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Evaluation of upper airway patency during Cheyne–Stokes breathing in heart failure patients

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ABSTRACT: **Little is known about the changes in upper airway calibre in Cheyne–Stokes respiration (CSR) during sleep in patients with congestive heart failure. This study aimed to test the hypothesis that upper airway closure occurs during central CSR events, by assessing upper airway calibre during sleep using the forced oscillation technique (FOT).**

Nine males with compensated heart failure (left ventricular ejection fraction mean±SEM 27.9±5.1%) and predominant central CSR (apnoea/hypopnoea index 43.9±4.2 events·h^{-1}) were studied during overnight polysomnography, which included pneumotachography, inductance plethysmography or oesophageal pressure and FOT-derived impedance signal (|Z|).

Baseline |Z| values during stable breathing in stage 2 sleep were 11.0±1.3 cmH_2O·s·L^{-1}. Mean |Z| increased to 31.9±6.7 cmH_2O·s·L^{-1} during obstructive apnoeas (7% of events, n=46). Increases in |Z| consistent with upper airway narrowing (more than two-fold baseline) were common during central apnoeas (50±12% of events) occurring in the middle or end of apnoeas and occurred during some central hypopnoeas (16±10% of events), typically in the expiratory phase.

These findings indicate that in heart failure patients, reductions in upper airway calibre are common during CSR apnoeas, and may also occur during central hypopnoeas.

KEYWORDS: **Central sleep apnoea, Cheyne–Stokes breathing, forced oscillation, upper airway**

Cheyne–Stokes respiration (CSR) during sleep is prevalent among patients with congestive heart failure (CHF) [1] and is associated with increased mortality [2, 3] The pathophysiology of CSR remains incompletely understood. A key factor triggering central apnoeas is a reduction in carbon dioxide tension below the apnoea threshold [1], which is related to sleep–wake instability, altered ventilatory and cerebrovascular carbon dioxide chemosensitivity, prolonged circulation time and stimulation from pulmonary irritant receptors [1, 4–6]. However, the observation that there may be a shift between obstructive and central apnoeas in CSR-CHF [7, 8], that CSR can be affected by posture, [9, 10] and that it may be suppressed by continuous positive airway pressure (CPAP) in some patients [11] suggests that upper airway instability may also play a role in this disorder. Dynamic changes in upper airway calibre might, therefore, be a further factor contributing to ventilatory instability in CSR-CHF.

Upper airway closure has previously been reported to occur in some forms of both spontaneous and experimentally induced central apnoea [7, 12–15]. However, upper airway patency during central apnoeas and hypopnoeas has not been systematically investigated in patients with CHF.

The forced oscillation technique (FOT) is a non-invasive method for instantaneous measurement of respiratory system mechanics which has been shown to be reliable in assessing upper airway calibre during sleep in patients with obstructive sleep apnoea (OSA) [16–18]. FOT systems have been developed which measure impedance (|Z| cmH_2O·s·L^{-1}) of the respiratory system during sleep in a continuous fashion without disturbing sleep architecture or altering upper airway muscle tone [19]. FOT has been shown to be a sensitive indicator of dynamic changes in upper airway calibre during obstructive events [17] and can be used to detect respiratory events and guide CPAP titration [16, 20, 21].

In the present study, we hypothesised that in CHF patients with CSR, upper airway closure would occur during central apnoeas and hypopnoeas. The objective of the study was to evaluate changes in upper airway calibre during CSR using FOT.

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METHODS

Subjects

Nine patients with stable chronic CHF being screened for the CANPAP study [11] were recruited from the Sleep Disorders and Cardiac Function Clinics of the McGill University Health Centre (Montreal, QC, Canada). The Research Ethics Board approved the study protocol and subjects provided written informed consent.

Eligibility requirements have been described in full elsewhere [22]. Briefly, subjects were adults with stable CHF due to ischaemic, idiopathic or hypertensive cardiomyopathy with left ventricular ejection fraction <40% (by radionuclide angiography) and ⩾15 apnoeas and hypopnoeas per hour of sleep (apnoea/hypopnoea index (AHI)), of which >50% were central at screening polysomnography (PSG). We recruited eligible subjects who either declined participation in the main study or were studied before randomisation within CANPAP.

Experimental protocol

After initial screening PSG to determine eligibility, each subject underwent a subsequent overnight (n=8) or daytime (n=1) conventional polysomnogram with the addition of oesophageal pressure (P_{oes}) monitoring when tolerated by the subject, and a sealed face mask connected to the FOT circuit for measurement of respiratory system impedance ($|Z|$).

Each polysomnogram was initially scored in a standard manner (sleep and respiratory events) [11] by a trained polysomnographic technologist. Following this, FOT-derived impedance values during respiratory events in non-rapid eye movement (REM) sleep were assessed as described below.

Measurements

Polysomnography

The following signals were included. 1) Electroencephalogram (C4A1, C3A2), chin electromyogram, electrocardiogram and electrooculogram which were recorded and scored for sleep stages and arousals according to standard criteria [23, 24]. 2) Nocturnal arterial oxygen saturation measured by pulse oximetry (Ohmeda Biox 3700; Roxon Inc., Montreal, ON, Canada). 3) Rib cage and abdominal movements by inductance plethysmography (Respitrace; Ambulatory Monitoring Inc., Ardsely NY, USA). 4) P_{oes} measured using a balloon-tipped catheter attached to a differential pressure transducer (Validyne, Northridge, CA, USA) and airflow and oscillatory impedance using the FOT device as described below. These variables were simultaneously recorded using a standard PSG system (Sandman, Ottawa, ON, Canada) and a second computerised system (CODAS; DATAQ Instruments, Akron, OH, USA) for subsequent respiratory signal processing. At least 3 h of sleep were required in order for PSG data to be included in the final analysis.

Oscillatory impedance measured using the FOT

FOT was applied as previously described [17, 18, 25]. A full-face mask was connected to a mesh wire-based pneumotachograph (resistance=0.522 $L \cdot s^{-1}$) connected to a T-piece. One arm of the T-piece was connected (Tb1) to a chamber with a loudspeaker (8BR40; Beyma, Valencia, Spain) and the other arm to a tube (Tb2) acting as a pneumatic low-pass filter. A continuous bias flow (0.4 $L \cdot s^{-1}$) through all the tubing was applied to the system in order to avoid rebreathing. A small amplitude (1 cmH_2O peak-to-peak) pressure oscillation of 5 Hz was generated with the loudspeaker and applied on the mask while the patient breathed spontaneously. Mask pressure and flow signals were measured with differential pressure transducers (range ± 9 and 2 cmH_2O, respectively; Validyne). The frequency responses at 5 Hz of the flow and pressure transducers were matched within 1% in gain and 1° in phase. Special attention was paid to avoid leaks by carefully fitting the full-face mask. The raw flow and pressure signals were analogically low-pass filtered (8-pole Butterworth, 32 Hz) and introduced into a microprocessor-based system for digital on-line computation of $|Z|$ [26]. This signal was recorded on the polygraph, as well as in the CODAS acquisition system as an additional channel.

Data analysis

Scoring of respiratory events

Scoring criteria for respiratory events were identical to those used in the CANPAP study [11], although with substitution in the present study of the pneumotachograph airflow signal for nasal pressure, and the availability of additional information concerning respiratory effort in subjects with P_{oes} catheters in place. CSR was defined as repetitive cycles of apnoeas and/or hypopnoeas, alternating with hyperpnoeas which had a crescendo/decrescendo pattern of tidal volume, occurring at a rate of >15 events·h^{-1} of sleep. Central apnoeas were defined as the absence of tidal volume for ⩾10 s without thoraco-abdominal motion and central hypopnoeas as a reduction of ⩾50% in tidal volume from baseline for ⩾10 s with flow paralleling P_{oes} and/or thoraco-abdominal displacement, and without clear inspiratory airflow limitation on the pneumotachograph signal. Apnoeas and hypopnoeas were classified as obstructive if there was out-of-phase motion of the rib cage and abdomen, incremental respiratory effort disproportionate to flow on P_{oes} tracing, or clear inspiratory airflow limitation on the pneumotachograph signal.

Measurements of impedance values $|Z|$ during apnoeas and hypopnoeas

We analysed impedance in one out of five CSR events in each patient, with the first event randomly selected then every fifth consecutive event analysed. For obstructive events, due to the small number, all events observed were analysed.

Impedance was measured during the apnoeic or hypopnoeic period of the CSR cycle. For apnoeas, measurements of impedance were performed by computing the mean $|Z|$ value of a 2-s window at the beginning, middle and end of the apnoea. For hypopnoeas, to determine the beginning and end of the measurement period, we defined a threshold flow as 50% of the mean of the 10 peak values of inspiratory flow during stable respiration (without CSR or OSA) in supine stage 2 sleep. A hypopnoea began with the first cycle that included a peak inspiratory flow below the threshold flow and it ended with the last cycle that contained a peak inspiratory flow below the threshold flow. To measure $|Z|$ values during hypopnoea, first, the mean mid-inspiratory $|Z|$ value (window=0.4 s at the middle of inspiration) for 10 consecutive breathing cycles of spontaneous normal breathing was averaged in order to obtain a normalised inspiratory value (stage 2 supine or awake if not available during sleep). The same analysis was performed with the corresponding expiratory cycle phases in order to obtain a

normalised mid-expiratory value. Then, inspiratory degree of occlusion was calculated by averaging the mid-inspiratory value (window=0.4 s) for each respiratory cycle during the event and expiratory degree of occlusion was calculated by averaging the mid-expiratory value (window=0.4 s) for each respiratory cycle during the event.

Previous studies in patients with OSA have indicated that major upper airway narrowing or collapse can be reliably identified when the impedance value increases to levels more than twice baseline values during tidal breathing [16, 27]. Therefore, for the various categories of respiratory events we determined the proportion of events for which |Z| exceeded this value.

Statistical analysis

FOT-derived impedance |Z| values were expressed as absolute values or as percentage of baseline |Z| value during stable breathing. |Z| values during stable breathing, central and obstructive apnoeas and hypopnoeas were normally distributed and mean values were compared using unpaired t-tests. Correlations between anthropometric or clinical measures and |Z| values were assessed using Pearson's product-moment coefficient. Data are expressed as mean±SEM, unless otherwise specified. A threshold of $p<0.05$ was used for statistical significance.

RESULTS

Subject characteristics are presented in table 1. On the original diagnostic polysomnograms, the apnoea index was 30.5±3.6 events·h^{-1}, total sleep time was 5.2±0.8 h and 66.3±3.6% of events were central. CHF aetiology was ischaemic in six subjects and idiopathic in three. New York Heart Association class was II in four subjects and III in five subjects. Placement of an oesophageal catheter was attempted in all subjects but was unsuccessful due to discomfort in four. Subject characteristics were not significantly different between those with *versus* those without oesophageal catheters.

Representative tracings of typical respiratory events are shown in figures 1–3. Figure 1a illustrates the impedance signal during central apnoeas during the CSR cycle in which the impedance value remained low throughout. In contrast, figure 1b shows central apnoeas during which the impedance signal increased substantially during the course of the events, followed by a rapid fall to baseline as soon as respiratory effort was initiated.

Figure 2 illustrates central hypopnoeas as evidenced by the changes in airflow paralleling changes in respiratory effort. Impedance values during hypopnoeas were often increased above baseline values during stable breathing, most often during the hypopnoeic phase of the CSR cycle (fig. 2a) but in some cases across the CSR cycle (fig. 2b). |Z| values tended to be higher during expiration and fell during inspiration. This pattern was observed in five of the eight subjects with central hypopnoeas. Overall, however, mean |Z| values during the expiratory phase were not significantly higher than during the inspiratory phase (15.7±0.8 *versus* 14.9±1.1 $cmH_2O \cdot s \cdot L^{-1}$; p=0.81).

We observed a small number of obstructive events in this patient group. One example is shown in figure 3 with the typical CSR pattern of effort during absent airflow, followed by a sudden resumption of airflow with airway re-opening. The impedance signal increases progressively during the obstructive event with, initially, impedance increasing during inspiratory effort and decreasing during the expiratory phase, followed by consistently high values indicative of persistent airway closure, followed by a rapid fall in impedance at airway re-opening.

A total of 647 events were analysed, the majority of which were central (table 1). As noted previously, for central events, every fifth event was analysed, while all obstructive events observed were analysed. All nine subjects demonstrated central apnoeas

TABLE 1 Subject characteristics and proportion of respiratory events with increased forced oscillation technique-derived impedance signal (|Z|)

Subject	Age yrs	BMI kg·m^{-2}	LVEF %	AHI# events per h	Central apnoeas¶		Central hypopnoeas¶		OAH+
					Events n	|Z| >2× proportion§	Events n	|Z| >2× proportion§	Events n
1	47	24.3	5	40.8	29	0.34	14	0.00	6
2	68	25.7	20	57.2	110	0.72	97	0.40	18
3	76	32.4	39	62.9	34	0.62	45	0.38	
4	84	31.2	33	48.9	60	0.20	29	0.07	
5	59	48.7	29	24.2	37	1.00			
6	70	24.3	38	28.0	16	0.00	2	0.00	
7	60	23.0	23	44.8	10	1.00	2	0.00	22
8	70	31.0	40	58.0	12	0.08	14	0.14	13
9	63	24.5	23	50.0	48	0.56	16	0.31	
Mean±SE	66.3±3.4	29.5±2.7	27.9±3.8	46.1±4.4		0.50±0.12		0.16±0.10	

BMI: body mass index; LVEF: left ventricular ejection fraction; AHI: apnoea/hypopnoea index; OAH: obstructive apnoeas and hypopnoeas. #: from original diagnostic polysomnogram; ¶: from study night, every fifth event analysed; +: from study night, all events analysed; §: proportion of events with |Z| greater than two-fold baseline values (see Methods).

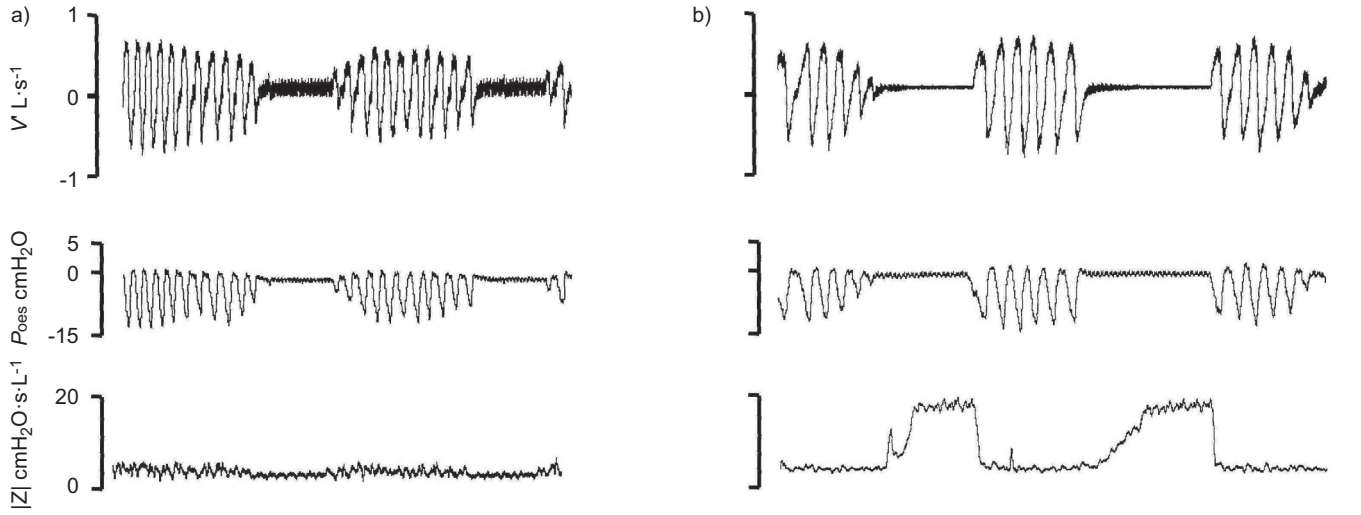

FIGURE 1. Examples of central Cheyne–Stokes respiration apnoeas with absence of airflow and respiratory effort from the same patient in which a) the forced oscillation technique-derived impedance signal (|Z|) remains low throughout the event, and b) |Z| increases during the course of the event. *V'*: gas flow (a positive value indicates inspiration); P_{oes}: oesophageal pressure.

(40±10 events analysed per subject), eight out of nine demonstrated central hypopnoeas (27±11 events analysed per subject), while four subjects demonstrated obstructive events (18±3 analysed per subject).

The mean baseline FOT-derived impedance value during stable breathing in non-REM sleep was 11.0±1.3 cm $H_2O \cdot s \cdot L^{-1}$. For the different categories of respiratory events, mean |Z| values for central hypopnoeas (34% of total events analysed), central apnoeas (55% of events), obstructive hypopnoeas (4% of events) and obstructive apnoeas (7% of events) were 15.3±1.7 $cmH_2O \cdot s \cdot L^{-1}$, 27.3±5.9 $cmH_2O \cdot s \cdot L^{-1}$, 30.6±11.5 $cmH_2O \cdot s \cdot L^{-1}$ and 31.9±6.7 $cmH_2O \cdot s \cdot L^{-1}$, respectively. All of these values were significantly greater than baseline ($p<0.005$).

Figure 4 shows mean values for |Z| during the first, middle and latter third of apnoeas for central *versus* obstructive apnoeas. While values during obstructive events tended to be higher, there were substantial increases in mean |Z| during central events indicating prominent degrees of upper airway closure.

Figure 5 illustrates the proportion of respiratory events during which upper airway closure occurred as defined by a criterion of |Z| reaching twice the baseline value during stable breathing. Given the small number of obstructive events, apnoeas and hypopnoeas were pooled for this analysis. For central hypopnoeas, five subjects demonstrated varying degrees of upper airway closure. For central apnoeas, the frequency of upper airway closure during events also varied between subjects, with upper airway closure occurring rarely or not at all in some subjects but in a majority of events in others. The upper airway was more likely to be occluded during central apnoeas than hypopnoeas as shown by the significantly higher proportion of events with |Z| values exceeding the baseline values for central apnoeas compared with hypopnoeas (0.50±0.12 *versus* 0.16±0.1, $p=0.03$).

There were no systematic differences in subject characteristics including age, body mass index, left ventricular ejection fraction, AHI or other measures of apnoea severity between subjects with frequent *versus* rare or absent upper airway closure during central events (table 1). Airway closure during central events was not consistently related to the occurrence of obstructive events in the same subjects. There was a trend to a positive correlation between body mass index and baseline pre-event |Z| value ($r=0.64$, $p=0.06$). No significant correlations were identified between anthropometric measures and the proportions shown in figure 5. For the four subjects who demonstrated occasional obstructive events, |Z| values during central apnoeas were high in two and low in the other two.

DISCUSSION

In this study, we applied the FOT to assess upper airway patency during predominantly central sleep apnoeas and hypopnoeas in subjects with compensated chronic CHF. We found that airway closure occurred, to a variable extent, during central apnoeas, with some patients frequently demonstrating airway closure, and others rarely demonstrating evidence of upper airway collapse. Upper airway narrowing was less common during CSR hypopnoeas than apnoeas, and during hypopnoeas, upper airway impedance tended to be higher during expiration than inspiration.

The FOT-derived impedance |Z| signal has previously been used to identify upper airway obstruction during sleep in OSA [17]. Upper airway closure is a dynamic process in OSA associated with an instantaneous large increase in respiratory resistance, which cannot be accounted for by other changes within the respiratory system. One limitation of our study is that we did not directly visualise the upper airway. However, invasive techniques such as video-endoscopy would probably be poorly tolerated in CHF patients whose sleep quality is generally poor. The values of the impedance signal observed during obstructive events in the present study were comparable with those previously described in severe OSA (|Z|=36±8 $cmH_2O \cdot s \cdot L^{-1}$) [12] supporting the conclusion that high impedance values observed during central events were indeed indicative of substantial upper airway narrowing.

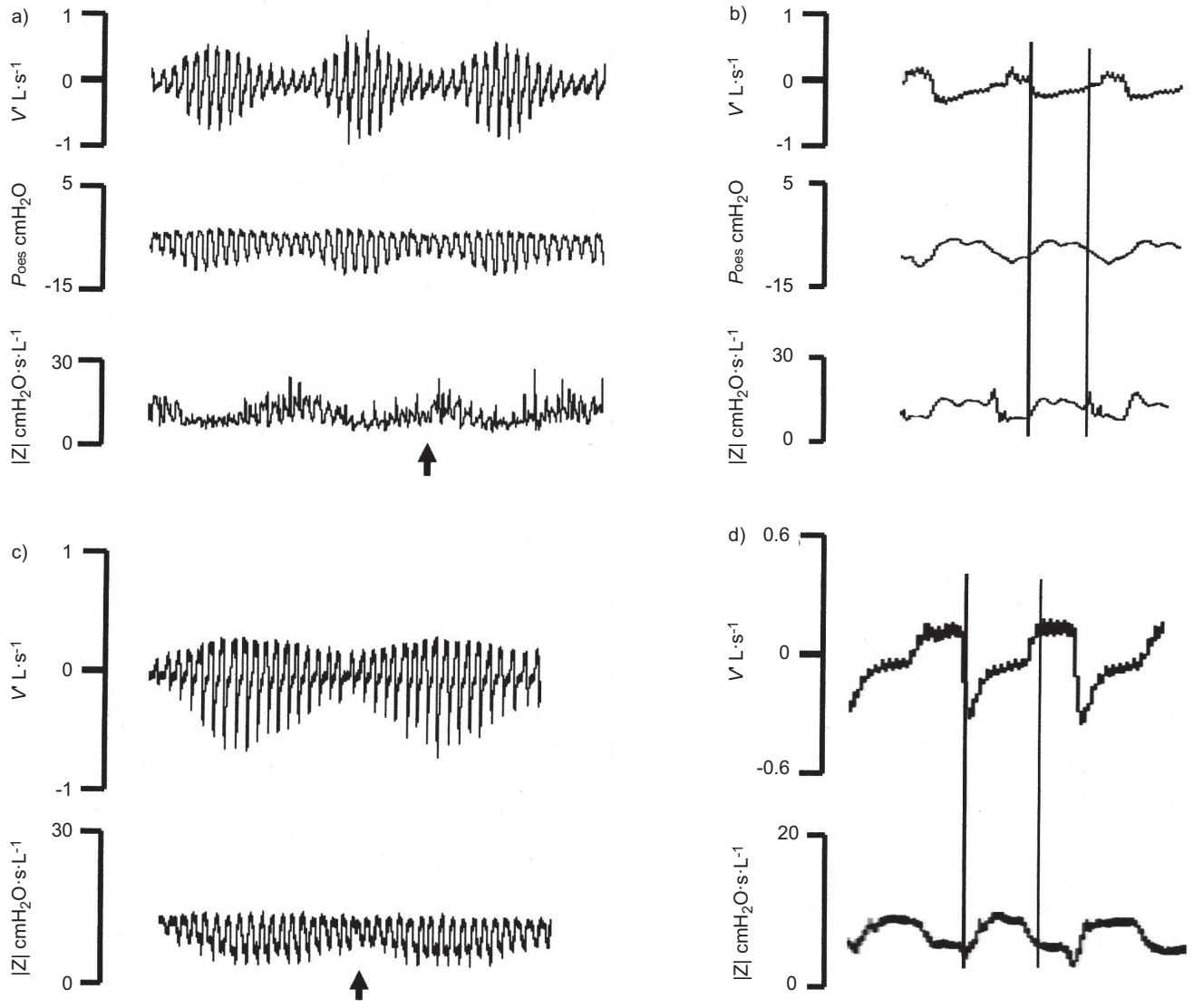

FIGURE 2. Representative tracings of central Cheyne–Stokes respiration (CSR) hypopnoeas with the variation in airflow paralleling respiratory effort. a) The forced oscillation technique-derived impedance signal (|Z|) increases in expiration during the hypopnoeic phase of the CSR cycle. b) Magnified view of the segment indicated by the arrow in (a) illustrating the increase in |Z| during the expiratory phase of the respiratory cycle. c) Tracings from another subject in whom expiratory |Z| values remain elevated across the CSR cycle with discrete reductions in |Z| during inspiration. d) Magnified view of the segment indicated by the arrow in (c). V': gas flow; P_{oes}: oesophageal pressure.

Another potential limitation of the study was the inability of four of the nine subjects to tolerate an oesophageal catheter, which can be a useful signal in distinguishing central from obstructive hypopnoeas. Only central apnoeas were observed in one of the four subjects without P_{oes}, and in the other three subjects the number of central apnoeas sampled/analysed outnumbered central hypopnoeas two-fold. Nonetheless, in the latter subjects we were confident of the central nature of the events so designated, based on the pneumotachography and inductance plethysmography signals, as well as the characteristic pattern of |Z| changes during these events (fig. 2 *versus* fig. 3). Another potential limitation of the study was the relatively small number of subjects which may have restricted our ability to identify anthropometric and other clinical factors in contributing to upper airway collapse.

The findings of the present study are in accordance with previous studies providing direct evidence of upper airway collapse during spontaneous or induced central apnoeas/hypopnoeas using acoustic or video-endoscopic techniques [13, 15]. More recently, VANDERVEKEN *et al.* [12] applied FOT in eight patients with predominantly OSA and demonstrated variable increases in |Z| during a small number of central apnoeas. However, to our knowledge, ours is the first study to assess upper airway calibre with FOT in a group consisting of exclusively stable CHF patients with predominantly central events.

FOT alone does not permit determination of the specific site of upper airway obstruction, or whether airway closure is passive or active. Reductions in pharyngeal cross-sectional area level have been observed by video-endoscopy during spontaneous

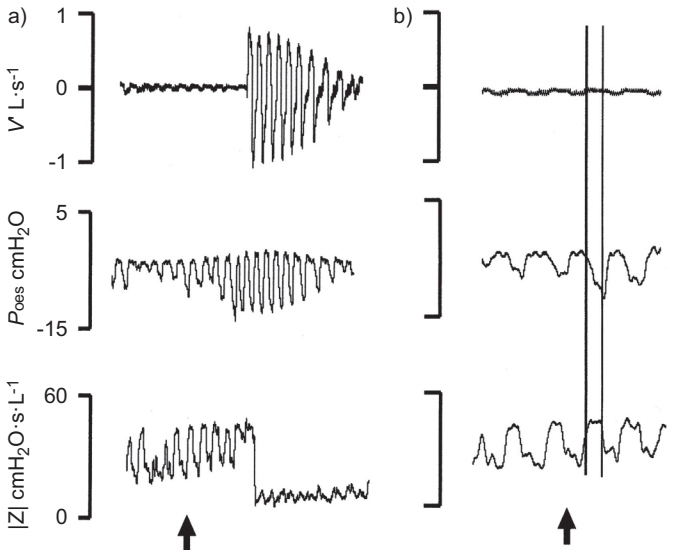

FIGURE 3. Representative tracings of an obstructive hypopnoea with a Cheyne–Stokes respiration pattern of respiratory effort. a) The forced oscillation technique-derived impedance signal (|Z|) increases in concert with increasing respiratory effort, followed by an abrupt fall signalling airway re-opening at the end of the obstructive event. b) Magnified view of the segment indicated by the arrow in (a). The marked increases in impedance are occurring during the inspiratory phase consistent with dynamic inspiratory airway collapse.

idiopathic central apnoeas [13, 15]. In one study [13], electromyogram recordings demonstrated that pharyngeal constrictors were inactive, suggesting passive airway closure. In addition, SANKRI-TARBICHI *et al.* [14] and BADR *et al.* [15] observed diminished pharyngeal cross-sectional area on video-endoscopy associated with increased upper airway resistance during induced central hypocapnic hypopnoea. Of note, retropalatal narrowing under these low drive/hypotonic conditions occurred predominantly during the expiratory phase [14]. In

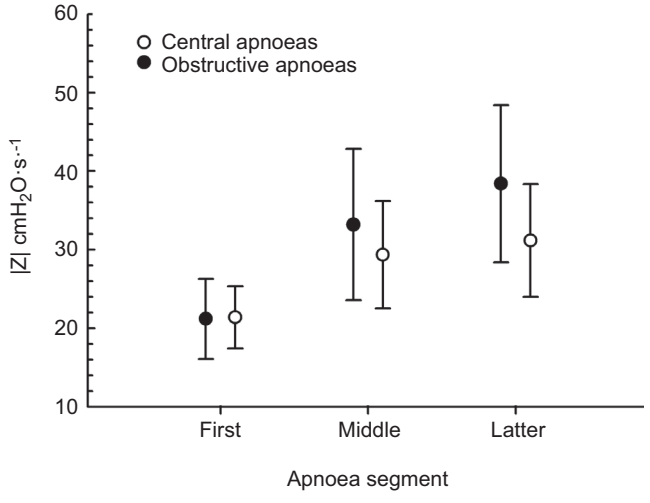

FIGURE 4. Group mean±SE values for the forced oscillation technique-derived impedance signal (|Z|) during the first, middle and latter third of Cheyne–Stokes respiration central apnoeas compared with obstructive apnoeas.

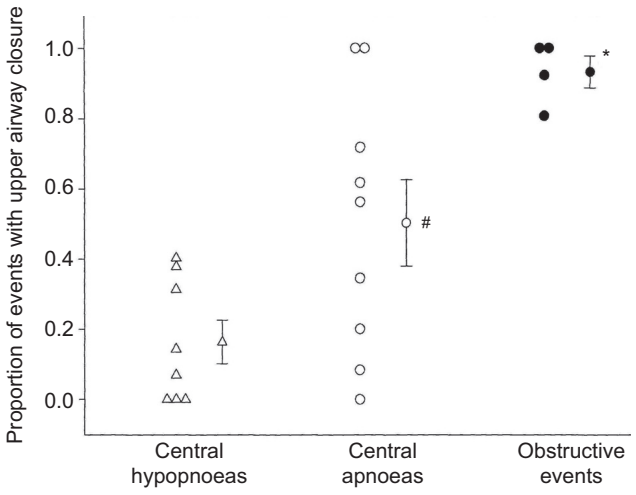

FIGURE 5. Proportion of respiratory events with forced oscillation technique-derived impedance signal (|Z|) increases consistent with upper airway closure (|Z| >2× baseline value) by event type. Symbols indicate individual patient values. Group mean±SE values are indicated by error bars. *: $p<0.05$ *versus* central events (hypopnoeas or apnoeas). #: $p<0.05$ *versus* central hypopnoeas.

our study, the development of upper airway closure during the course of central apnoeas, with immediate airway re-opening associated with the onset of inspiratory effort and airflow (figs 1b and 4) could be consistent with passive pharyngeal collapse during the apnoea phase followed by active re-opening of the airway as inspiratory drive resumes.

During CSR hypopnoeas, some subjects demonstrated substantial increases in |Z| values compared with stable breathing periods at similar lung volumes as judged from respiratory inductance plethysmography signals, consistent with upper airway narrowing. This was most prominent during the hypopnoeic phase of the cycle (fig. 2), and impedance tended to be higher in expiration and fall during inspiration. Lung volume changes could potentially have contributed to the inspiratory decrease in |Z|, and the increased expiratory impedance during the hypopnoeic phase could reflect dynamic narrowing of intrathoracic large airways although this seems unlikely in the context of reduced drive. It seems more likely that the expiratory increase in |Z| is reflective of passive upper airway narrowing during the period of reduced drive. The inspiratory fall could also represent active inspiratory airway opening. Our observations during both CSR apnoeas and hypopnoeas are, therefore, consistent with passive upper airway narrowing due to withdrawal of inspiratory drive to the pharyngeal dilators.

However, upper airway calibre could also be actively diminished at the laryngeal level since it has been shown that vocal cord adductors are activated and abductors are suppressed during induced hypocapnia in animals [28], as well as in humans [29].

While this seems somewhat less likely in the context of CSR, the mechanisms and site of upper airway closure in central sleep apnoea-CSR may differ between individuals, depending upon upper airway anatomy, carbon dioxide responsiveness

and other factors [14, 15]. Ideally, innovative noninvasive imaging techniques should be combined with electromyographic studies to further characterise upper airway narrowing in CSR-CHF.

The observation of supine-dependence of central sleep apnoea-CSR [9, 10] and responses to fixed CPAP in some patients [11] suggest that upper airway narrowing during CSR events may contribute to the pathogenesis of this condition. This could be mediated through reflex inhibitory effects of upper airway closure, which may precipitate or prolong central apnoeas [30]. Variations in upper airway calibre could be a contributing factor to ventilatory instability, promoting ventilatory overshoot with abrupt decreases in upper airway resistance or dampening compensatory responses in the context of high resistance [31]. The frequent occurrence of reduced airway calibre during central CSR events in some subjects with central CSR also sheds light on the previously reported overlap between CSR and OSA [7, 8]. When airway calibre is reduced, conceivably only small changes in airway dimensions related to respiratory drive, tissue fluid shifts or changes in lung volume would be required to either promote or alleviate an inspiratory obstructive component to periodic breathing.

The findings of this study also suggest potential clinical applications for FOT in CSR-CHF patients. For diagnostic purposes, FOT-derived impedance during CSR hypopnoeas could assess inspiratory upper airway obstruction. Increased impedance could potentially be a marker for a response of CSR to fixed CPAP [11], although this remains to be tested. In addition, FOT-driven auto-CPAP has been used successfully in OSA [32]. Conceivably, FOT-derived impedance could be incorporated into servo-ventilation algorithms to adjust end-expiratory pressure levels to assure upper airway patency during the treatment of CSR.

In conclusion, our findings support the hypothesis that in CHF patients with CSR, upper airway closure occurs commonly during CSR apnoeas, and may also occur during central hypopnoeas in non-REM sleep. Further studies are needed to identify the specific site and mechanism of occlusion and the possible contribution of upper airway closure to the pathophysiology of CSR.

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STATEMENT OF INTEREST

A statement of interest for R.J. Kimoff and the study itself can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

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