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ORIGINAL RESEARCH

Occurrence of Coronary Collaterals in Acute Myocardial Infarction and Sleep Apnea

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BACKGROUND: In patients with acute myocardial infarction (MI), cardioprotective effects of obstructive sleep apnea are postulated on account of hypoxemic preconditioning. The aim of this single-center substudy was to investigate a potential association between obstructive sleep apnea and the presence of coronary collaterals in patients with first-time acute MI who have been enrolled in an ongoing, multicenter clinical trial.

METHODS AND RESULTS: In TEAM-ASV I (Treatment of Sleep Apnea Early After Myocardial Infarction With Adaptive Servo-Ventilation Trial; NCT02093377) patients with first acute MI who received a coronary angiogram within 24 hours after onset of symptoms underwent polygraphy within the first 3 days. Coronary collaterals were classified visually by assigning a Cohen-Rentrop Score (CRS) ranging between 0 (no collaterals) and 3. Of 94 analyzed patients, 14% had significant coronary collaterals with a CRS ≥2. Apnea-Hypopnea Index (AHI) score was significantly higher in patients with CRS ≥2 compared with those with CRS <2 (31/hour [11–54] versus 13/hour [4–27]; *P*=0.032). A multivariable regression model revealed a significant association between obstructive AHI and CRS ≥2 that was independent of age, sex, body mass index, and culprit lesion left anterior descending artery (odds ratio [OR], 1.06; 95% CI, 1.01–1.12; *P*=0.023), but no significant association between coronary collaterals and central AHI (OR, 1.02; 95% CI, 0.97–1.08; *P*=0.443).

CONCLUSIONS: Patients with first-time acute MI had more extensive coronary collateralization with an increased AHI or rather an increased obstructive AHI. This finding supports the hypothesis that obstructive sleep apnea exerts potential cardioprotective effects, in addition to its known deleterious effects, in patients with acute MI.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02093377.

Key Words: coronary collaterals ■ hypoxic preconditioning ■ myocardial infarction ■ sleep-disordered breathing

Early after myocardial infarction (MI) the heart seems especially sensitive to the adverse effects of obstructive sleep apnea (OSA). This leads to microvascular obstruction, prolonged myocardial ischemia, less salvaged myocardium, and a smaller reduction of infarct size despite successful percutaneous coronary intervention (PCI).[1–4] Conversely, cardioprotective effects of OSA have also been postulated. Recurrent nocturnal oxygen desaturations might precondition the myocardium to hypoxemia, which may help to attenuate the myocardial damage caused by ischemia in patients with MI.[5–7] It is hypothesized that higher levels of circulating endothelial progenitor cells, angiogenic T cells, and vascular endothelial growth factor may support the formation of coronary collaterals in patients with OSA.[8]

Two small studies, one including patients with total chronic coronary occlusion and one including patients with acute MI, found more coronary collaterals in patients with OSA.[9,10] However, these studies neither discriminated between obstructive and central sleep apnea nor adjusted for potentially confounding clinical factors that may influence collateralization.

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CLINICAL PERSPECTIVE

What Is New?

- Patients with first-time acute myocardial infarction and elevated Apnea-Hypopnea Index scores had more extensive coronary collateralization.
- This finding was independent of age, sex, body mass index, and culprit lesion left anterior descending artery.

What Are the Clinical Implications?

- The study supports the hypothesis that obstructive sleep apnea exerts potential cardioprotective effects, in addition to its known deleterious effects, in patients with acute myocardial infarction.

Nonstandard Abbreviations and Acronyms

AHI	Apnea-Hypopnea Index
CRS	Cohen-Rentrop Score
SDB	sleep-disordered breathing
TEAM-ASV	Treatment of Sleep Apnea Early After Myocardial Infarction With Adaptive Servo-Ventilation Trial

The aim of the present study was to investigate the potential association between OSA and the presence of significant coronary collaterals in a larger sample of patients with first-time acute MI.

METHODS

Study Design

Data are available upon request from the authors. TEAM-ASV I (Treatment of Sleep Apnea Early After Myocardial Infarction With Adaptive Servo-Ventilation Trial I) is a multicenter, randomized, parallel group, open-label trial to compare treatment with PCI and optimal medical therapy versus PCI, optimal medical therapy, and adaptive servo-ventilation in patients with acute MI and sleep-disordered breathing (SDB).[11] The present cross-sectional analysis is a single-center substudy of baseline data from patients who were enrolled in TEAM-ASV I at the University Hospital Regensburg.

The trial was approved by the institutional ethics committee at the University of Regensburg (approval number: 11-101-0229) and is being conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. All patients provided written informed consent before undergoing study investigations. This trial is registered at clinicaltrials.gov (NCT02093377).

Study Population

Consecutive patients in stable hemodynamic condition who had experienced a first acute MI (ST-segment–elevation in the ECG or acute occlusion of coronary artery) were assessed for eligibility and included in the TEAM-ASV I trial if aged between 18 and 80 years and if a primarily successful PCI had been achieved within 24 hours after onset of symptoms.[11] Ad hoc PCI was performed in the culprit lesion and additionally in nonculprit subtotal stenoses. Chronic totally occluded coronary arteries were not intervened in the first examination. Exclusion criteria included previous MI or myocardial revascularization (PCI or surgical), indication for surgical revascularization, cardiogenic shock, mean supine blood pressure <60 mm Hg or New York Heart Association class IV, an implanted cardiac device or other contraindication (known allergies or contraindication to contrast dye) for cardiac magnetic resonance imaging, and previous stroke.[11] Patients with contraindications for positive airway pressure support, severe obstructive or restrictive airway disease, heart failure due to primary valve disease; patients on or with indication for oxygen therapy, mechanical or noninvasive ventilation, nocturnal positive airway pressure support, or diurnal symptoms of OSA requiring immediate treatment; patients awaiting heart transplantation; and pregnant patients were also excluded.[11] For troponin I as well as for creatine kinase and creatine kinase muscle-brain type, the respective peak value within 72 hours after MI was recorded.[12] Because of a change in laboratory testing from sensitive troponin I to high-sensitive troponin I during the study period, the troponin I value is given as "times upper limit of normal.".[13] Three-vessel disease was diagnosed if there was a stenosis of at least 50% in all 3 main epicardial coronary vessels. "Canadian Cardiovascular Society grading of angina pectoris" refers to the period of 14 days before the infarct-related event. All clinical data were collected from the medical files of the enrolled study patients.

Assessment of Sleep-Disordered Breathing

All patients underwent an overnight polygraphy (SOMNOscreen plus RC, SOMNOmedics, Randersacker, Germany) within 3 days after PCI. Polygraphy evaluation includes breathing parameters (such as pressure cannula for oronasal airflow, microphone for snoring, measurement of thoracic and abdominal respiratory effort), oxygen saturation, ECG, recording of body position, and light detection.[11]

Apneas and hypopneas were scored according to the internationally accepted American Academy of Sleep Medicine 2014 criteria,[14] by the same experienced sleep technician who was blind to baseline clinical characteristics. An apnea was defined as an air flow reduction ≥90% for >10 seconds, and a hypopnea was defined as an air flow reduction ≥30% for >10 seconds and ≥4% oxygen desaturation.[15] The Apnea-Hypopnea Index (AHI) was calculated as the sum of apneas and hypopneas divided by hours of sleep, the apnea index measured only apneas per hour of sleep. For obstructive AHI, the number of obstructive apneas and hypopneas per hour of sleep was calculated, central AHI measured all central apneas and hypopneas. A central apnea was defined by the absence of thoracoabdominal excursions. If the central component of an apnea already satisfied the definition of a central apnea (ie, ≥10 seconds), 3 consecutive obstructive breaths were needed to classify the event as an obstructive apnea. Just 1 or 2 obstructed breaths at the end of an apnea did not change the classification to an obstructive event.[16] Obstructive versus central hypopneas were determined based on the presence/absence of snoring during the event, and/or increased inspiratory flattening of the nasal pressure or positive airway pressure device flow signal compared with baseline breathing, and/or associated paradoxical thoracoabdominal movements during the event but not during preevent breathing on respiratory inductance plethysmography.[16,17] SDB was defined as AHI ≥15/hour. OSA was diagnosed if the obstructive AHI was greater than or equal to the central AHI, central sleep apnea was determined if the central AHI was greater than the obstructive AHI.

Assessment of Coronary Collaterals

Coronary angiograms from the acute MI were analyzed retrospectively by 2 interventional cardiologists who were blind to all other clinical data. At least 4 standardized projections of the left coronary artery and 2 of the right coronary artery were obtained. The extent of coronary collateralization was classified visually using the 4 grades set by the Cohen-Rentrop Score (CRS): CRS 0 (no filling of collateral vessels), CRS 1 (filling of collateral vessels without any opacification of the epicardial recipient artery), CRS 2 (partial filling of the target epicardial artery by collateral vessels), and CRS 3 (complete epicardial filling of the recipient artery by collaterals) (Figure 1).[18] A CRS ≥2 describes an at least partially retrograde filling of the occluded coronary. The score assigned to the collateral circulation was based on the imaging that best illustrated the occluded vessel. The collaterals of the culprit lesion were assessed.

Statistical Analysis

Data are presented as mean±SD for normal distributed continuous variables or as frequencies (with percentage) for categorical variables. Nonnormally distributed variables are presented as median and interquartile range (q1–q3). Normality was assessed visually by using Q-Q plots and density plots. To analyze baseline differences between patients with and without significant coronary collaterals, *t* tests were used for normally distributed continuous variables, and nonnormally distributed variables were compared using the Mann-Whitney *U* test. For categorical variables the chi-square test for independence was applied. Univariable logistic regression models were used to identify possible modulators for the presence of coronary collaterals. To check whether the association between presence of coronary collaterals and AHI was significant after adjusting for clinically selected modulators (age, male sex, body mass index [BMI], and culprit lesion left anterior descending artery), a multivariable logistic regression analysis was applied. Results are shown as odds ratios per 1-unit change with corresponding 95% CIs. No multiplicity adjustment was applied. A 2-sided *P*-<0.05 was considered statistically significant for all tests. All data were analyzed using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

RESULTS

Patient Characteristics

Between March 2014 and July 2019 147 patients with first-time acute MI were tested for eligibility for participation in TEAM-ASV I at the Regensburg study center, of whom 111 were eligible and enrolled in the study (Figure 2). Owing to withdrawal of consent or inadequate quality of the polygraphy recordings, 17 patients were excluded from the present analysis (Figure 2). The remaining set of 94 patients was 81% male with a mean age of 58±9 years and a mean BMI of 29±5 kg/m^2 (Table 1). Median AHI was 14/hour (interquartile range 5–31) and 49% had at least moderate SDB (Table 2). Median percentage of night-time spent with peripheral blood oxygen saturation below 90% was 6% (interquartile range 1–16) (Table 2).

Patients′ Characteristics According to Collaterals

Although 81 patients (86%) had no coronary collaterals or only side branches of the occluded vessel filled with contrast medium (CRS 0/1), 13 (14%) presented with at least partial or complete retrograde filling of the occluded coronary artery (CRS 2/3) (Table 1). Patients in the 2 groups did not differ significantly with respect to age, sex, and BMI (Table 1). There were also no

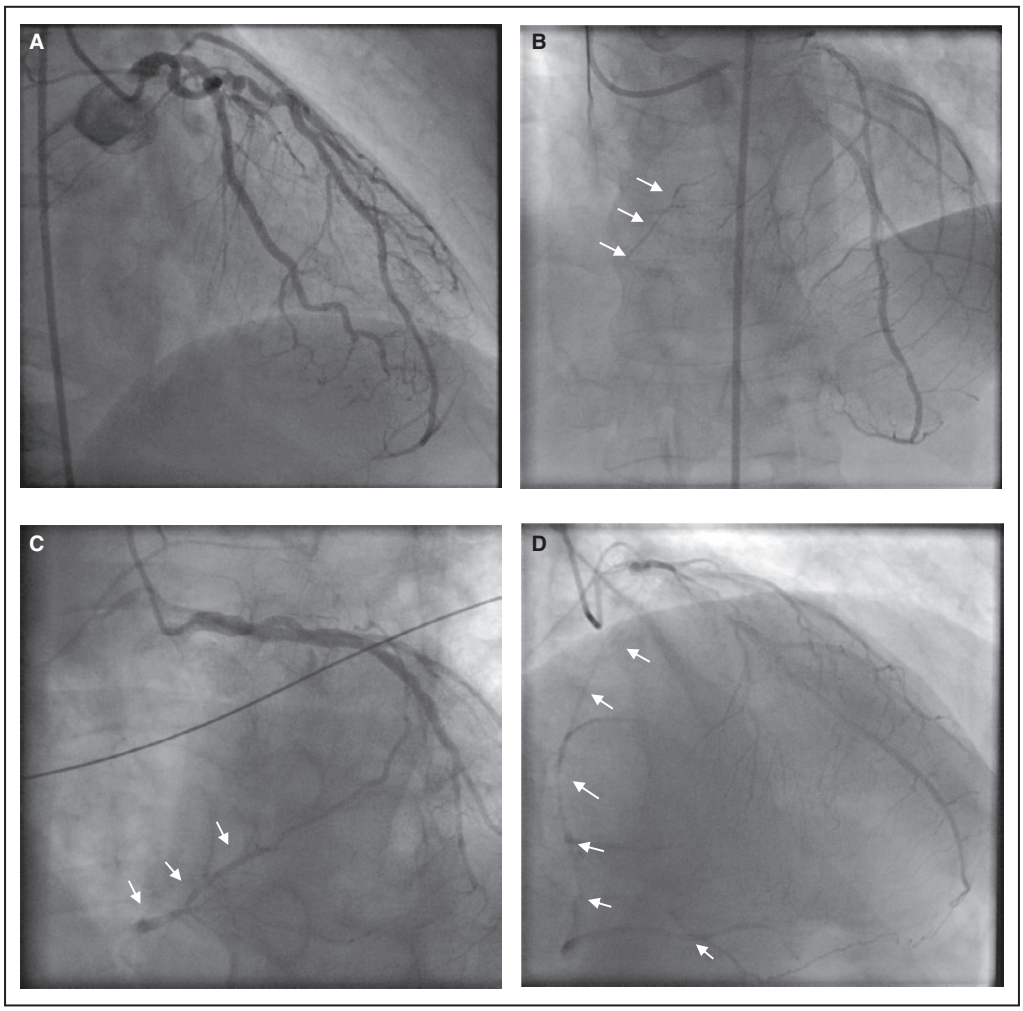

Figure 1. Coronary collaterals classified to the Cohen-Rentrop Score.[18]
Shown are cranial projections in which the left anterior descending artery collateralizes the occluded right coronary artery. Arrows mark the collaterals. **A**, grade 0=no filling of collateral vessels; **B**, grade 1=filling of collateral vessels without any opacification of the epicardial recipient artery; **C**, grade 2=partial filling of the target epicardial artery by collateral vessels; **D**, grade 3=complete epicardial filling of the recipient artery by collaterals.[10]

significant differences in respect to cardiovascular risk factors such as hypertension, smoking status, hyperlipidemia, low-density lipoprotein, and blood pressure. Of note, all 12 patients with known diabetes mellitus were graded with CRS 0/1. ST-segment–elevation MI was more frequent in patients with CRS 0/1 (Table 1).

Maximum troponin I, creatin kinase, and creatine kinase muscle-brain, the Canadian Cardiovascular Society grading of angina pectoris, and the pain-to-balloon time were similar between the 2 groups (each $P>0.05$; Table 1). Further details on interventional strategies and medication are presented in Table 1.

Nocturnal Respiratory Characteristics and Collaterals

Patients who have acute MI with CRS 2/3 had a significantly higher AHI than patients with CRS 0/1 (median: 31/hour versus 13/hour; $P=0.032$) (Table 2). Considering that the difference in central AHI was not significant between the 2 groups ($P=0.275$), this finding was driven by obstructive AHI, which was significantly higher in the CRS 2/3 group ($P=0.007$; Table 2). In both the univariable logistic regression analysis and the multivariable logistic regression model that accounted for age, sex, BMI, and culprit lesion left anterior descending artery, only the AHI was a significant modulator for the presence of relevant coronary collaterals ($P=0.024$ and $P=0.022$, respectively) (Table 3, Tables S1 through S3). In addition, we performed a second multivariable regression model to evaluate the association between the severity of OSA (obstructive AHI) and the severity of central sleep apnea (central AHI) with higher grade coronary collaterals (CRS 2/3) (Table 4). After accounting for age, sex, BMI, and culprit lesion left anterior

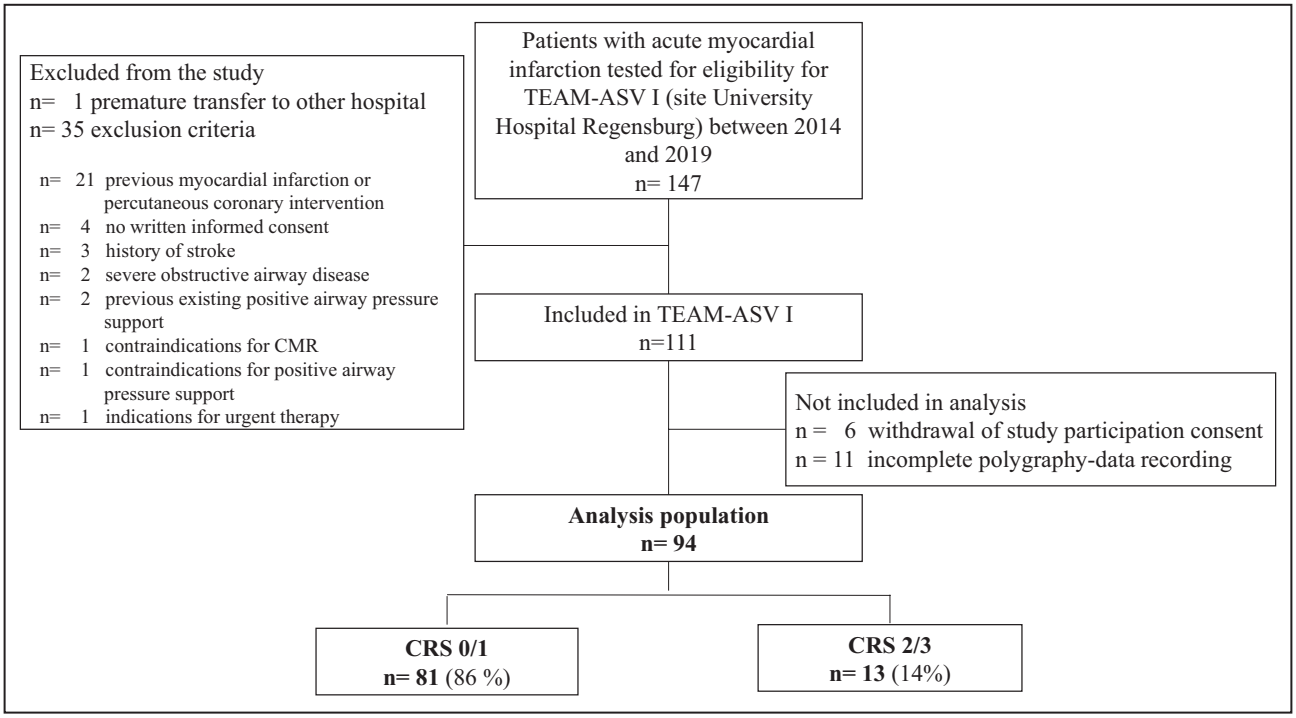

Figure 2. Study flow chart.
CMR indicates cardiac magnetic resonance imaging; CRS, Cohen-Rentrop Score; and TEAM-ASV I, Treatment of Sleep Apnea Early After Myocardial Infarction With Adaptive Servo-Ventilation Trial.

descending artery only obstructive AHI was significantly associated with CRS 2/3 (P=0.023), whereas central AHI was not (P=0.443) (Table 4).

The minimum and mean peripheral oxygen saturation and the percentage of recording time spent with a peripheral blood oxygen saturation below 90% were similar in the 2 groups (Table 2). The oxygen desaturation index was numerically higher in the CRS 2/3 group than in the CRS 0/1 group (Table 2). Neither minimum/mean peripheral oxygen saturation nor percentage of recording time spent with a peripheral blood oxygen saturation below 90% were significant modulators for the presence of significant coronary collaterals (each P>0.05) (Tables S4 through S7).

DISCUSSION

This study of patients with first-time acute MI revealed several new findings. AHI was significantly higher in patients who have acute MI with extensive coronary collateralization (CRS 2 or 3) but only AHI and obstructive AHI, not central AHI, were associated with the presence of significant collaterals. Critically, these associations were independent of selected clinically relevant modulators.

This finding supports and builds upon observations from previous studies. Steiner et al reported that coronary collateral vessel development is augmented in patients with total chronic coronary occlusion and OSA.[9] In contrast to the present study, Steiner et al investigated a heterogeneous group of 34 patients who underwent elective coronary angiography that uncovered a chronic coronary occlusion.[9]

Consistent with the present study, Ben Ahmed et al investigated 71 patients and reported that coronary collaterals during inaugural acute MI were more frequent in subjects with OSA.[10] Ben Ahmed et al performed the polygraphy up to 15 days after acute MI, versus 3 days in the TEAM-ASV I study.[10] We consider the temporal proximity of the polygraphy to the MI as a strength of the present study, because type and severity of SDB change in the early course after MI, as cardiac function improves.[19] In order to classify the extent of coronary collateralization, Ben Ahmed et al compared CRS ≥1 versus no coronary collaterals, whereas most other studies, including TEAM-ASV I, have used CRS ≥2 as a threshold for defining the presence of relevant collaterals.[10,20,21] Unlike previous studies, the TEAM-ASV I study additionally discriminated between central and obstructive respiratory events and found a significant association between coronary collaterals and obstructive, but not central, AHI.[9,10] Steiner and colleagues investigated only obstructive sleep apnea.[9] Ben Ahmed and colleagues excluded patients with central sleep apnea.[10] However, the number of patients with central

Table 1. Clinical Characteristics of the 94 Patients With First-Time Acute Myocardial Infarction Grouped According to CRS Grading of Coronary Collaterals

	Total (n=94)	CRS 0/1 (n=81)	CRS 2/3 (n=13)	*P* Value*
Age, y	58±9	58±9	60±9	0.431
Male sex, n (%)	76 (81)	64 (79)	12 (92)	0.258
Body mass index, kg/m^2	29±5	29±5	28±4	0.477
Hypertension, n (%)	57 (61)	49 (61)	8 (62)	0.943
Current smoker, n (%)	57 (61)	50 (62)	7 (54)	0.589
Family history of coronary heart disease, n (%)	38 (40)	33 (41)	5 (39)	0.876
Chronic obstructive pulmonary disease, n (%)	2 (2)	1 (1)	1 (8)	0.134
Diabetes mellitus, n (%)	12 (13)	12 (15)	0 (0)	0.137
Hyperlipidemia, n (%)	50 (53)	44 (54)	6 (46)	0.584
Low-density lipoprotein, mg/dL	129±34	129±34	133±38	0.657
Heart rate, /min	71±7	71±7	70±8	0.630
Systolic blood pressure, mm Hg	122±13	123±12	118±13	0.147
Diastolic blood pressure, mm Hg	70±8	70±7	66±9	0.057
Left ventricular ejection fraction in echocardiography, n (%)				0.627
>45%	74 (80)	63 (79)	11 (85)	
<45%	19 (20)	17 (21)	2 (15)	
Atrial fibrillation, n (%)	4 (4)	3 (4)	1 (8)	0.508
ST-segment–elevation myocardial infarction, n (%)	81 (86)	73 (90)	8 (62)	0.006
Maximum troponin [times upper limit of normal]	872 [115–2936]	879 [91–2956]	860 [421–4747]	0.338
Maximum CK, U/L	1300 [586–2829]	1256 [496–2726]	1569 [953–3438]	0.239
Maximum CK-muscle-brain type, ng/mL	109 [39–275]	110 [35–324]	103 [82–265]	0.494
Thrombus aspiration, n (%)	20 (21)	16 (20)	4 (31)	0.368
Glycoprotein IIb/IIIa inhibitor, n (%)	21 (22)	15 (19)	6 (46)	0.026
Infarct-related artery				0.004
Left main coronary artery, n (%)	0 (0)	0 (0)	0 (0)	
Left anterior descending artery, n (%)	42 (45)	40 (49)	2 (15)	
Left circumflex artery, n (%)	10 (11)	8 (10)	2 (15)	
Right coronary artery, n (%)	28 (30)	19 (24)	9 (69)	
Multivessel, n (%)	14 (15)	14 (17)	0 (0)	
Number of vessels diseased	2±1	2±1	2±1	0.123
Three-vessel disease, n (%)	26 (28)	20 (25)	6 (46)	0.108
Canadian Cardiovascular Society grading of angina pectoris, n (%):				0.188
0	67 (71)	60 (74)	7 (54)	
1	18 (19)	15 (19)	3 (23)	
2	5 (5)	3 (4)	2 (15)	
3	2 (2)	2 (3)	0 (0)	
4	2 (2)	1 (1)	1 (7)	
Pain-to-balloon time, min	224 [160–354]	220 [145–321]	285 [178–728]	0.168

Results are provided as mean±SD or median [q1–q3], unless otherwise stated. Coronary arteries with stenoses greater than or equal to 50% were designated as diseased vessel. CK indicates creatine kinase; and CRS, Cohen-Rentrop Score.

**P* value comparing CRS 0/1 vs CRS 2/3.

sleep apnea (n=2 of 73 monitored patients) seems rather low in comparison to other reports of up to 50% central sleep apnea in patients with SDB after acute MI.[19,22] In the present analysis, only obstructive, but not central, AHI was found to be associated with relevant coronary collaterals in patients who have acute MI. This might be explained by the fact that OSA is typically already existing before MI, whereas central apnea tends to occur after MI, owing to resulting heart failure.[23]

In contrast to the 2 previous studies, in this study multivariable regression analyses revealed an association between AHI and the presence of significant

Table 2. Nocturnal Respiratory Data of the 94 Patients With First-Time Acute Myocardial Infarction Grouped According to CRS Grading of Coronary Collaterals

	Total (n=94)	CRS 0/1 (n=81)	CRS 2/3 (n=13)	*P* Value*
Interval between percutaneous coronary intervention and polygraphy, d	2±1	2±1	2±1	0.559
AHI, /h	14 [5–31]	13 [4–27]	31 [11–54]	**0.032**
Obstructive AHI, /h	7 [2–16]	6 [2–13]	17 [10–32]	**0.007**
AI, /h	7 [2–22]	6 [2–20]	17 [6–35]	**0.040**
Obstructive AI, /h	4 [1–8]	3 [1–7]	8 [4–17]	**0.012**
Sleep-disordered breathing, n (%)	46 (49)	37 (46)	9 (69)	0.115
Obstructive sleep apnea, n (%)	28 (30)	22 (27)	6 (46)	0.961
Central sleep apnea, n (%)	18 (19)	15 (19)	3 (23)	0.961
Oxygen desaturation index, /h	9 [3–19]	9 [3–18]	13 [5–36]	0.120
Minimum SpO_2 (%)	82±7	82±7	83±3	0.730
Mean SpO_2, %	93±2	93±2	92±2	0.157
Percentage of recording time spent with a peripheral blood oxygen saturation below 90%, %	6 [0–16]	6 [1–15]	5 [2–39]	0.427

Results are provided as mean±SD or median [q1–q3], unless otherwise stated. AI indicates apnea index; AHI, Apnea-Hypopnea Index; CRS, Cohen-Rentrop Score; and SpO_2, peripheral oxygen saturation.

Bold indicates statistical significant values (*P*<0.05).

**P* value comparing CRS 0/1 vs CRS 2/3.

coronary collaterals that was independent of potential confounding factors.[9,10] Of note, all patients with diabetes mellitus belonged to the group with CRS grade 0/1. This is in line with previous studies describing less extensive coronary collateral formation in patients with diabetes mellitus,[24,25] although previous studies are contradictory.[26]

Coronary collaterals are interarterial connections that can provide an alternative source of blood supply to myocardium that has been jeopardized by failure of the original vessel.[27] Therefore, several studies have proposed cardioprotective effects of coronary collaterals in patients with coronary stenosis or coronary artery disease.[27,28] As coronary collateral formation is augmented in patients with OSA, OSA might contribute to this phenomenon of cardioprotection.

Animal models have shown that hypoxemic preconditioning owing to intermittent hypoxia could be a possible pathophysiological mechanism for angiogenesis and therefore responsible for the development of coronary collaterals.[29] Hypoxemic preconditioning, also experienced by patients with OSA owing to intermittent nocturnal hypoxia, may result in milder cardiac injury during an acute, nonfatal MI, and in an age decline relative mortality risk in sleep apnea.[5,6] Coronary collaterals may play an essential role in this context.

Table 3. Modulators for the Presence of Coronary Collaterals (Cohen-Rentrop Score ≥2) in 94 Patients With First-Time Acute Myocardial Infarction

Variable	Multivariable Analysis (Adjusted for Age, Male Sex, BMI, and Culprit Lesion LAD)	
Independent	**OR (95% CI)**	***P* Value**
AHI [/h, continuous]	1.04 (1.01–1.07)	**0.022**
Age, y	1.03 (0.96–1.12)	0.396
Male sex	3.98 (0.36–43.63)	0.259
BMI, kg/m²	0.88 (0.75–1.04)	0.139
Culprit lesion LAD	0.08 (0.01–0.45)	0.004

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were AHI (continuous variable), age, male sex, BMI, and culprit lesion LAD. Culprit lesion LAD vs non-LAD. Shown are the odds ratios (OR), 95% CIs, and *P* values. The ORs are per 1-unit-change. AHI indicates Apnea-Hypopnea Index; BMI, body mass index; and LAD, left anterior descending artery.

Bold indicates statistical significant values (*P*<0.05).

Table 4. Multivariable Logistic Regression Analyses in 94 Patients With First-Time Acute Myocardial Infarction: Severity of Central and Obstructive Sleep Apnea

Variable	Multivariable Analysis (Adjusted for Age, Male Sex, BMI, and Culprit Lesion LAD)	
Independent	**OR (95% CI)**	***P* Value**
Obstructive AHI [/h, continuous]	1.06 (1.01–1.12)	**0.023**
Central AHI [/h, continuous]	1.02 (0.97–1.08)	0.443
Age, y	1.03 (0.95–1.12)	0.441
Male sex	3.96 (0.35–45.48)	0.269
BMI, kg/m²	0.87 (0.74–1.03)	0.105
Culprit lesion LAD	0.07 (0.01–0.45)	0.005

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were obstructive AHI (continuous variable), central AHI, age, male sex, BMI, and culprit lesion LAD. Culprit lesion LAD vs non-LAD. Shown are the Odds ratios (OR) by logistic regression analysis, 95% CIs, and *P* values. The ORs are per 1-unit-change. AHI indicates apnea-hypopnea-index; BMI, body mass index; and LAD, left anterior descending artery.

Bold indicates statistical significant values (*P*<0.05).

Angiogenesis, which leads to coronary collateral formation, could be triggered by the hypoxia inducible factor-1 alpha, which is sensitive to hypoxia and regulates the production of vascular endothelial growth factor.[5] Increased levels of vascular endothelial growth factor can be found in patients with OSA.[30–34] In addition to increased vascular endothelial growth factor expression, other angiogenetic factors such as an increased number of endothelial progenitor cells and angiogenic T cells were detected in the monocytes of patients with acute MI and SDB.[8] Therefore, various angiogenetic factors may contribute to coronary collateral formation in patients with SDB. However, because Buchner et al found significantly less salvaged myocardium and a smaller reduction in infarct size in patients with acute MI and SDB, we assume that coronary collaterals may attenuate the established deleterious effects[1–4] of SDB after acute MI. The fact that no significant difference between the 2 groups was detected when comparing maximum troponin I, creatin kinase, and creatine kinase muscle-brain in the present study could be a sign for the collaterals not being efficacious enough to compensate the target diseased vessel and protect the corresponding myocardium. In addition, collaterals may play a different role in plaque rupture and chronic progressive occlusion. Different pathomechanisms underlying ST-segment–elevation MI and non–ST-segment–elevation MI (as the latter more often results from chronic occlusion[35]) may have implications for collateral formation. This might possibly explain the more frequent occurrence of ST-segment–elevation MI in patients without significant collaterals in the present study.

Several limitations of the present study warrant discussion. The number of patients in the group with relevant coronary collaterals was rather small and different from those without relevant collaterals in some baseline characteristics; however, after multivariable adjustment the findings according to sleep apnea were still significant. For diagnosis of SDB, patients underwent an overnight polygraphy instead of a full polysomnography, which is considered the most precise diagnostic tool. Nevertheless, portable respiratory devices are well established and validated for assessing SDB in the absence of overnight polysomnography in an inpatient setting.[36–38] Recent studies have shown good sensitivity and specificity of portable SDB monitoring devices in diagnosing OSA, but diagnostic accuracy for central sleep apnea is less well established. The divergent results that were observed for obstructive AHI and central AHI indicate a low rate of misclassification, because misclassification would confer a conservative bias that might obscure any differences between OSA and central sleep apnea.[39] Potentially, angiographic collateralization is not protective against myocardial ischemia in patients with SDB in the same way it might be for patients without SDB.[1] This could result in selection bias as there are possibly more patients with SDB presenting with collateralized MI. There are no hemodynamic data such as myocardial wall stress in this analysis that could explain the development of collaterals.

CONCLUSIONS

In summary, patients with first-time acute MI had more extensive coronary collateralization with an increased AHI or rather an increased obstructive AHI. Our finding supports the hypothesis that OSA may also exert potential cardioprotective effects in addition to its known deleterious effects[1–4] in acute MI.

Further studies are needed to investigate whether OSA triggers coronary collateralization, and if so, whether such collaterals are cardioprotective.

ARTICLE INFORMATION

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Author contributions: Summerer, Arzt, and Stadler were involved in the conception, hypotheses formulation, and design of the present work; the analysis and interpretation of preexisting data from the TEAM-ASV I patient cohort in Regensburg; and writing this article. Fox, Oldenburg, Buchner, and Debl were involved in designing TEAM-ASV I. Zeman was involved in the statistical analysis. Role of the Sponsor: The principal investigator (Arzt) has full control of the design and conduct of the study; the collection, management, analysis, and interpretation of data; the preparation, review, and approval of the article; and the decision to submit the article for publication.

Compliance with ethical standards: TEAM-ASV I was approved by the ethics committee of the University of Regensburg (approval no. 11-101-0229) and was conducted in accordance with the ethical principles outlined in Good Clinical Practice and the Declaration of Helsinki. Informed consent: Written informed consent was provided by all patients before enrolment. Open access funding enabled and organized by ProjektDEAL.

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Supplementary Material

Tables S1–S7

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SUPPLEMENTAL MATERIAL

Table S1. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and number of vessels diseased)**	
independent	OR (95% CI)	*p* Value
AHI [/h, continuous]	1.03 (1.00; 1.06)	**0.038**
Age [years]	1.01 (0.94; 1.09)	0.751
Male sex	2.69 (0.30; 24.14)	0.376
BMI [kg/m²]	0.92 (0.79; 1.07)	0.259
Number of vessels diseased	1.45 (0.69; 3.08)	0.330

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were AHI, age, male sex, BMI, and number of vessels diseased. Coronary arteries with stenoses greater than or equal to 50% were designated as diseased vessel. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

AHI: apnea-hypopnea-index; BMI: body mass index.

Table S2. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and pain-to-balloon-time)**	
independent	OR (95% CI)	*p* Value
AHI [/h, continuous]	1.03 (0.10; 1.06)	0.089
Age [years]	1.02 (0.95; 1.09)	0.606
Male sex	2.88 (0.32; 26.26)	0.349
BMI [kg/m²]	0.91 (0.78; 1.06)	0.245
Pain-to-balloon time [min]	1.00 (0.10; 1.00)	0.185

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were AHI, age, male sex, BMI, and pain-to-balloon time. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

AHI: apnea-hypopnea-index; BMI: body mass index.

Table S3. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and CCS)**	
independent	OR (95% CI)	*p* Value
AHI [/h, continuous]	1.03 (1.00; 1.06)	0.077
Age [years]	1.02 (0.95; 1.10)	0.531
Male sex	2.77 (0.31; 24.58)	0.359
BMI [kg/m²]	0.92 (0.79; 1.07)	0.274
CCS	1.25 (0.66; 2.38)	0.492

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were AHI, age, male sex, BMI, and CCS. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

AHI: apnea-hypopnea-index; BMI: body mass index; CCS: Canadian Cardiovascular Society grading of angina pectoris.

Table S4. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and culprit lesion LAD)**	
independent	OR (95% CI)	*p* Value
T90 (%)	1.02 (0.99; 1.05)	0.232
Age [years]	1.05 (0.97; 1.13)	0.221
Male sex	8.90 (0.67; 118.57)	0.098
BMI [kg/m²]	0.92 (0.78; 1.07)	0.266
Culprit lesion LAD	0.10 (0.02; 0.50)	0.005

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were T90, age, male sex, BMI, and culprit lesion LAD. Culprit lesion LAD versus non-LAD. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

BMI: body mass index; LAD: Left anterior descending artery; T90: percentage of recording time spent with a peripheral blood oxygen saturation below 90%.

Table S5. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and number of vessels diseased)**	
independent	OR (95% CI)	*p* Value
T90 (%)	1.02 (0.99; 1.05)	0.221
Age [years]	1.03 (0.96; 1.11)	0.424
Male sex	4.51 (0.46; 44.02)	0.195
BMI [kg/m²]	0.95 (0.82; 1.09)	0.427
Number of vessels diseased	1.43 (0.67; 3.03)	0.352

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were T90, age, male sex, BMI, and number of vessels diseased. Coronary arteries with stenoses greater than or equal to 50% were designated as diseased vessel. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

BMI: body mass index; T90: percentage of recording time spent with a peripheral blood oxygen saturation below 90%.

Table S6. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction with the dependent variable Cohen-Rentrop-Score 0/1 vs 2/3.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and pain-to-balloon time)**	
independent	OR (95% CI)	*p* Value
T90 (%)	1.01 (0.98; 1.05)	0.376
Age [years]	1.03 (0.96; 1.11)	0.346
Male sex	4.60 (0.47; 45.48)	0.192
BMI [kg/m²]	0.93 (0.81; 1.08)	0.365
Pain-to-balloon time [min]	1.00 (1.00; 1.00)	0.171

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were T90, age, male sex, BMI, and pain-to-balloon time. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

BMI: body mass index; T90: percentage of recording time spent with a peripheral blood oxygen saturation below 90%.

Table S7. Modulators for the presence of coronary collaterals (Cohen-Rentrop-Score ≥2) in 94 patients with first-time acute myocardial infarction with the dependent variable Cohen-Rentrop-Score 0/1 vs 2/3.

Variable	**Multivariable analysis (adjusted for age, male sex, BMI, and CCS)**	
independent	OR (95% CI)	*p* Value
T90 (%)	1.02 (0.99; 1.05)	0.201
Age [years]	1.04 (0.97; 1.12)	0.243
Male sex	4.71 (0.48; 45.99)	0.183
BMI [kg/m²]	0.95 (0.82; 1.09)	0.447
CCS	1.49 (0.85; 2.62)	0.167

Multivariable logistic regression analyses. The variables used in the multivariable regression analyses were T90, age, male sex, BMI, and CCS. Shown are the Odds ratios (OR), 95% confidence intervals (95% CI) and p values. The ORs are per 1-unit-change.

BMI: body mass index; CCS: Canadian Cardiovascular Society grading of angina pectoris; T90: percentage of recording time spent with a peripheral blood oxygen saturation below 90%.