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Resolution of ST deviation after myocardial infarction in patients with and without sleep-disordered breathing

Electronic supplementary material

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Statement of significance

What is already known about this subject? After ST elevation myocardial infarction treated with percutaneous coronary intervention, sleep-disordered breathing is associated with repetitive hypoxia, increased cardiac workload, and less myocardial salvage.

What does this study add? Patients with sleep-disordered breathing have prolonged resolution of ST deviation and higher frequencies of microvascular obstruction in the first days after ST elevation myocardial infarction.

How might this impact on clinical practice? In an ongoing multicenter randomized controlled trial of adaptive servoventilation in patients with acute myocardial infarction and sleep-disordered breathing (TEAM-ASV; NCT02093377) the question is investigated whether prompt diagnosis and early treatment can prevent further myocardial damage after acute myocardial infarction.

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This observational study was performed at the Universitätsklinikum Regensburg.

Introduction

In patients with ST elevation myocardial infarction (STEMI), prognosis is highly dependent on the extent of the necrotic area in the myocardium [1]. Timely reperfusion of the infarcted area using percutaneous coronary intervention (PCI) is the clinical standard to limit expansion of infarct size [2]. Salvage of vital myocardium and limitation of the myocardial necrotic area contributes to improved prognosis [2, 3]. After successful PCI resulting in reperfusion of the infarcted myocardium, necrotic areas and vital myocardium at risk for necrosis can coexist [4].

An early and well-known marker of the extent of myocardial ischemia in patients with STEMI is ST segment deviation on an electrocardiogram (ECG) [5, 6]. The extent and early resolution of ST segment deviation, as well as residual ST deviation, are strong predictors of prognosis in patients with STEMI [7, 8] and correlate with infarct size and microvascular obstruction (MVO) assessed by cardiovascular magnetic resonance (CMR) [9, 10].

Sleep-disordered breathing (SDB) is common in patients with acute myocardial infarction, with a prevalence of up to 66% [11–13]. It is known that SDB is associated with nocturnal myocardial ischemia [14] and is an independent predictor for the occurrence of acute myocardial infarction [15, 16]. SDB results in repetitive oxygen desaturations, as well as surges in heart rate and blood pressure and thus in cardiac workload [17]. The resulting mismatch of oxygen sup-

Abbreviations	
AHI	Apnea–hypopnea index
CMR	Cardiac magnetic resonance imaging
ECG	Electrocardiogram
LV	Left ventricular
MVO	Microvascular obstruction
NT-proBNP	N-terminal pro-brain natriuretic peptide
PCI	Percutaneous coronary intervention
SD	Standard deviation
SDB	Sleep-disordered breathing
STEMI	ST elevation myocardial infarction

ply and demand associated with SDB may have additional negative effects on myocardium at risk that could be possibly salvaged [17]. Thus, SDB is associated with impaired recovery of left and right ventricular function [18, 19], myocardial salvage, and larger infarct size after acute myocardial infarction [20], as determined by CMR. Untreated pre-existing SDB is also associated with less resolution of ST elevation in STEMI patients assessed 30 min after PCI [21]. However, it is not known whether exposure to SDB harms the myocardium at risk in STEMI patients by promoting continued ischemia within the first days after successful PCI and whether SDB is associated with MVO.

Thus, the objective of this study was to test the hypothesis that STEMI patients with SDB have a higher extent of residual ST segment deviation after PCI and more MVO than similar patients without SDB.

Methods

Study design

This analysis was undertaken as part of a prospective observational study from March 2009 to December 2011 in patients with first acute myocardial infarction (ST elevation on ECG, or complete occlusion of coronary artery in non-STEMI) who were admitted to the Universitätsklinikum Regensburg and underwent a primary PCI within the first 24 h after symptom onset [20] (Supplementary Figure S1). Key exclusion criteria were a previous myocardial infarction or previous myocardial revascularization, indication for surgical myocardial revascularization, cardiogenic shock, contraindications for CMR, known and treated SDB, and follow-up not feasible [20]. For this subanalysis, patients with non-STEMI were excluded.

Within the first 5 days after PCI, all eligible patients underwent an overnight in-laboratory sleep study (polysomnography). CMR studies were performed on days 3–5 after PCI and 12 weeks later [20]. Data from routine ECGs performed as part of regular clinical practice immediately before PCI until 5 days after PCI were used for the present analysis.

The primary endpoint of this analysis was the extent of residual ST deviation within 24 h and more than 24 h after PCI. This primary endpoint was chosen because high residual ST deviation indicates prolonged ischemia and is associated with worse prognosis [22]. Secondary endpoints were the relative resolution of ST deviation, the extent of MVO, and the N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration before and after PCI.

Percutaneous coronary intervention and medical management of STEMI

PCI and medical management of STEMI were performed according to contemporary guidelines [23]. The use of thrombectomy and glycoprotein IIb/IIIa inhibitors was at the discretion of the interventional cardiologist, depending on the presence of high thrombus burden in the infarct-related artery. All patients were treated with aspirin, intravenous heparin, and adenosine diphosphate (ADP) receptor inhibitors.

Polysomnography

Polysomnography was performed in all subjects using standard techniques (Alice System, Respironics, Pittsburgh, USA) [20]. Respiratory efforts were measured with the use of respiratory inductance plethysmography, and airflow by nasal pressure cannula. Sleep stages, arousals, and apneas and hypopneas were determined according to American Academy of Sleep Medicine (AASM) criteria by one experienced sleep technician blinded to the clinical data [24]. Apnea was defined as a cessation of inspiratory airflow for ≥10 s. A hypopnea required a 30% or more reduction in nasal pressure signal associated with a ≥4% desaturation (hypopnea definition A, AASM 2007) [24]. The apnea–hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of sleep. An AHI of ≥15 events per hour indicates at least a moderate degree of SDB. Patients were stratified into those without (AHI < 15/h) and with SDB (AHI ≥ 15/h) [25].

ECG acquisition and analysis

ST deviations in routine 12-lead ECGs were analyzed according to standard criteria [8, 26] before PCI, at 0–24 h, and more than 24 h after PCI. Elevations and depressions of the ST segment were measured according to infarct location in all affected leads of the ECG. The analysis of ST deviations was blinded to other clinical data.

The extent of ST deviation was measured at the J point. Mean ST deviation was calculated according to infarct location. In order to obtain the most accurate results, ST depression in reciprocal leads was also taken into consideration [8]. For anterior infarction, mean ST deviation was calculated as the mean of ST elevations in leads I, aVL, V1–V6, and reciprocal ST depressions in the leads II, III, and aVF. For non-anterior infarctions, mean ST deviation was calculated as the mean of ST elevations in leads II, III, aVF, V5, and V6, and reciprocal ST depressions in leads V1–V4 [8]. Routine clinical ECGs were grouped into three time periods. Relative resolution of ST deviation was categorized into three groups of prognostic importance: *complete resolution*, *partial resolution*, and *no resolution* [7, 8]. *Complete resolution* was defined as ≥70% resolution of ST deviation compared to ECG before PCI, *partial resolution* as >30% to <70% resolution of ST deviation, and *no resolution* as <30% resolution of ST deviation [7].

To measure the extent of ST deviation in digitalized 12-lead ECGs, a program was used which performs as a digital magnifier and enables precise measurement of ST deviation with an accuracy of 0.001 mV (Measure 2.1 d, DatInf GmbH, Tübingen, Germany).

Cardiovascular magnetic resonance acquisition and analysis

Details of CMR acquisition and analysis have been published previously [20]. Briefly, CMR studies were performed on a clinical 1.5-Tesla scanner (Avanto, Siemens Healthcare Sector, Erlangen, Germany) using a 32-channel phased-array receiver coil. Calculation of left ventricular (LV) volumes was performed

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Resolution of ST deviation after myocardial infarction in patients with and without sleep-disordered breathing

Abstract

Objective. The objective of this study was to test the hypothesis that ST elevation myocardial infarction (STEMI) patients with sleep-disordered breathing (SDB) have less resolution of ST segment deviation and more microvascular obstruction (MVO) after percutaneous coronary intervention (PCI) than STEMI patients without SDB.
Methods. In this prospective observational study, patients with STEMI and successful PCI were stratified based on the presence (apnea–hypopnea index [AHI] ≥ 15/h) or absence (AHI < 15/h) of SDB. ST deviations in electrocardiograms (ECGs) were analyzed according to standard criteria before PCI, and at 0–24 h and >24 h after PCI. MVO was assessed by cardiac magnetic resonance imaging.
Results. A total of 35 patients were enrolled, 18 with SDB and 17 with no SDB. Before PCI, median ST deviation was similar in the no SDB and SDB groups (0.094 [0.063–0.144] vs. 0.106 [0.055–0.132] mV, $p = 0.88$). The no SDB group had significantly less residual ST deviation compared to the SDB group, both within 24 h (0.018 [0.012–0.039] vs. 0.052 [0.035–0.077] mV, $p = 0.01$) and more than 24 h after PCI (0.016 [0.005–0.029] vs. 0.045 [0.017–0.097] mV, $p = 0.006$). Multivariable linear regression models including established determinants for infarct size and myocardial ischemia showed that AHI was independently associated with higher ST deviation >24 h after STEMI (B [95% confidence interval, CI] 0.82 [–0.12; 1.51], $p = 0.024$) and MVO (B [95% CI] 0.08 [0.01; 0.160]; $p = 0.036$).
Conclusion. SDB is associated with a lower relative reduction in ST deviations and more MVO after STEMI. The present findings suggest that SDB-related myocardial ischemia on the myocardium at risk takes place in the first days after STEMI.

Keywords

ST elevation myocardial infarction · Sleep apnea · Ischemia · Electrocardiography · Magnetic resonance imaging

Rückbildung von ST-Veränderungen nach Myokardinfarkt bei Patienten mit und ohne schlafbezogene Atmungsstörung

Zusammenfassung

Ziel. Ziel der vorliegenden Studie war es, die Hypothese zu untersuchen, dass Patienten mit ST-Hebungs-Infarkt („ST elevation myocardial infarction", STEMI) und schlafbezogener Atmungsstörung (SBA) seltener eine Rückbildung der ST-Strecken-Veränderung und häufiger eine mikrovaskuläre Obstruktion (MVO) nach perkutaner Koronarintervention (PCI) aufweisen als STEMI-Patienten ohne SBA.
Methoden. In der vorliegenden prospektiven Beobachtungsstudie wurden Patienten mit STEMI und erfolgreicher PCI – je nach Vorliegen einer SBA (Apnoe-Hypopnoe-Index, AHI: ≥ 15/h) oder nicht (AHI < 15/h) – stratifiziert. Die ST-Abweichungen im Elektrokardiogramm (EKG) wurden entsprechend den Standardkriterien vor PCI sowie 0–24 h und >24 h nach PCI ausgewertet. Die Beurteilung einer MVO erfolgte anhand der kardialen Magnetresonanztomographie.
Ergebnisse. Es wurden 35 Patienten in die Studie aufgenommen, 18 mit SBA und 17 ohne SBA. Vor der PCI war die mediane ST-Abweichung in der Gruppe ohne SBA ähnlich wie in der Gruppe mit SBA (0,094 [0,063–0,144] vs. 0,106 [0,055–0,132] mV; $p = 0,88$). Die Gruppe ohne SBA wies signifikant weniger residuale ST-Abweichungen auf als die Gruppe mit SBA, sowohl innerhalb von 24 h (0,018 [0,012–0,039] vs. 0,052 [0,035–0,077] mV; $p = 0,01$) als auch mehr als 24 h nach PCI (0,016 [0,005–0,029] vs. 0,045 [0,017–0,097] mV, $p = 0,006$). Multivariate lineare Regressionsmodelle einschließlich etablierter Determinanten für die Infarktgröße und Myokardischämie zeigten, dass der AHI in unabhängiger Weise mit einer größeren ST-Abweichung >24 h nach STEMI (B [95 %-Konfidenzintervall, 95 %-KI] 0,82 [–0,12; 1,51]; $p = 0,024$) und einer MVO (B [95 %-KI] 0,08 [0,01; 0,160]; $p = 0,036$) assoziiert war.
Schlussfolgerung. SBA sind mit einer geringeren relativen Rückbildung der ST-Abweichungen und mit einer größeren MVO nach STEMI assoziiert. Die vorliegenden Befunde weisen darauf hin, dass eine SBA-bedingte Myokardischämie im entsprechend gefährdeten Myokard in den ersten Tagen nach STEMI auftritt.

Schlüsselwörter

ST-Hebungs-Myokardinfarkt · Schlafapnoe · Ischämie · Elektrokardiographie · Magnetresonanztomographie

in serial short-axis slices using commercially available software (Syngo Argus, version B15; Siemens Healthcare Sector, Erlangen, Germany). The extent of delayed enhancement was quantified with custom analysis software (VPT, Siemens Corporate Research, Princeton, NJ, USA) [27]. On the delayed enhancement imaging, myocardial infarction was defined as a signal intensity of hyperenhanced myocardium greater than five standard deviations (SD) above the mean signal intensity of the remote region [20], and MVO was defined as a hypoenhanced region within infarcted myocardium. All measurements were expressed as a percentage of the total LV myocardial volume.

Statistical analysis

Normally distributed quantitative data are expressed as mean ± SD. Non-normally distributed quantitative data are expressed as median and interquartile range. Categorical data are expressed as frequencies with percentages. Comparison of quantitative variables between SDB and no SDB patients were made using an unpaired Student's *t*-test for normally distributed variables or a non-parametric statistical test (Mann–Whitney) for skewed variables. Comparison between categorical variables was performed using the exact unconditional Pearson chi-squared statistic.

Table 1 Patient and sleep characteristics at baseline

	No SDB ($n = 17$)	SDB ($n = 18$)	p-value
Age, years	53 ± 10	56 ± 9	0.470
Body mass index, kg/m^2	27 ± 3	29 ± 4	0.281
Male gender, *n* (%)	13 (77)	16 (89)	0.330
Heart rate, beats/minute	73 ± 14	80 ± 18	0.223
Systolic blood pressure, mm Hg	121 ± 26	131 ± 26	0.272
Diastolic blood pressure, mm Hg	77 ± 14	78 ± 14	0.833
Hypertension, *n* (%)	10 (59)	9 (50)	0.600
Current smoker, *n* (%)	11 (65)	8 (44)	0.229
Diabetes mellitus, *n* (%)	1 (6)	3 (17)	0.316
Hypercholesterolemia, *n* (%)	5 (29)	2 (11)	0.176
Symptom-to-balloon time, h (IQR)	4.5 (2.95–7.13)	3.84 (2.79–9.86)	0.869
Non-LAD infarction, *n* (%)	9 (53)	8 (44)	0.615
TIMI flow before PCI, *n* (%)	–	–	0.258
Grade 0	13 (76)	16 (89)	–
Grade 1	3 (18)	1 (6)	–
TIMI flow post PCI, *n* (%)	–	–	0.316
Grade 2	1 (6)	3 (17)	–
Grade 3	16 (94)	15 (83)	–
Thrombus aspiration, *n* (%)	9 (53)	11 (61)	0.625
Glycoprotein IIb/IIIa inhibitor, *n* (%)	13 (77)	15 (83)	0.612
CK at admission, U/L (IQR)	247 (170–1071)	394 (138–2050)	0.869
Apnea–hypopnea index, 1/h	6 ± 4	33 ± 15	<0.001
Mean oxygen saturation, %	93 ± 3	93 ± 1	0.634
Minimum oxygen saturation, %	87 ± 4	84 ± 5	0.130
Total sleep time, min	392 ± 87	327 ± 74	0.216
Rapid eye movement sleep, min	17 ± 7	15 ± 6	0.389

Data are *n* (%), mean ± standard deviation or median (interquartile range)
CK creatinine kinase; *LAD* left anterior descending; *PCI* percutaneous coronary intervention; *SDB* sleep-disordered breathing; *TIMI* Thrombolysis in Myocardial Infarction, *IQR* interquartile range

Multivariable linear regression analyses were performed to identify predictors of ST deviation within 24 h and after more than 24 h post PCI, and for MVO in baseline CMR. Known potential confounders and risk factors that can affect myocardial ischemia [28, 29] and infarct size [20, 30] were entered into the adjusted models. Categorical variables included infarct location, TIMI flow before and after PCI, and current smoking. Continuous variables included symptom onset to reperfusion time, ST deviation before PCI, and AHI/h.

For graphical illustration, boxplots and scatterplots were used. All reported p-values were two-sided, and a p-value of 0.05 was considered the threshold for statistical significance. Data entry and calculation were performed with the software package SPSS 22.0 (IBM Corp., Armonk, NY, USA).

Results

In total, 57 STEMI patients fulfilled the inclusion and exclusion criteria of the observational study [20], of whom 35 could be included in the current analysis (Supplementary Figure S1). Of these patients, 18 had an AHI ≥15/h and were included in the SDB group. ST deviation pre PCI was measured in the ECG which was performed immediately before PCI. Mean time of measurement was similar in the no SDB and the SDB groups for the periods 0–24 h post PCI (5.1 ± 5.5 vs. 5.2 ± 4.2 h, $p = 0.964$) and >24 h post PCI (87.3 ± 48.3 vs. 88.2 ± 36.8 h, $p = 0.953$).

Patient characteristics

Baseline patient, sleep, and respiratory characteristics are presented in **Table 1**. There were no significant differences between patients with and without SDB with respect to age, gender, body mass index, coronary risk factors, and hemodynamic findings. There were also no significant differences between groups for time from symptom onset to revascularization, infarct-related artery, TIMI flow pre or post PCI, thrombus aspiration, or use of glycoprotein IIb/IIIa inhibitors during PCI. All patients were receiving similar medical therapy.

ST deviation and relative resolution of ST deviation

The extent of ST deviation before PCI was similar in the no SDB and SDB groups (0.094 [0.063–0.144] vs. 0.106 [0.055–0.132] mV, $p = 0.88$; **Fig. 1**). The no SDB group had significantly lower ST deviation compared to the SDB group both within the first 24 h after PCI (0.018 [0.012–0.039] vs. 0.052 [0.035–0.077] mV, $p = 0.01$) and more than 24 h after PCI (0.016 [0.005–0.029] vs. 0.045 [0.017–0.097] mV, $p = 0.006$).

Relative resolution of ST deviation was significantly higher in the no SDB group than in the SDB group within the first 24 h after PCI (74 [58–89] vs. 51 [24–69]%, $p = 0.004$; **Fig. 2**) and more than 24 h post PCI (86 [67–95] vs. 50 [13–84]%, $p = 0.037$). Complete resolution of ST deviation occurred significantly more frequently in the no SDB group than in the SDB group (0–24 h post PCI: 65 vs. 22%, $p = 0.011$; >24 h post PCI: 76 vs. 39%, $p = 0.025$; Supplementary Figure S2).

Although ST deviation pre PCI and 0–24 h post PCI did not correlate with the final infarct size determined by CMR 12 weeks after infarction, there was a significant correlation between 12-week infarct size and ST deviation at more than 24 h after PCI ($r = 0.751$, $p < 0.001$; **Fig. 3**).

Microvascular obstruction

After PCI the no SDB group showed significantly lower MVO compared to

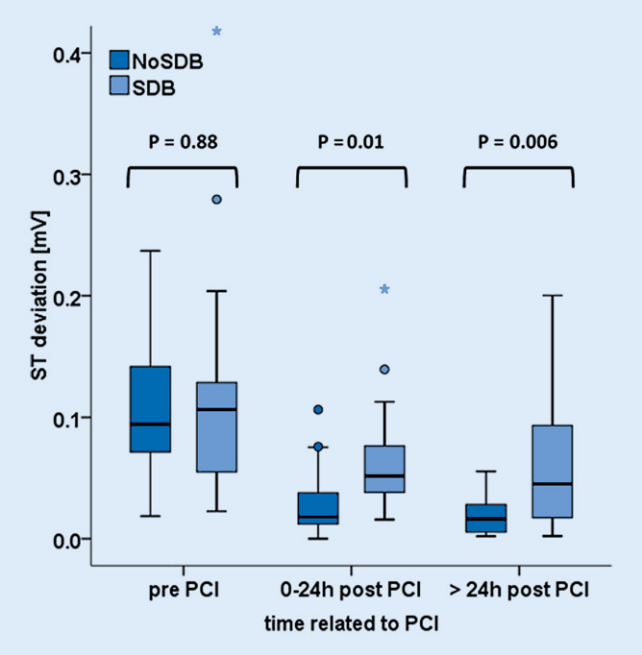

Fig. 1 ▲ Mean absolute ST deviation [mV] before, within 24 h, and >24 h after percutaneous coronary intervention (*PCI*). *SBD* sleep-disordered breathing

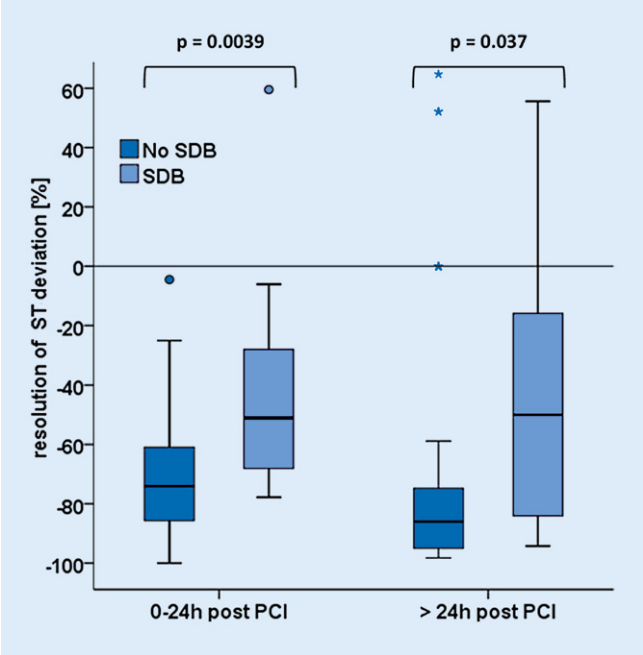

Fig. 2 ▲ Median relative resolution of ST deviation within the first 24 h and >24 h after percutaneous coronary intervention (*PCI*). *SBD* sleep-disordered breathing

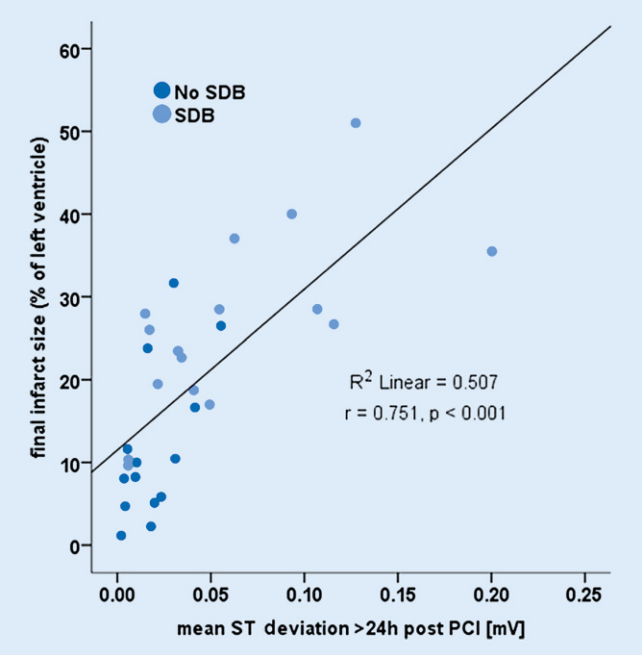

Fig. 3 ◀ Scatterplot of the correlation between ST deviation >24 h after percutaneous coronary intervention (*PCI*) and final size of necrotic myocardium 12 weeks after ST elevation myocardial infarction. *SBD* sleep-disordered breathing

the SDB group (0.0 [0.0–1.07] vs. 1.74 [0.23–6.16]%, $p = 0.027$; **Fig. 4**). The extent of MVO was significantly correlated with the extent of ST deviation at more than 24 h post PCI ($r = 0.496$, $p = 0.005$). There was also a significant correlation between MVO at baseline and the infarct size at 12 weeks ($r = 0.754$, $p < 0.001$).

NT-proBNP

There was no significant difference between the no SDB and SDB groups in NT-proBNP concentrations before PCI (108 [38–995] vs. 195 [51–1150] pg/mL, $p = 0.64$) and within the first 24 h after PCI (765 [463–1351] vs. 1328 [777–3142] pg/mL, $p = 0.19$; **Fig. 5**). However, at more than 24 h after PCI, the no SDB group had a significantly lower NT-proBNP concentration (810 [326–1000] vs. 1231 [690–2229] pg/mL, $p = 0.026$).

Predictors of ST deviation and MVO

Multiple linear regression analyses were used to identify independent predictors of residual ST deviation within 24 h and more than 24 h after PCI and MVO (**Table 2**). Symptom-to-balloon time and ST deviation pre PCI were independent predictors of ST deviation 0–24 h after PCI. Symptom-to-balloon time was also an independent predictor of ST deviation more than 24 h after PCI, whereas ST deviation pre PCI was not an independent predictor of ST deviation more than 24 h after PCI. Other independent predictors for ST deviation more than 24 h after PCI were infarct location, TIMI flow pre and post PCI, and current smoking. Although AHI was not an independent predictor of ST deviation 0–24 h post PCI, there was a significant association between AHI

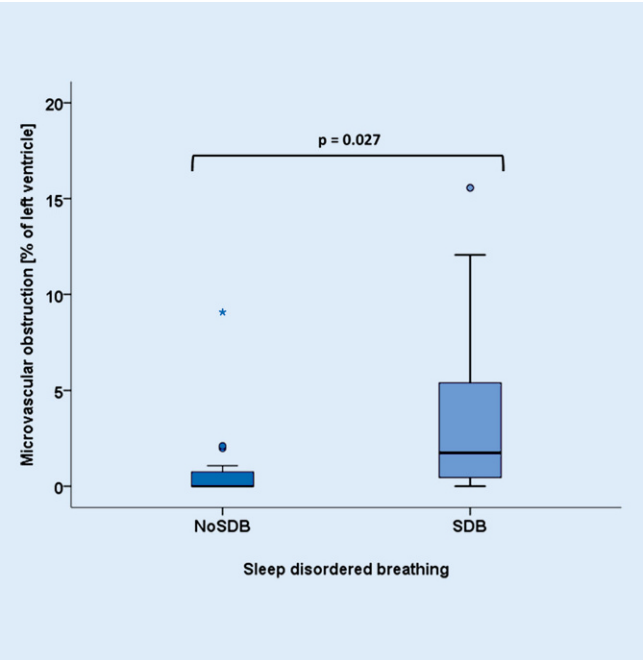

Fig. 4 ▲ Microvascular obstruction (in %) of left ventricular mass at baseline according to the presence of sleep-disordered breathing (*SBD*)

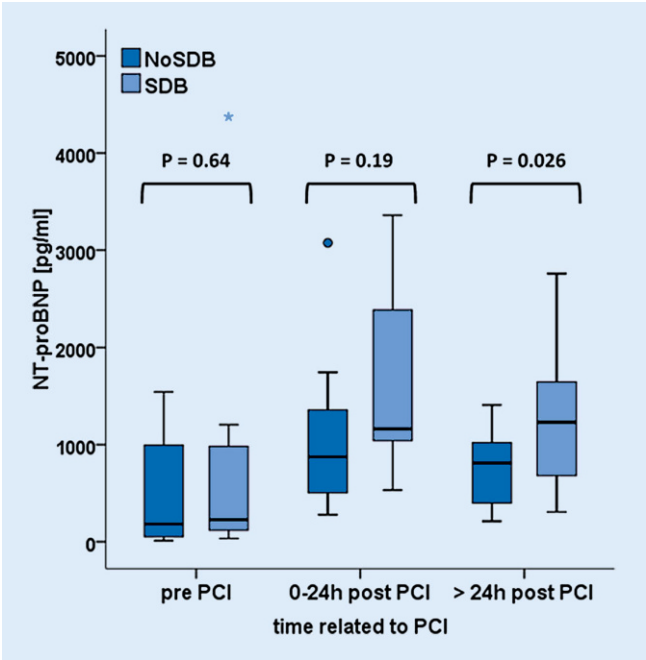

Fig. 5 ▲ Activity of N-terminal pro-brain natriuretic peptide (*NT-proBNP*) before percutaneous coronary intervention (*PCI*), within the first 24 h and >24 h after PCI

and ST deviation more than 24 h after PCI. Significant predictors of MVO were TIMI flow post PCI and AHI.

Discussion

This study reports a number of major novel observations. First, patients with SDB had a higher absolute ST deviation and less relative resolution of ST deviation compared to patients without SDB within the first 24 h and more than 24 h after PCI; this finding was independent of known risk factors for myocardial ischemia and infarct size. Secondly, residual ST deviation more than 24 h after PCI was significantly associated with final infarct size after 12 weeks. Thirdly, early after PCI, MVO was more frequent and affected more myocardium in patients with SDB than in those without SDB; the number of apneas and hypopneas per hour (AHI) was an independent predictor of MVO early after PCI. Finally, patients with SDB had higher serum levels of NT-proBNP more than 24 h after PCI.

A previous study by Nakashima et al. showed that STEMI patients with obstructive sleep apnea (OSA) had a higher incidence of relative ST resolution <50% at 30 min after successful PCI than those without OSA [21]. Given that the patient does not sleep in the 30 min between PCI and measurement of resolution of ST deviation, an immediate effect of SDB on ST resolution is unlikely. The findings of the current study extend those of Nakashima et al., in that they represent novel data on resolution of ST deviation in patients with and without SDB in the first days after PCI with exposure to SDB before the measurements of ST deviation.

The differences in resolution of ST deviation seen in STEMI patients with and without SDB in the first 24 h after PCI were similar to those reported by Nakashima and colleagues 30 min after PCI. More than 24 h after PCI, residual ST deviation remained significantly higher in SDB patients. Prolonged time to resolution of ST deviation after STEMI is associated with a worse prognosis [7]. Almost complete resolution of ST deviation, a favorable prognostic marker [7, 8], was very rare in SDB patients in this study, both within 24 and more than 24 h after PCI. Because AHI is an independent predictor of the extent of residual ST deviation more than 24 h after PCI, it is possible that early treatment of SDB in the very first nights after STEMI may improve resolution of ST deviation and lead to a more favorable prognosis.

It has been shown that the extent of early ST segment resolution is a good predictor of the final size of the necrotic area in infarcted myocardium [9]. In this study, residual ST deviation more than 24 h after PCI correlated well with final infarct size measured using CMR 12 weeks after STEMI, whereas there was no correlation between final infarct size and earlier measurements of ST deviation. These data suggest that an important proportion of the negative impact of SDB on final infarct size occurs early, in the first days after STEMI.

After acute myocardial infarction, the presence of MVO inhibits myocardial healing and LV remodeling [31, 32]. The higher frequency of MVO within a few days after successful reperfusion in patients with SDB in this study supports the suggestion that SDB has a negative impact on damaged myocardium very early after STEMI.

Natriuretic peptides are markers of heart failure [33]. However, an early increase of NT-proBNP levels also reflects acute myocardial ischemia in patients with acute coronary syndrome [34, 35], and correlates with area at risk [36]

Table 2 Predictors of different outcomes after PCI

Predictors of endpoint	ST deviation 0–24 h post PCI (µV)		ST deviation >24 h post PCI (µV)		Microvascular obstruction (%)	
	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*
Symptom-to-balloon time	2.00 [0.28; 3.71]	*0.025*	1.90 [0.35; 3.46]	*0.019*	0.05 [–0.14; 0.25]	0.586
Anterior infarction	25.44 [–3.83; 54.71]	0.086	45.92 [19.43; 72.42]	*0.001*	–0.02 [–3.14; 3.11]	0.992
TIMI flow pre PCI[a]	–25.22 [–70.41; 19.98]	0.261	–55.49 [–96.40; –14.58]	*0.010*	–3.01 [–7.36; 1.33]	0.165
TIMI flow post PCI[b]	–32.82 [–85.97; 20.33]	0.215	–57.87 [–105.98; –9.76]	*0.020*	–5.09 [–9.85; –0.33]	*0.037*
Current smoking	21.35 [–9.53; 52.23]	0.167	39.11 [11.16; 67.05]	*0.008*	1.43 [–1.68; 4.55]	0.351
ST deviation pre PCI (µV)	0.27 [0.07; 0.48]	*0.012*	0.16 [–0.03; 0.34]	0.097	Not included	–
AHI/h	0.45 [–0.32; 1.22]	0.240	0.82 [0.12; 1.51]	*0.024*	0.08 [0.01; 0.16]	*0.036*
Model summary[c]	$R^2 = 0.45$; F = 2.97		$R^2 = 0.59$; F = 5.20		$R^2 = 0.35$; F = 2.04	

Significant *p*-values are shown in italics
AHI apnea–hypopnea index; *B* regression coefficient; *CI* confidence interval; *PCI* percutaneous coronary intervention; *TIMI* Thrombolysis in Myocardial Infarction.
[a]TIMI grade 0 vs TIMI grade 1
[b]TIMI grade 2 vs TIMI grade 3
[c]Linear regression model: R^2 coefficient of determination; *F* F-test

and predicts ST segment resolution [37]. Higher levels of NT-proBNP in patients with SDB after STEMI have already been observed [38]. In this study, patients with SDB also had significantly higher serum levels of NT-proBNP within the first week after STEMI. This suggests prolonged myocardial ischemia in patients with SDB in the first days after myocardial infarction.

Pathophysiological considerations

Prompt reperfusion therapy is the key to a favorable prognosis in acute myocardial infarction [2], but does not overcome all the factors that can negatively influence the damaged myocardium. The prolonged resolution of ST deviation and greater extent of MVO in STEMI patients with SDB documented in this study might be caused by an increased mismatch of oxygen demand and supply. SDB causes increased sympathetic activation, arousals from sleep, and intermittent hypoxia, associated with acute surges in heart rate, blood pressure, and LV afterload [39]. In patients without cardiac disease and early after acute myocardial infarction, 24-hour blood pressure, heart rate, and cardiac workload, and thus myocardial oxygen demand [40, 41], are significantly increased in the presence of SDB [17, 42]. In addition, mechanical stress caused by negative intrathoracic pressures during nocturnal apnea episodes may also increase myocardial oxygen demand [39]. Increased oxygen demand is paralleled by reduced oxygen supply to damaged myocardial cells during nocturnal apneas and hypopneas which lead to intermittent hypoxia. It has been demonstrated that an obstructive apnea is associated with an 8-second delay between an increase in myocardial workload and the associated increase in coronary blood flow [43], and that SDB can impair myocardial tissue perfusion in STEMI patients [21]. Coronary vasodilatation as a physiological reaction to myocardial hypoxia is reduced by endothelial dysfunction [44] and arteriosclerosis [45], both of which are significantly associated with the severity of SDB [46, 47]. The apnea-related mismatch of oxygen demand and supply may be the crucial hit to cells in the myocardium at risk of infarction in the first days immediately after STEMI. This may lead to a larger final extent of necrotic myocardium and to more severe heart failure.

Study limitations

Differences in resolution of ST deviation and the extent of MVO in STEMI patients with and without SDB were striking, but these findings have to be interpreted in the light of the following limitations. Because of the observational study design, the results can only show that there is an association between SDB and less resolution of ST deviation and more MVO in the first days after STEMI, but it is not possible to establish a cause-and-effect relationship. In addition, the sample size in this study was small.

Conclusion

This study documented prolonged resolution of ST deviation and a greater extent of MVO after STEMI in patients with SDB. The present findings suggest that SDB-related myocardial ischemia on the myocardium at risk takes place in the first days after STEMI. This raises the question of whether prompt diagnosis of unknown SDB and early treatment after STEMI may prevent further myocardial damage. Such questions are currently being investigated in an ongoing multicenter randomized controlled trial of adaptive servoventilation in patients with acute myocardial infarction and SDB (TEAM-ASV; NCT02093377).

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Compliance with ethical guidelines

Conflict of interest. M. Arzt receives grant support from ResMed (Martinsried, Germany), Philips Home Healthcare Solutions (Murrysville, PA, USA), and the German Foundation for Cardiac Research (Deutsche Stiftung für Herzforschung). M. Arzt is the holder of an endowed professorship from the Free State of Bavaria at the University of Regensburg that was donated by ResMed (Martinsried, Germany) and Philips Home Healthcare Solutions (Murrysville, PA, USA). M. Arzt has previously received lecture fees from Philips Home Healthcare Solutions (Murrysville, PA, USA) and ResMed (Martinsried, Germany). U. Sterz, S. Buchner, A. Hetzenecker, A. Satzl, K. Debl, A. Luchner, O. Husser, O.W. Hamer, C. Fellner, F. Zeman, and L.S. Maier declare that they have no competing interests.

The local institutional ethics committee reviewed and approved the study protocol, and all research was carried out in accordance with Good Clinical Practice and the principles outlined in the 1964 Declaration of Helsinki and its later amendments. All patients provided written informed consent before enrolment in the study.

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