SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

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Reduction of sleep-disordered breathing following effective percutaneous mitral valve repair with the MitraClip system

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Abstract

Purpose This study tested the hypothesis that a reduction of pulmonary congestion achieved by a reduction of mitral regurgitation (MR) severity in heart failure (HF) patients is associated with reduced event lengths of sleep-disordered breathing (SDB).
Methods We prospectively enrolled 20 consecutive HF patients who underwent MitraClip implantation. Patients underwent cardiorespiratory polygraphic recording prior to and after percutaneous mitral valve repair (PMVR). Beyond routinely established indicators of apneas and hypopneas per hour (respiratory event index), we manually analyzed apnea event lengths.
Results MitraClip implantation led to marked reduction of MR severity and a reduction in left atrial pressure. These hemodynamic changes were accompanied by changes in SDB: the subtype of SDB switched from CSA to OSA in 4 patients. Likewise, quantitative indicators of SDB were altered in both forms of SDB with a reduction in circulatory delay (CSA 38 ± 14 vs. 33 ± 15 s.; $p = 0.002$ and OSA 34 ± 9 vs. 28 ± 6 s.; $p = 0.02$) and a corresponding reduction in ventilation lengths in CSA patients (42 ± 15 vs. 37 ± 13 s.; $p = 0.05$).
Conclusion A reduction of pulmonary congestion as achieved by a decrease of left atrial pressure through successful MitraClip implantation is associated with a reduction in respiratory event lengths, further pointing towards a relation between SDB and HF.

Abbreviations
REI	Respiratory event index
AL	Apnea length
CD	Circulatory delay
CL	Cycle length
CSA	Central sleep apnea
CSR	Cheyne-Stokes respiration
EROA	Effective regurgitant orifice area
HF	Heart failure
LVEF	Left ventricular ejection fraction
MR	Mitral regurgitation
NYHA	New York Heart Association
OSA	Obstructive sleep apnea
PISA	Proximal isovelocity surface area
PG	Polygraphic recording
PMVR	Percutaneous mitral valve repair
RV	Regurgitation volume
SDB	Sleep-disordered breathing
RVEDD	Right ventricular end-diastolic diameter
TTPV	Time-to-peak-ventilation
VL	Ventilation length

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Introduction

Sleep-disordered breathing (SDB) that comprises central sleep apnea (CSA) and obstructive sleep apnea (OSA) is a common

comorbidity in heart failure (HF) [1, 2]. Observational studies suggested a link between CSA and surrogate markers of HF severity and several smaller studies suggested favorable effects of CSA treatment on surrogate markers of HF severity [3–7]. In fact for CSA, a close link has been shown between severity of CSA and pulmonary congestion (as a direct consequence of backward failure) due to HF [8]. This is particularly evident when respiratory event lengths are measured quantitatively instead of the traditionally applied number of apneas and hypopneas per hour [8]. A prolonged circulation time (circulatory delay) may directly modify respiratory feedback mechanisms (as a key element in the pathophysiology of CSA) and cause an increase in the duration of CSA with longer cycle lengths, ventilation lengths, apnea lengths and time to peak ventilation [8]. Untreated OSA represents an independent risk factor for the occurrence of malignant arrhythmias and increased cardiac mortality [9]. More recently, a correlation between cycle lengths and signs of HF was also suggested to be involved in OSA [6].

Therefore, the aim of the current study was (1) to unmask potential correlations between signs of HF and respiratory event lengths in both OSA and CSA and (2) to show that reductions in filling pressures as achieved by successful percutaneous mitral valve repair (PMVR) in HF patients with symptomatic mitral regurgitation (MR) lead to reductions in respiratory event lengths with a particular focus on circulatory delay as this has been shown to be uniquely interrelated to cardiac function [6, 8].

Methods

Study population

We prospectively included 23 consecutive patients with clinically relevant MR who underwent PMVR with the MitraClip system between December 2016 and June 2017. Three patients did not complete the examinations (with the reason being intolerance of the polygraphic recording system) and were excluded. Thus, our final patient group consisted of 20 patients who underwent PMVR completing all examinations. All patients were classified inoperable or at high-risk for surgery by our interdisciplinary heart team and gave written informed consent for data acquisition and analysis. The study was approved by the local Ethics Committee of the University of Düsseldorf and carried out in accordance with the Declaration of Helsinki. All data were included in a registry, which is registered at www.clinicaltrials.gov (NCT02033811).

Study protocol

Patients underwent cardiorespiratory polygraphic recording (PG) within 5 days prior to and after MitraClip implantation. All patients were supposed to show at least mild sleep apnea (respiratory event index (REI) > 5 events/h) on the initial PG.

A comprehensive echocardiographic examination was performed prior to and after MitraClip implantation. Hemodynamic measures were retrieved from right heart catheterization prior MitraClip implantation and from the procedure itself. Therein, the interventionists (R.W. and P.H.) carried out left atrial (LA) pressure measurements prior to and after MitraClip implantation whenever technically feasible.

Echocardiographic measurements

Echocardiographic examinations were performed using a GE Vivid S6/E9, or a Philips iE33. All echocardiographic data were obtained in digital format and then stored on a workstation for offline analysis (Xcelera Cardiology Information Management, Philips). Left ventricular volumes and ejection fraction (LVEF) were calculated using the Simpson biplane method. Right ventricular dysfunction was considered present when the tricuspid annular plane systolic excursion (TAPSE) was ≤ 14 mm. Assessment of MR was performed according to current guidelines [7]. MR was graded as mild, moderate or severe according to the guidelines of the European Society of Cardiology (ESC) [7, 10].

Measurement of sleep-disordered breathing patterns

Cardiorespiratory polygraphy recordings were performed as described earlier using a six-channel device (MiniScreen plus, FA Löwenstein medical, Germany) [6]. Nasal airflow, chest and abdominal efforts, finger pulse oximetry (averaging time 4 s; sampling frequency 3 Hz), ECG, snoring, and body position were recorded continuously. The transient loss of one channel, except nasal airflow, was deemed acceptable. Recordings were analyzed and reviewed by two sleep specialists (J.S. and S.K.) who were adequately trained within the Institute for Sleep Medicine and Neuromuscular Disorders at the University Hospital of Muenster by an attending in sleep medicine (M.B.). Respiratory event scoring followed the guidelines of the American Academy of Sleep Medicine (AASM) [11–13]. Apnea was defined as a reduction in nasal airflow by > 90% of baseline for > 90% of the event's duration and > 10 s. Apneas were classified as obstructive if there was a continued or increased inspiratory effort throughout the entire period of absent airflow. If this was not the case apneas were classified as central. Hypopnea was defined as 30% fall from baseline in airflow signal for 90% of the event's duration of at least 10 s and 3% desaturation from pre-event baseline. Patients were classified as having OSA if > 50% of all apneas were obstructive in origin, while they were classified as having CSA if > 50% of all apneas were central. Cycle lengths were measured as previously described by our group [8]. In short, cycle length was defined as the time from the beginning of an apnea to the end of the following ventilation; therefore, cycle lengths represent the sum of apnea length and the following ventilation lengths. Time from

resumption of airflow to the following peak in airflow was defined as TTPV. Circulatory delay was the time from the first breath after apnea to the following nadir of oxygen saturation. Data on respiratory event lengths shown represent an average of up to 24 separate (up to 6 apnea events per time window of 2 h from 10 p.m. to 6 a.m.)—manually and carefully selected—apnea measurements obtained throughout the night. In patients classified as having predominantly OSA, obstructive apneas events were measured whereas in CSA patients central apnea events were measured. Figure 1 shows a scheme of central and obstructive apnea respiratory event lengths measurements.

Statistical analysis

All analyses were performed using Sigma Plot software (Version 13.0, Systat Software Ltd). Results are expressed as mean ± standard deviation for continuous variables or percentages for categorical variables unless otherwise specified. Before analysis, normality distribution was tested with Kolmogorov-Smirnov test. The differences between two groups were compared for significance with a two-tailed paired t test. Pearson product moment correlation was used for correlation analysis. A value of $p < 0.05$ was considered statistically significant.

Results

The demographic and clinical data of the cohort are summarized in Table 1. Mean age was 80 ± 6 years. The majority of

patients (85%) presented with New York Heart Association (NYHA) functional class III or IV and reduced LVEF ($38 \pm 9\%$). Mean NT-proBNP was 4893 (1256–5271) pg/ml. Seven patients (35%) presented with degenerative MR, while 13 patients (65%) had functional MR. MitraClip implantation was associated with a significant reduction in MR severity (80 vs. 10% MR grade 3+; $p < 0.001$) as well as LA pressure (16 ± 6 vs. 12 ± 5 mmHg; $p = 0.006$) and systolic pulmonary artery pressure (49 ± 17 vs. 44 ± 9 mmHg; $p = 0.04$).

Association between sleep-disordered breathing and heart failure at baseline

All patients showed at least mild SDB (apnea-hypopnea index > 5 events/h) on the initial PG with the majority of them (11/20 patients) presenting with predominant OSA (Table 2 and Fig. 2). At baseline, positive correlations were found between respiratory event length and cardiac function in both CSA and OSA patients: In CSA patients, apnea length ($r = -0.08$; $p = 0.03$; Fig. 3a) and ventilation length ($r = -0.08$; $p = 0.04$; Fig. 3b) increased with worsening cardiac index. However, no correlations were found between echocardiographic parameters of HF severity and respiratory event length.

In OSA patients, there was no correlation between cardiac index and respiratory event length. Instead, cycle length increased with reduced LVEF ($r = -0.6$; $p = 0.04$; Fig. 3c). Furthermore, cycle length increased with signs of right ventricular overload (increased right ventricular end-diastolic diameter

Fig. 1 Scheme of obstructive (left) and central (right) respiratory apnea event lengths (**a**) nasal airflow, (**b**) peripheral oxygen saturation, (**c**) chest effort, and (**d**) abdominal effort in sleep apnea in heart failure patients. CD, circulatory delay; CL, cycle length; AL, apnea length; VL, ventilation length; TTPV, time to peak ventilation
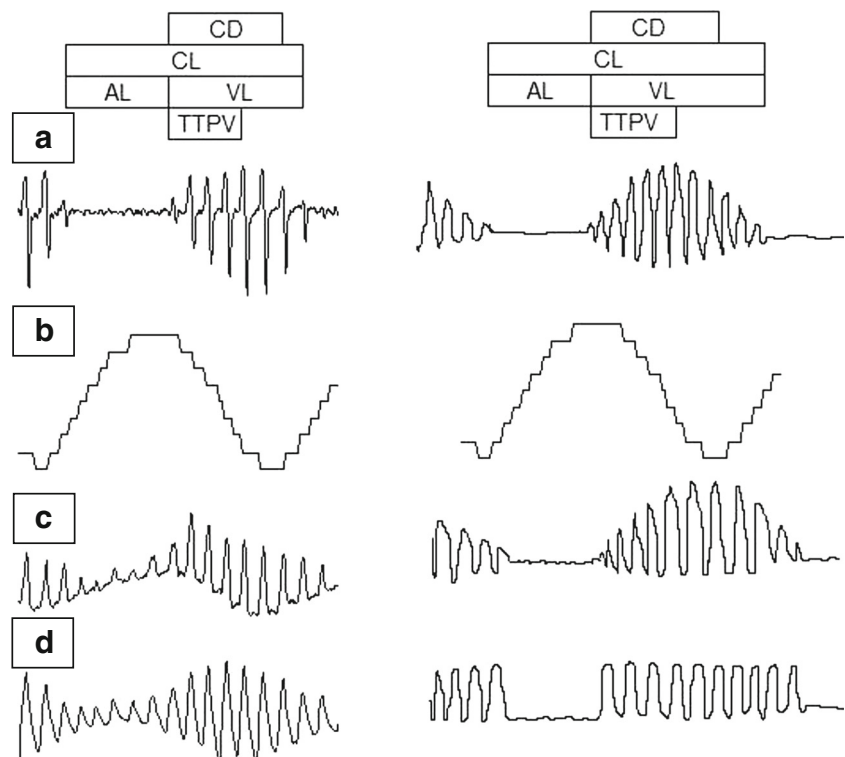
Table 1 Demographic and clinical parameters at baseline

	HF patients ($n = 20$)
Clinical characteristics	
Age [years]	80 ± 6
Female [%]	30
BMI [kg/m^2]	27 ± 3
NYHA class II [%]	15
NYHA class III [%]	80
NYHA class IV [%]	5
MLWHFQ	
Good [%]	30
Moderate [%]	35
Poor [%]	35
ESS > 10 [%]	25
Systolic BP [mmHg]	139 ± 27
Diastolic BP [mmHg]	69 ± 11
Sinus Rhythm [%]	30
Pacemaker/ICD [%]	40
VC [% predicted]	82 ± 25
FEV1/VC [n.u.]	77 ± 14
Logistic EuroSCORE I [%]	25 ± 17
Previous cardiac history	
Previous CABG [%]	30
Previous valve surgery [%]	15
CV risk factors	
Hypertension [%]	85
Diabetes [%]	40
Smoking	
Current [%]	10
Former [%]	20
Echocardiographic findings	
DMR vs. FMR [%]	35 vs. 65
LA area [cm^2]	27 ± 5
LVEDD [mm]	52 ± 9
LVEF [%]	38 ± 9
MR severity at rest	
Moderate [%]	20
Severe [%]	80
EROA [mm^2]	30 ± 15
PISA [mm]	7.2 ± 1.4
RV [ml]	46 ± 22
RVEDD [mm]	37 ± 6
TAPSE [mm]	18 ± 6
TAPSE ≤ 14 mm [%]	25
TR severity at rest	
Mild [%]	50
Moderate [%]	30
Severe [%]	20
Laboratory assessment	
NT-proBNP [pg/ml]	4893 (1256–5271)
Hemoglobin [mg/dl]	13 ± 2

Table 1 (continued)

	HF patients ($n = 20$)
Serum creatinine [mg/dl]	1.3 ± 0.4
eGFR [mL/min/1.73 m^2]	53 ± 18
HsCRP [mg/dl]	1 ± 2

Data are presented as mean¡ SD or %, unless otherwise stated. *PVMR*, percutaneous mitral valve repair; *BMI*, body mass index; *NYHA*, New York Heart Association; *MLWHFQ*, Minnesota Living with Heart Failure Questionnaire; *ESS*, Epworth Sleepiness Scale; *BP*, blood pressure; *LA*, left atrial volume; *LVEDD*, left ventricular end-diastolic diameter; *LVEF*, left ventricular ejection fraction; *DMR*, degenerative mitral regurgitation; *FMR*, functional mitral regurgitation; *MR*, mitral regurgitation; *RVEDD*, right ventricular end diastolic diameter; *TAPSE*, tricuspid annular plane systolic excursion; *VC*, vital capacity; *FEV1*, forced expiratory volume in 1 s; *ICM*, ischemic cardiomyopathy; *DCM*, dilated cardiomyopathy; *CABG*, coronary artery bypass graft; *CV*, cardiovascular; *CAD*, coronary artery disease; *NT-proBNP*, N-terminal pro-brain natriuretic peptide; *eGFR*, estimated glomerular filtration rate; *hsCRP*, high-sensitivity C-reactive protein

(RVEDD)) ($r = 0.7$; $p = 0.03$; Fig. 3d). In addition, ventilation length increased with worsening LVEF ($r = -0.6$; $p = 0.05$).

In contrast to these findings, no correlations between cardiac function and severity of OSA or CSA were found when traditionally used markers of SDB severity (event counts/h) were applied. Moreover, we did not detect a direct association between parameters of MR severity and SDB.

Changes in sleep-disordered breathing after MitraClip implantation

Echocardiographic, hemodynamic and respiratory changes associated with MitraClip implantation are summarized in Table 2. Successful reduction in MR was associated with a change in the subtype of SDB with fewer patients presenting with predominantly CSA after PMVR (Table 2 and Fig. 2). Again, no significant changes in severity of SDB were found when standard metrics of SDB severity, as defined by event counts per hour, were analyzed. However, when we conducted in-depth quantitative analysis of apnea event lengths, we deciphered alterations in circulatory delay in both, central apneas (38 ± 14 vs. 33 ± 15 s.; $p = 0.002$; Fig. 4a) and obstructive apneas (34 ± 9 vs. 28 ± 6 s.; $p = 0.02$; Fig. 4b) following PMVR. In patients with central apneas, ventilation length was also shorter after MitraClip implantation (42 ± 15 vs. 37 ± 13 s.; $p = 0.05$).

Discussion

In the present study, we evaluated the association between HF severity and SDB and the effect of PMVR on SDB in patients with clinically relevant MR undergoing PMVR with the MitraClip. We demonstrate that in HF patients with symptomatic MR, both obstructive and central respiratory event lengths are related to hemodynamic and echocardiographic

Table 2 Echocardiographic, hemodynamic, and respiratory results

	Pre MitraClip	Post MitraClip	*p* value
Echocardiographic parameters			
MR severity at rest			< 0.001
Mild [%]	0	15	
Moderate [%]	20	75	
Severe [%]	80	10	
MVPG [mmHg]	1.7 ± 0.8	3.4 ± 2	0.002
MVPG > 5 mmHg [%]	0	15	
Systolic PAP [mmHg]	49 ± 16	44 ± 9	0.04
Hemodynamic measurements			
Cardiac Index [L/min/m^2]	1.9 ± 0.4	n.a.	
Mean RAP [mmHg]	10 ± 6	n.a.	
RVEDP [mmHg]	12 ± 11	n.a.	
Mean PAP [mmHg]	37 ± 11	n.a.	
PVR [dyn*s/cm^5]	284 ± 170	n.a.	
SVR [dyn*s/cm^5]	2012 ± 463	n.a.	
AO [SaO2%]	92 ± 13	n.a.	
PA [SaO2%]	59 ± 8	n.a.	
Mean LA pressure [mmHg]*	16 ± 6	12 ± 5	0.006
Standard respiratory results		–	
SDB [%]	100	100	0.99
Predominantly OSA [%]	55	75	0.08
Predominantly CSA [%]	45	25	0.08
AHI [events/h]	35 ± 21	37 ± 21	0.48
AI [events/h]	22 ± 21	19 ± 16	0.38
oAI [events/h]	8 ± 8	10 ± 10	0.31
cAI [events/h]	12 ± 15	8 ± 9	0.83
HI [events/h]	13 ± 6	18 ± 11	0.06
Mean [SaO2%]	93 ± 3	92 ± 3	0.10
Minimum [SaO2%]	76 ± 8	75 ± 9	0.73
In-depth analysis of respiratory event lengths			
Obstructive event lengths*			
Cycle lengths [sec.]	53 ± 11	50 ± 9	0.39
Apnea lengths [sec.]	19 ± 4	18 ± 5	0.64
Ventilation lengths [sec.]	34 ± 8	32 ± 10	0.58
Time to peak ventilation [sec.]	12 ± 2	12 ± 3	0.77
Circulatory delay [sec.]	34 ± 9	28 ± 6	0.02
Central event lengths*			
Cycle lengths [sec.]	65 ± 20	59 ± 17	0.08
Apnea lengths [sec.]	23 ± 8	23 ± 8	0.56
Ventilation lengths [sec.]	42 ± 15	37 ± 13	0.05
Time to peak ventilation [sec.]	12 ± 2	12 ± 3	0.77
Circulatory delay [sec.]	38 ± 14	33 ± 15	0.002

Data are presented as mean¡SD or %, unless otherwise stated. *p*, p value; $p \leq 0.05$ is considered statistically significant < *MR*, mitral regurgitation; *EROA*, effective regurgitant orifice area; *PISA*, proximal isovelocity surface area; *RV*, regurgitant volume; *RAP*, right atrial pressure; *RVEDP*, right ventricular end-diastolic pressure; *PAP*, pulmonary arterial pressure; *PVR*, pulmonary vascular resistance; *SVR*, systemic vascular resistance index; *AO SaO2%*, aortal oxygen saturation; *PA SaO2%*, pulmonary arterial oxygen saturation; *LAP*, left atrial pressure (*paired values for LAP were available in 10 patients); *SDB*, sleep-disordered breathing; *CSA*, central sleep apnea; *OSA*, obstructive sleep apnea; *AHI*, apnea hypopnea index; *AI*, apnea index; *oAI*, obstructive apnea index; *cAI*, central apnea index; *HI*, hypopnea index; *SaO2*, oxygen saturation.

*Apnea event lengths in patients with predominantly obstructive (*n* = 11) sleep apnea and with predominantly central sleep apnea (*n* = 9) were carefully selected and averaged for each patient (for details see "Methods" section).

P-values marked in italics were considered statistically significant (*p* < 0.05).

Fig. 2 Patient flow chart and changes in the subtype of sleep apnea after MitraClip implantation. PMVR, percutaneous mitral valve repair
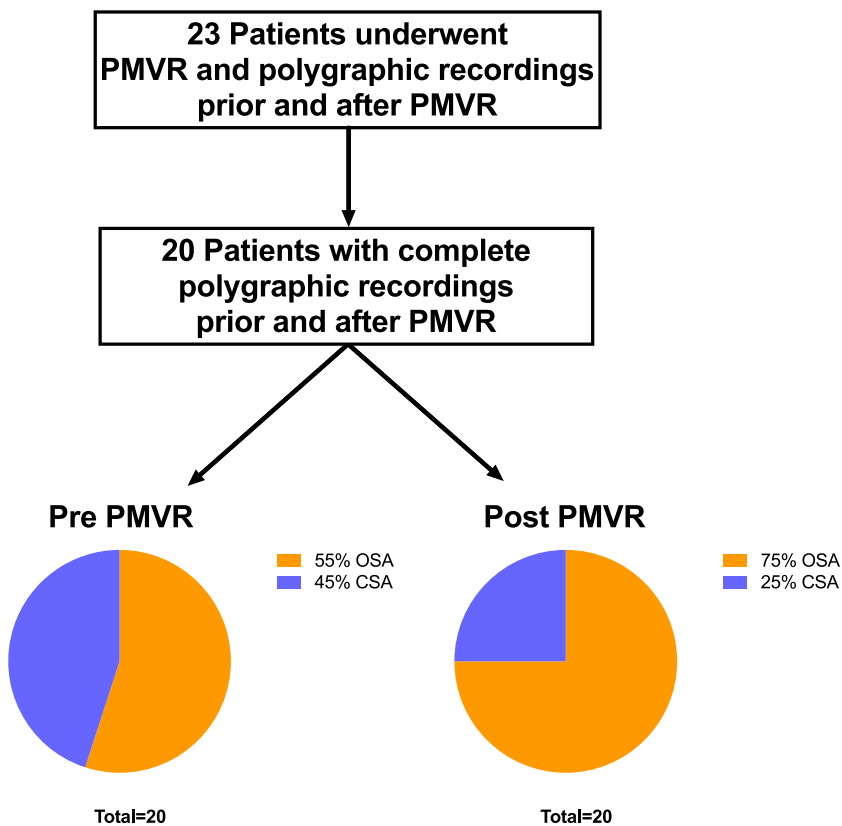

Fig. 3 Correlations between apnea lengths and cardiac index (**a**) and ventilation length and cardiac index in 9 CSA patients (**b**). Correlations between cycle lengths and left ventricular ejection fraction (**c**) and cylce length and right ventricular end-diastolic diameter as a sign of right ventricular overload in 11 OSA patients (**d**). Each data point represents an average of up to 24 separate–manually and carefully selected–apnea measurements obtained throughout the night
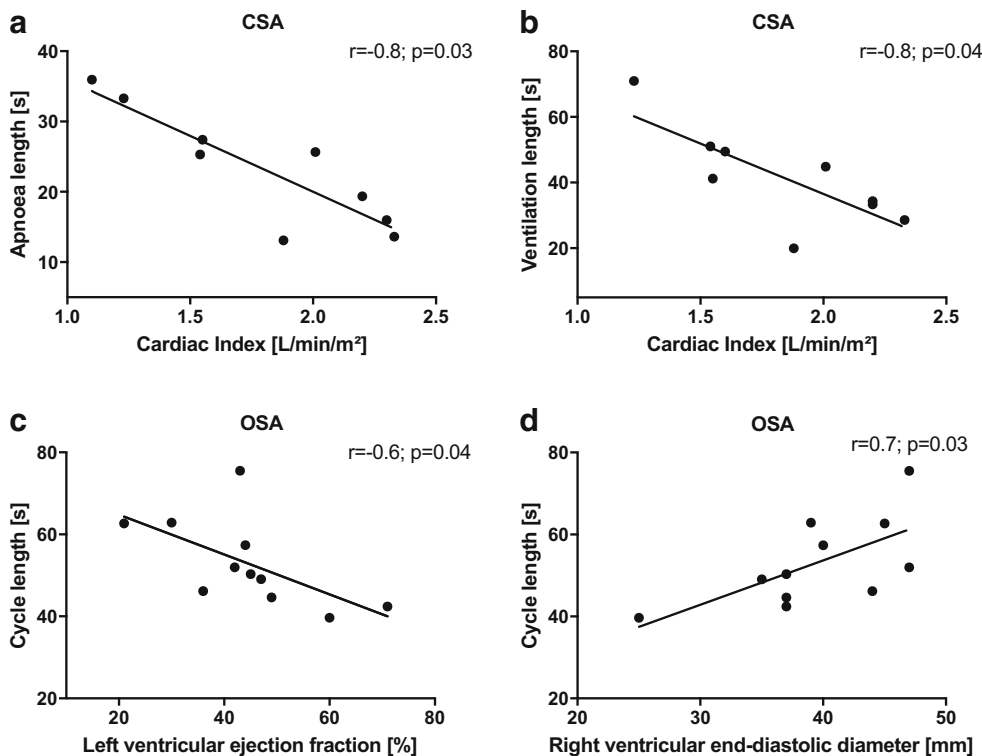
Fig. 4 Differences in circulatory delay between pre and post MitraClip implantation in patients with predominantly OSA (**a**) (*n* = 11) and patients with predominantly CSA (**b**) at baseline (*n* = 9). Each data point represents an average of up to 24 separate–manually and carefully selected–apnea measurements obtained throughout the night
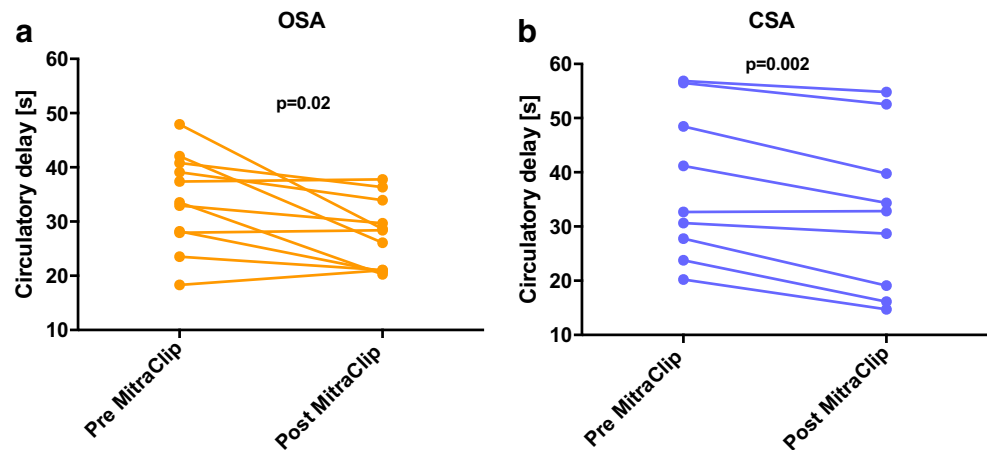
parameters of right- and left ventricular function (in contrast to respiratory events/h). Furthermore, we show that a reduction of filling pressures achieved by a reduction in MR severity through PMVR is associated with a reduction of respiratory event lengths, further underscoring the interrelation between SDB and HF.

Association between sleep-disordered breathing and heart failure at baseline

The phenomenon of a correlation between HF severity and respiratory event lengths in both OSA and CSA has been studied before. Wedewardt et al. demonstrated an association of central apnea event lengths with left ventricular systolic function which is in line with our findings [8]. In fact, the Academy of Sleep Medicine (AASM) acknowledges the superiority of cycle lengths over REI in reflecting severity of CSA in HF in its current guidelines [12]. Central respiratory event lengths lengthen along with deteriorating left ventricular systolic function [12]. The pathophysiology of CSA in HF is complex and still incompletely understood. Pulmonary congestion is thought to lead to increased central respiratory drive entering into a vicious circle of hyperventilation with subsequent central apneas in response to small increases in carbon dioxide at night [3, 14]. J-receptors sense pulmonary congestion, clinically indicated by increased post-capillary wedge pressure and foster central respiratory drive [3]. Circulatory delay might explain best why respiratory cycle lengths (as opposed to the REI) correlate with HF severity in CSA. As left ventricular function deteriorates, circulatory delay increases leading to a less efficient feedback system of any respiratory changes. Of note, a previous cross-sectional study has shown that there is substantial inter-correlation between circulatory delay and apnea length and ventilation length owing to the fact that a less efficient feedback system with longer circulatory delay may lead to longer overall cycle lengths too [8].

In contrast to CSA, the association of OSA severity with HF severity is less clear [1]. In this regard, Efken et al. and Ryan et al. studied obstructive apnea event lengths in HF and demonstrated a robust correlation between obstructive apnea event lengths and pulmonary congestion with the main reason for this correlation being increased circulatory delay [6, 15]. In this regard, our findings of a correlation between right ventricular overload and circulatory delay along with a correlation between left ventricular function and cycle lengths supports the hypothesis that that a longer circulation time leads to delayed report of gas tensions and this does also contribute to longer cycle lengths in OSA. This would only explain why OSA ventilation lengths correlate with HF severity. In this regard, a correlation with HF severity as invasively measured by pulmonary congestion has only been demonstrated for cycle length and ventilation lengths and not for apnea lengths [6]. This finding is in line with our results and underlines that, in contrast to CSA where both apnea lengths and ventilation lengths were found to correlate with HF severity, in OSA, apnea lengths depend on complex regulatory pathways that determine upper airway stability [8]. Despite the fluid shift theory that strengthens the thesis that HF severity directly contributes to upper airway instability and hence prolonged apnea lengths, even in OSA this theory alone does not explain apnea lengths in OSA [16].

Changes in sleep-disordered breathing after MitraClip implantation

Successful MitraClip implantation led to a reduction of MR severity as shown by echocardiography and invasive measurement of LA pressure as well as a reduction of systolic pulmonary artery pressure. Figure 5 displays a representative case of a patient's finding on PG recording and invasive hemodynamics as well as echocardiographic severity of MR before and after successful PMVR. The fact that MitraClip implantation was associated with a change in the subtype of SDB in 4 patients from CSA to OSA is in line with previous reports, showing that improvements in cardiac function can lead to lesser CSA, thereby

Pre PMVR   Post PMVR

SpO2
Heart rate
Puls wave
Flow
Thorax
Abdomen

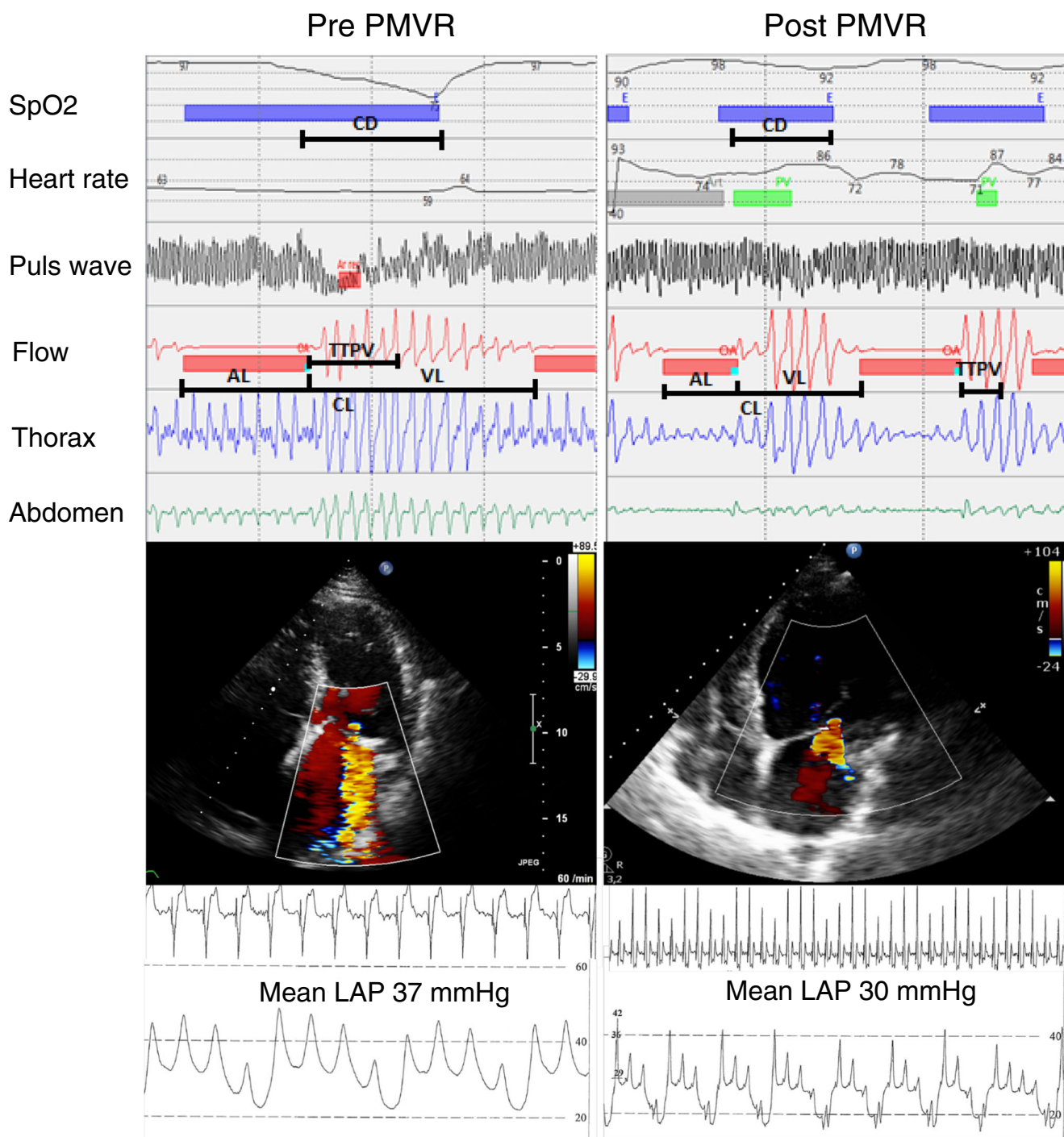Mean LAP 37 mmHg   Mean LAP 30 mmHg

Fig. 5 Representative data of a patient with severe MR, increased left atrial pressure (LAP) and long CSA cycle lengths before PMVR with the MitraClip system (right) and only mild MR, lower LA pressure and shorter CSA cycle lengths after successful MitraClip implantation (left). From top to down polygraphic data show the following signals: (a) nasal airflow, (b) peripheral oxygen saturation, (c) chest effort, and (d) abdominal effort. CD, circulatory delay; CL, cycle length; AL, apnea length; VL, ventilation length; TTPV, time to peak ventilation; LAP, left atrial pressure; PMVR, percutaneous mitral valve repair

unmasking pre-existing OSA. This was shown by Fox et al. in patients with improved cardiac function following successful cardioversion of atrial fibrillation and atrial flutter [17]. Likewise, resolution from CSA was demonstrated in patients following implantation of left ventricular assist device, cardiac transplantation, successful diuretic therapy for acute decompensated HF, and more recently, after treatment of HF with sacubitril/valsartan [18–21]. This was also demonstrated after valvuloplasty in patients with mitral stenosis albeit with the limitation that respiratory event lengths were not quantified [22, 23].

Our finding of a significant change in both cycle lengths and circulatory delay and not apnea lengths in central respiratory event lengths following reduction in MR severity along with a decrease in LA pressure (indicating pulmonary decongestion) is of importance: First, it provides further evidence that in CSA, ventilation lengths and hence central respiratory drive is influenced by the degree of pulmonary congestion (LA pressure) with shorter ventilation lengths as pulmonary congestion decreases due to a reduction of MR. Second, we demonstrate that this holds true for ventilation lengths but not for apnea lengths. In this regard, apnea lengths were found to be relatively consistent at approximately 20 s in previous cross-sectional studies of CSA cycle lengths in HF and to be less dependent from HF severity than ventilation lengths, which is in line with our results [24]. The significant change in circulatory delay in CSA event lengths with shorter circulatory delays following PMVR is likely to be the direct consequence of reduced MR, lower LA pressure and consecutively improved cardiac function with faster response to changes in gas tensions. This might also be one of the mechanisms behind the significantly shorter ventilation lengths following PMVR. Faster response to any changes in gas tensions through improved cardiac function with shorter circulatory delay through less MR could explain shorter ventilation lengths in CSA patients after MitraClip implantation. In patients with predominately OSA, we detected shorter circulatory delays without any significant changes in ventilation lengths or apnea lengths following MitraClip implantation. This could be caused by an improved cardiac function after PMVR leading to shorter circulatory delays also in obstructive events. However, ventilation lengths and apnea lengths might not be solely influenced by cardiac function as they depend on complex regulatory pathways that determine upper airway stability and that also include fluid shift from the legs to the neck at night [16]. In this regard, we strengthen the findings of Efken et al. by demonstrating that the correlations were also found in longitudinal design and not only in cross-sectional studies [6].

Limitations

There are several limitations of this study. We applied multi-channel cardiorespiratory polygraphy recordings instead of polysomnography. Therefore, data on sleep, sleep quality, and arousals are not available. This implies that total REI could be underestimated because total sleep time might be shorter than total recording time. Despite this, for the purpose of measuring obstructive and central respiratory patterns, high-quality polygraphy recordings provide all the important information required. The small sample size is a further limiting factor. Final inclusion of 20 patients implies that multivariate analysis is impossible; thus, analysis of potential confounding factors is beyond the scope of this manuscript. However, this study is the first to assess cycle lengths in

OSA in patients with symptomatic MR along the course of successful treatment by PMVR.

Conclusion

In HF patients with symptomatic MR, both obstructive and central respiratory event lengths (in contrast to respiratory events counts per hour) are related to left ventricular function. A reduction of pulmonary congestion as indicated by a reduction in LA pressure following successful PMVR is associated with a reduction in respiratory event lengths, further pointing towards a relation between SDB and HF.

Compliance with ethical standards

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