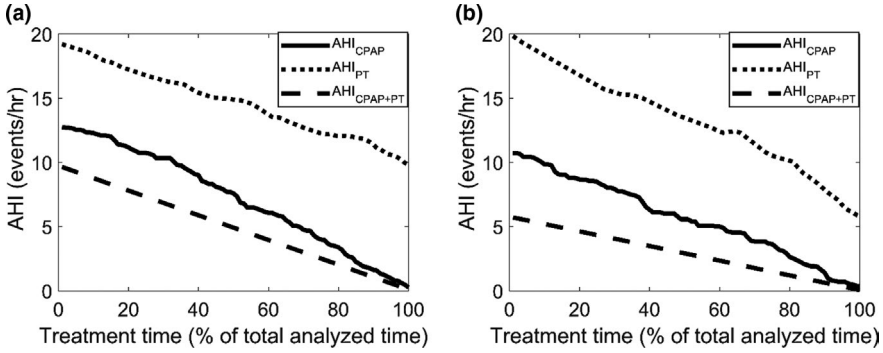

FIGURE 1 *Median apnea–hypopnea index (AHI) values of the whole population with respect to simulated treatment time at baseline (a) and after weight change (b). AHI_{CPAP} denotes continuous positive airway pressure (CPAP) treatment simulation, AHI_{PT} denotes positional therapy simulation, and $AHI_{CPAP+PT}$ denotes simulation of combined CPAP treatment and positional therapy. In positional therapy simulation, time point 0 represents supine AHI (sleeping in a supine position for the whole night). The amount of non-supine time is increased towards time point 100, which represents non-supine AHI. % of total analysed time denotes the percentage of the total analysed time starting from the beginning of the analysed recording and continuing until the end of the recording*

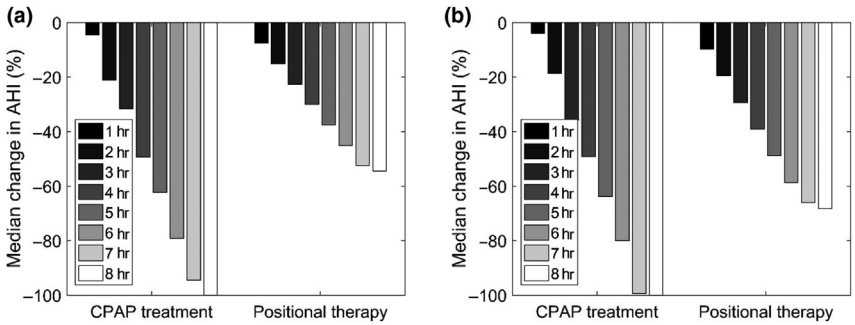

FIGURE 2 Computational simulation results on median apnea–hypopnea index (AHI) change during simulated continuous positive airway pressure (CPAP) treatment and positional therapy, with cumulative usage with 1-hr step increases (cumulative usage depicted with different colours) at baseline (a) and after follow-up (b). Positional therapy was simulated starting with a supine position only (non-supine time 0 hr) and continuing with cumulative 1-hr increases in time spent in a non-supine position

sized groups were >7% weight loss, 0%–7% weight loss and weight gain. The effect of weight change on the AHI was then evaluated based on the polygraphy recordings at baseline and after the follow-up of 5 years.

Continuous positive airway pressure treatment was computationally simulated for individual patients with Matlab (v.2016a Mathworks) (Kulkas et al., 2018). The simulation started from the beginning of the analysed time and the breathing cessation events inside the simulated CPAP period were considered to be totally prevented (AHI 0 events/hr during CPAP simulation time). The events during the rest of the night after the simulated period were considered to remain as they were in the original polygraphy recording. Simulated CPAP AHI was then calculated for each individual patient by dividing the number of events remaining after the CPAP simulation period by the total analysed time. To show the effects of the simulated CPAP treatment, the simulation was first performed for individual patients with 1-hr cumulative step increases. For more detailed analysis the simulated CPAP treatment period was selected to be 3.3-hr from the beginning of the analysed period based on the average CPAP adherence in the SAVE study (McEvoy et al., 2016). In addition to the 3.3-hr CPAP treatment time simulation, the CPAP simulation was also performed on mild and moderate OSA patients separately using previously determined (simulated) thresholds for sufficient CPAP treatment in different OSA severity categories (3.3, 5.6 and 6.5-hr for mild, moderate and severe patients, respectively) (Kulkas et al., 2018). The non-supine AHI was considered to represent the effect of simulated positional therapy on the AHI. In the combination of simulated CPAP treatment and positional therapy, AHI of 0 events/hr inside the simulated CPAP treatment period and non-supine AHI in the remaining part of the analysed time were utilized to compute the simulated total AHI. Baseline polygraphies were used to compute the AHI at baseline ($AHI_{baseline}$) and the follow-up polygraphies to compute the effect of weight change (AHI_W). The simulations were computed at baseline and after the follow-up. The simulations computed on the baseline polygraphies represent the simulated CPAP treatment (AHI_{CPAP}), simulated positional therapy (AHI_{PT}) and their combination ($AHI_{CPAP+PT}$). The simulations computed on the follow-up polygraphies represent the weight change combined with simulated CPAP treatment (AHI_{W+CPAP}), weight change combined with simulated positional therapy (AHI_{W+PT}) and weight change combined with simulated CPAP treatment and simulated positional therapy ($AHI_{W+CPAP+PT}$).

The Wilcoxon signed-ranks test was used to estimate the statistical significance of the differences in the AHI in the different

treatment scenarios. The Kruskal-Wallis test was used to compare the groups at baseline and the Mann–Whitney test in cases where the Kruskal-Wallis test showed statistically significant differences. The chi-square test was used to estimate the differences in the frequency of patients in different OSA severity classes between the weight change groups. $p < .05$ was considered as the limit of statistical significance. For statistical testing, SPSS version 25 (SPSS Inc) was used.

3 | RESULTS

An example of the simulated change in the AHI with respect to total analysed time is depicted in Figure 1. The median change in the AHI with cumulative 1-hr step increases in the simulated positional or CPAP treatment time is shown in Figure 2. The individual patient-specific CPAP simulation results for the AHI with 1-hr step increases in the CPAP simulation time are shown in Figure 3. The median (range) weight change in the three different weight-change groups was −10.1% (−25.7% to −7.0%), −2.9% (−6.5% to −0.7%) and 4.0% (0.4% to 18.7%). There were no statistically significant differences in the patient demographics between the groups at baseline, except for the non-supine AHI, which was lower in the weight-gain group compared to both weight-loss groups ($p < .05$) (Table 1.) At baseline, out of the included 54 patients, 38 patients had mild OSA and 16 patients had moderate OSA. In both weight-loss groups there were 11 mild and six moderate OSA patients and in the weight-gain group there were 16 mild and two moderate OSA patients. The number of mild and moderate OSA patients was not statistically significantly different between the weight-change groups (chi-squared test, $p = .214$). At baseline, there were eight, 10 and nine positional OSA patients having twice as high supine AHI compared to non-supine AHI at baseline, in the three weight-change groups, respectively.

Weight loss of >7% resulted in a 43.5% ($p < .05$) decrease in the AHI compared to baseline, whereas in the 0%–7% weight-loss group the reduction was 18% and did not reach statistical significance. Weight gain (median 4%) resulted in 84.7% higher AHI ($p < .05$) compared to baseline (Table 2, Figure 4). Simulated CPAP treatment (AHI_{CPAP}) resulted in 42.4% ($p < .05$), 35.5% ($p < .05$) and 35.1% ($p < .05$) reduction in the AHI at baseline in the weight loss >7%, weight loss 0%–7% and weight gain > 0% groups, respectively (Table 2, Figure 4). Simulated positional therapy (AHI_{PT}) resulted in 13.5% ($p < .05$), 30.7% ($p < .05$) and 33.7% ($p < .05$) decrease in the AHI at baseline in the groups, respectively (Table 2, Figure 4). A combination of simulated CPAP treatment and positional therapy ($AHI_{CPAP+PT}$) resulted in reduction of 53.3% ($p < .05$), 60.4% ($p < .05$) and 64.4% ($p < .05$) in the AHI in the groups, respectively (Table 2, Figure 4).

The combination of weight change and simulated CPAP treatment (AHI_{W+CPAP}) led to 69.4% ($p < .05$) and 48.8% ($p < .05$) AHI reduction in the weight-loss groups, respectively, and a 9.6% increase in the AHI in the weight-gain group (Table 2, Figure 4). The combination of weight change and simulated positional therapy (AHI_{W+PT}) resulted in 84.9% ($p < .05$), 43.4% and 9.2% AHI reduction in the groups, respectively (Table 2, Figure 4). The combination of all three treatments (i.e., weight change, simulated CPAP treatment and simulated positional therapy, $AHI_{W+CPAP+PT}$) reduced the AHI by 92.2% ($p < .05$), 72.7% ($p < .05$) and 50.3% ($p < .05$) compared to baseline AHI in the two weight-loss groups and one weight-gain group, respectively (Table 2, Figure 4).

When weight loss (AHI_W) was >7% it resulted in a reduction in the AHI that was similar to simulated CPAP treatment (AHI_{CPAP}), whereas in the other groups simulated CPAP treatment (AHI_{CPAP}) was superior (Table 2, Figure 4) compared to the other treatment modalities. Simulated positional therapy (AHI_{PT}) was not as effective as weight loss (AHI_W) or simulated CPAP treatment (AHI_{CPAP}) in the >7% weight-loss group (Table 2, Figure 4). In the 0%–7% weight-loss group, weight loss (AHI_W) and simulated positional therapy (AHI_{PT}) were equally effective, whereas simulated CPAP treatment was superior in reducing the AHI (Table 2, Figure 4). In the weight-gain group, simulated CPAP treatment (AHI_{W+CPAP}) and simulated positional therapy (AHI_{W+PT}) were able to compensate for the AHI increase due to the weight gain and resulted in a similar AHI to that at baseline (Table 2, Figure 4).

The effects of different simulated adherence levels of CPAP treatment in mild and moderate OSA patients are presented in Table 3. Increasing simulated CPAP treatment time statistically significantly decreases the AHI. As the disease severity increases, a higher adherence level to treatment is needed to normalize the AHI.

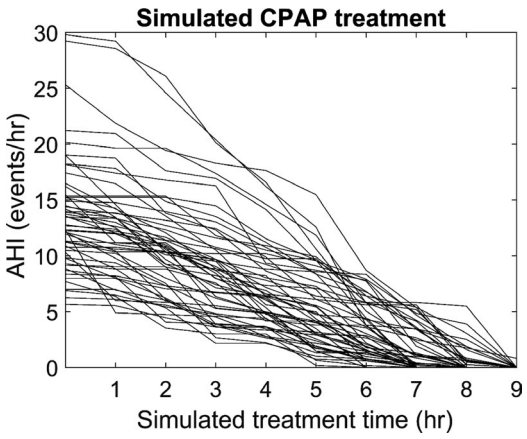

FIGURE 3 Patient-specific continuous positive airway pressure (CPAP) simulation results for the apnea–hypopnea index (AHI) with 1-hr step increases in the simulated CPAP treatment time for 54 patients at baseline. Each solid line represents an individual patient

4 | DISCUSSION

In this study, we compared the effects of lifestyle intervention-based weight loss, computational simulation of CPAP treatment, positional therapy, and their combinations on severity of OSA (i.e., values of AHI). In the >7% weight-loss group, weight loss and simulated CPAP

TABLE 1 Patient demographics (median (range)) at baseline in different weight-change groups

	Weight loss > 7%	Weight loss 0%–7%	Weight gain > 0%
Patients (females)	18 (6)	18 (5)	18 (4)
Height (m)	1.7 (1.6–1.8)	1.8 (1.5–1.9)	1.7 (1.6–1.9)
Age (yr)	54.5 (44.5–63.9)	53.6 (32.5–68.8)	51.4 (32.5–66.2)
Weight (kg)	92.5 (74.6–137.7)	92.2 (78.6–130.6)	93.5 (75.0–118.1)
BMI (kg/m^2)	32.1 (28.6–41.6)	31.9 (27.1–39.0)	32.5 (26.0–39.0)
AHI (events/hr)	13.2 (6.7–29.8)	13.9 (8.0–25.3)	11.3 (5.7–17.4)
Supine AHI (events/hr)	19.6 (0.0–52.5)	22.0 (6.7–80.5)	18.7 (8.2–44.0)
Non-supine AHI (events/hr)	10.0 (1.1–33.0)	11.8 (0.2–21.7)	5.9 (0.2–14.2)
ODI (events/hr)	12.2 (6.6–23.9)	13.2 (8.0–20.3)	10.9 (4.6–16.3)
Total analysed time (min)	436.4 (358.0–583.6)	436.4 (325.0–533.0)	437.7 (380.1–590.6)
Non-supine time (min)	323.8 (10.9–489.2)	268.6 (60.0–465.0)	295.4 (72.7–435.2)
Supine time (min)	112.0 (0.0–512.3)	149.3 (10.1–404.0)	182.3 (18.0–347.7)

Note: No statistically significant differences were observed in any parameter values between the groups (Kruskal-Wallis test), except for non-supine AHI values, which were lower in the weight-gain group compared to both weight-loss groups ($p < .05$ Mann–Whitney test). AHI, apnea–hypopnea index; BMI, body mass index; ODI, oxygen desaturation index.

TABLE 2 Apnea–hypopnea index (AHI) values (median (range)) at baseline and in different weight-change groups with different treatment modalities

	Weight loss > 7%	Weight loss 0%–7%	Weight gain > 0%
$AHI_{baseline}$	13.2 (6.7–29.8)$^{\#}$	13.9 (8.0–25.3)	11.3 (5.7–17.4)$^{\#}$
AHI_{W}	6.4 (1.5–22.0)*	11.8 (5.3–33.0)	17.1 (7.8–56.1)*
AHI_{CPAP}	8.3 (2.2–18.7)*	8.7 (2.8–18.2)$^{*,\#}$	7.4 (2.4–10.2)$^{*,\#}$
AHI_{PT}	10.0 (1.1–33.0)$^{*,\#}$	11.8 (0.2–21.7)*	5.9 (0.2–14.2)$^{*,\#}$
$AHI_{CPAP+PT}$	5.9 (0.7–20.5)*	6.0 (0.1–12.6)$^{*,\#}$	3.2 (0.2–8.2)$^{*,\#}$
AHI_{W+CPAP}	3.9 (0.8–15.3)$^{*,\#}$	7.6 (1.6–23.8)$^{*,\#}$	9.6 (4.0–39.1)$^{\#}$
AHI_{W+PT}	2.4 (0.0–18.7)$^{*,\#}$	7.7 (0.7–41.8)	12.0 (1.1–37.8)$^{\#}$
$AHI_{W+CPAP+PT}$	1.1 (0.0–7.2)$^{*,\#}$	3.9 (0.3–24.5)$^{*,\#}$	6.3 (0.7–25.8)$^{*,\#}$

Note: $AHI_{baseline}$ denotes AHI at baseline, AHI_{W} denotes AHI after weight change, AHI_{CPAP} denotes AHI after simulated CPAP treatment, AHI_{PT} denotes AHI after simulated positional therapy, $AHI_{CPAP+PT}$ denotes AHI after simulated CPAP and positional therapy, AHI_{W+CPAP} denotes AHI after weight change and simulated CPAP treatment, AHI_{W+PT} denotes AHI after weight change and simulated positional therapy, $AHI_{W+CPAP+PT}$ denotes AHI after weight change, simulated CPAP treatment, and simulated positional therapy.

*Indicates statistically significantly different from AHI at baseline ($p < .05$).

#Indicates statistically significantly different from AHI after weight change (AHI_{W}) ($p < .05$).

therapy with 3.3-hr adherence level were equally effective in reducing the AHI, whereas positional therapy was not as effective. In the 0%–7% weight-loss group, simulated CPAP treatment with a 3.3-hr adherence level was superior compared to weight loss or simulated positional therapy. In the weight-gain group, simulated CPAP treatment with a 3.3-hr adherence level and positional therapy were able to compensate for the AHI increase caused by weight gain. In general, the combination of all treatment modalities resulted in the greatest decrease in AHI values.

Weight loss is an effective way to reduce the AHI, whereas weight gain often leads to an increase in the AHI. However, the relationship between weight change and the AHI has been shown to be nonlinear (Kulkas et al., 2013, 2014; Newman et al., 2005). Weight-loss levels of 4% to 24% have been shown to reduce the AHI by 10%–75% (Joosten et al., 2017). Our results on the effect of weight loss on the AHI are in line with these previous findings. A weight loss greater than 7% produced a similar AHI reduction to simulated CPAP treatment with a 3.3-hr adherence level, whereas both of these treatments were superior to simulated positional therapy. In the 0%–7% weight-loss group, simulated CPAP treatment with a 3.3-hr adherence level provided greater AHI reduction compared to weight loss or simulated positional therapy. Weight loss can be hard to achieve and sustain, as shown by a 2-year follow-up study with four different types of diets randomly assigned to overweight adults (Sacks et al., 2009). In that follow-up, study subjects were able to lose 7% (6 kg on average) of their initial weight in 6 months, but at 2 years the average weight loss had reduced to 4 kg (Sacks et al., 2009). This indicates that although weight loss is an effective

way to manage OSA, it is hard to apply in clinical practice as even an intervention with guidance and dietary instruction only produced limited weight loss in the long term (Sacks et al., 2009).

In a recent study, CPAP treatment was found to be inefficient in terms of preventing cardiovascular risk, which might be partially because adherence was limited to an average of 3.3-hr per night (McEvoy et al., 2016). We have previously shown in a simulation study that the required levels of CPAP usage to normalize the AHI are 3.3, 5.6 and 6.5-hr for mild, moderate, and severe OSA patients, respectively (Kulkas et al., 2018). In the present study, the typical CPAP adherence level of 3.3-hr was used in the simulation of CPAP treatment based on the adherence levels witnessed in the SAVE study (McEvoy et al., 2016). With this adherence level, simulated CPAP treatment was able to lower the AHI in all weight-change groups and compensate for the AHI increase in the weight-gain group. In the simulation of CPAP treatment all breathing cessation events were considered to be prevented during the simulated period. However, it has been shown that during CPAP treatment there can be residual events (McEvoy et al., 2016), which could lead to slightly higher AHI values than the simulated CPAP treatment shows. In addition, the adherence to CPAP therapy is patient specific and therefore using a 3.3-hr adherence level might not always fully represent the actual clinical situation. It is known that lower levels of CPAP adherence lead to a greater AHI, whereas higher adherence levels reduce the AHI more. Based on the additional simulations conducted separately for the mild and moderate OSA patient groups, it was seen that the previously determined adherence level of 3.3-hr was sufficient to reduce the AHI to close to the normal level in mild OSA patients, whereas a 5.6-hr adherence level was needed with patients having moderate OSA. However, it is very important to note that there is substantial individual variation in the required levels to normalize the AHI and therefore individualized treatment plans and optimized adherence levels are needed. This further highlights the potential clinical value of the present simulation approach. The computational simulation can be adjusted individually at a patient level with different adherence levels and provide an estimate of the AHI reduction to motivate the individual patient to have sufficient CPAP treatment adherence (Figure 3) (Kulkas et al., 2018).

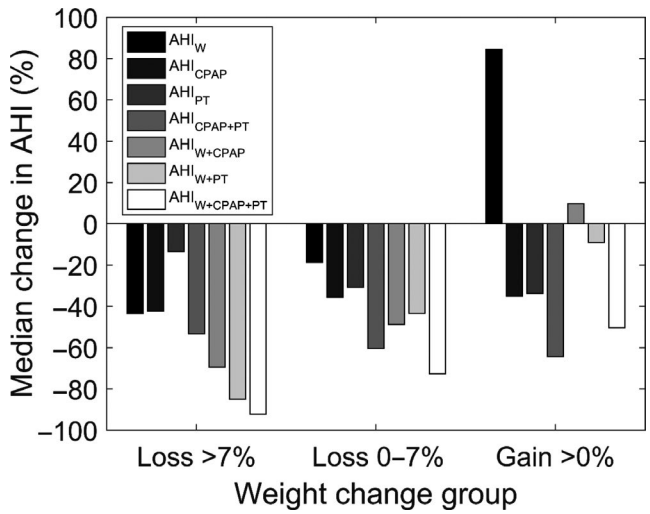

FIGURE 4 Median change in the apnea–hypopnea index (AHI) compared to baseline AHI after different treatments and their combinations. AHI_W denotes AHI after weight change, AHI_{CPAP} denotes AHI after simulated continuous positive airway pressure (CPAP) treatment, AHI_{PT} denotes AHI after simulated positional therapy, $AHI_{CPAP+PT}$ denotes AHI after simulated CPAP and positional therapy, AHI_{W+CPAP} denotes AHI after weight change and simulated CPAP treatment, AHI_{W+PT} denotes AHI after weight change and simulated positional therapy, $AHI_{W+CPAP+PT}$ denotes AHI after weight change, simulated CPAP treatment, and positional therapy

CPAP has been shown to be a more effective treatment than positional therapy (Barnes et al., 2017). Our results also support this, showing greater reductions in the AHI in the weight-loss groups with simulated CPAP treatment compared to simulated positional therapy. However, it has been shown that in severe OSA some patients could gain even greater benefits from positional therapy compared with using CPAP with suboptimal adherence (Oksenberg, Gadoth, Töyräs, & Leppänen, 2019). In the weight-gain group, simulated positional therapy was able to compensate for a weight-related increase in the AHI. In the present study, the non-supine AHI was utilized as a simulation of positional therapy. However, avoiding the supine sleeping position for the whole night is a challenging task and non-adherence to positional therapy can limit the success of the therapy (Omobomi & Quan, 2018). Therefore, the current results might overestimate the effect of positional therapy to some extent. In our cohort there were differences between the groups in the baseline values of the non-supine AHI, with the lowest non-supine AHI values being in the weight-gain group. This could also lead to some overestimation of the effect of simulated positional therapy in the weight-gain group compared to

TABLE 3 Simulated effect of continuous positive airway pressure (CPAP) treatment on the apnea–hypopnea index (AHI) (median (range)) at different adherence levels in mild (n = 38) and moderate (n = 16) OSA patients

	$AHI_{baseline}$	$AHI_{CPAP3.3h}$	$AHI_{CPAP5.6h}$	$AHI_{CPAP6.5h}$
Mild OSA (n = 38)	11.3 (5.7–14.9)	6.6 (2.2–12.7)*	2.7 (0.0–8.6)*	1.0 (0.0–6.3)*
Moderate OSA (n = 16)	18.2 (15.0–29.8)	11.8 (6.8–18.7)*	5.7 (0.4–10.2)*	1.4 (0.0–7.4)*

Note: Applied adherence levels are based on a previously published simulation study (Kulkas et al., 2018). $AHI_{baseline}$ denotes AHI at baseline, $AHI_{CPAP3.3h}$ denotes AHI after 3.3-hr of simulated CPAP treatment, $AHI_{CPAP5.6h}$ denotes AHI after 5.6 hr of simulated CPAP treatment, and $AHI_{CPAP6.5h}$ denotes AHI after 6.5 hr of simulated CPAP treatment. OSA, obstructive sleep apnea.
*Indicates statistically significant difference compared to $AHI_{baseline}$ ($p < .05$).

the weight loss groups. It is acknowledged that the success of positional treatment is dependent on the baseline situation with regards to the number of events and time spent during the night in the supine position. With simulation tools the level of adherence to positional therapy and the individual variation in the baseline can be taken into account and the treatment outcomes in terms of AHI reduction can be individually predicted for each patient.

In the current study, there were 38 mild and 16 moderate OSA patients at baseline. In both weight-loss groups there were 11 mild and six moderate OSA patients and in the weight-gain group 16 mild and two moderate OSA patients. The differences in the number of mild and moderate OSA patients between the weight-change groups might affect the results. However, there were no statistically significant differences in AHI values, nor in the number of mild and moderate OSA patients, between the weight-change groups, indicating similar OSA severity. Therefore, the differences in the numbers of mild and moderate patients between the groups are not expected to significantly undermine the present results. As there were no severe OSA patients in the current study population, further research is needed to generalize our findings also to severe OSA patients. The computational simulations presented in this study can, however, be performed for all patients irrespective of OSA severity.

The combination of simulated CPAP treatment, simulated positional therapy and weight loss provided the highest reduction in the AHI in the weight-loss groups. In the weight-gain group, the combination of simulated CPAP treatment and positional therapy was able to reduce the AHI even when weight gain increased the AHI substantially compared to baseline. Individualized solutions are needed to provide optimal treatment results in OSA patients. Estimation of the capability of an individual to comply with long-term weight-loss schemes, and adherence to CPAP treatment or positional therapy at a sufficient level to reduce the severity of OSA, is a challenging clinical task. With computational simulation tools, clinicians could estimate the effectiveness of different treatment modalities and their combinations at different adherence levels in advance and produce an optimal treatment plan for individual patients to reduce OSA severity and to prevent the harmful consequences of OSA. The simulation data could be used for personalized, preventive and patient-centric management of OSA to make optimized individualized treatment plans and to find optimal individualized solutions together with the patient. This would further enable us to take into account the patient's ability and motivation to comply with the selected treatment at a sufficient level in advance. On the other hand, the simulation results could be also used to motivate the patients to comply with the selected treatment at a sufficient level. With the present simulation approach, treatment plans could be further optimized and individualized based on the adherence levels witnessed during the actual treatment phase.

The management of OSA is a complex process with different treatment modalities available. Weight loss, CPAP treatment, and positional therapy are all valid tools for treatment of OSA, but they all have their limitations. Tools that could provide estimates of the treatment success of different modalities and their combinations at the individual patient level could aid clinicians to determine individually sufficient treatment levels and modalities. In computational simulations the levels of adherence to CPAP treatment and positional therapy can be adjusted and the analysis performed at the individual patient level to predict the treatment success in terms of AHI reduction. Utilizing the information on different treatment levels and modalities could encourage clinicians to evaluate the treatment effectiveness at different levels of adherence in advance and motivate patients individually to comply with the treatment at sufficient levels to reduce OSA severity and the related health risk.

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CONFLICTS OF INTEREST

The authors declare that they do not have any conflicts of interest.

AUTHOR CONTRIBUTIONS

AK conceived and designed the research and drafted the manuscript. All the authors participated in analysis and interpretation of data. All the authors revised the manuscript critically and approved the manuscript in its final form.

ETHICAL APPROVAL

The Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland, approved the data collection (127/2004 and 1034/2019) and the patients gave their written consent to participate in the lifestyle intervention. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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