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WYDZIAŁ LEKARSKI

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Ocena wybranych czynników ryzyka sercowo- naczyniowego u pacjentów z bruksizmem sennym

ROZPRAWA DOKTORSKA

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Składam serdeczne podziękowania wszystkim, dzięki którym realizacja badań wchodzących w skład niniejszej pracy doktorskiej była możliwa:

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SPIS TREŚCI

1. LISTA PUBLIKACJI WCHODZĄCYCH W SKŁAD CYKLU PRAC:

1.1. **Monika Michałek-Zrąbkowska**, Mieszko Więckiewicz, Joanna Smardz, Paweł Gać, Rafał Poręba, Anna Wojakowska, Grzegorz Mazur, Helena Martynowicz.
Determination of Inflammatory Markers, Hormonal Disturbances, and Sleepiness Associated with Sleep Bruxism Among Adults.
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1.2. **Monika Michałek-Zrąbkowska**, Mieszko Więckiewicz, Piotr Macek, Paweł Gać, Joanna Smardz, Anna Wojakowska, Rafał Poręba, Grzegorz Mazur, Helena Martynowicz.
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1.3. **Monika Michałek-Zrąbkowska**, Mieszko Więckiewicz, Paweł Gać, Joanna Smardz, Rafał Poręba, Anna Wojakowska, Katarzyna Gosławska, Grzegorz Mazur, Helena Martynowicz.
Effect of Sleep Bruxism Intensity on Blood Pressure in Normotensives.
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1.4. **Monika Michałek-Zrąbkowska**, Helena Martynowicz, Mieszko Więckiewicz, Joanna Smardz, Rafał Poręba, Grzegorz Mazur.

Cardiovascular Implications of Sleep Bruxism- A Systematic Review with Narrative Summary and Future Perspectives.

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2. WYKAZ STOSOWANYCH SKRÓTÓW

ABPM- Ambulatory blood pressure monitoring (24- godzinny ambulatoryjny pomiar ciśnienia tętniczego)

BEI- Bruxism episode index (indeks epizodów bruksizmu/ godzinę snu)

BMI- Body mass index (wskaźnik masy ciała)

CRP- C- reactive protein (białko C-reaktywne)

EAS- European Atherosclerosis Society (Europejskie Towarzystwo Miażdżycowe)

ESC- European Society of Cardiology (Europejskie Towarzystwo Kardiologiczne)

GABA- Gamma-aminobutyric acid (kwas gamma-aminomasłowy)

HOMA-IR- Homeostasis model assessment insulin resistance index (wskaźnik insulinooporności- ocena modelu homeostazy oporności na insulinę)

RMMA- Rhythmic masticatory muscle activity (rytmiczna aktywność mięśni żwaczy)

SCORE- Systematic COronary Risk Evaluation (skala oceny ryzyka sercowo-naczyniowego)

3. OMÓWIENIE PUBLIKACJI WCHODZĄCYCH W SKŁAD ROZPRAWY DOKTORSKIEJ

Choroby układu krążenia są główną przyczyną umieralności w Polsce i innych krajach wysokorozwiniętych. Wczesne rozpoznanie czynników ryzyka sercowo- naczyniowego u poszczególnych pacjentów ma istotne znaczenie w praktyce klinicznej, ponieważ pozwala ocenić, czy w ciągu najbliższych 10 lat wystąpią groźne powikłania chorób sercowo-naczyniowych, w tym zgon.[1] Zachorowalność na choroby układu krążenia wzrasta wraz z wiekiem. Działania profilaktyczne na wczesnym etapie życia oraz redukcja już istniejących czynników ryzyka sercowo- naczyniowego są kluczowe by obniżyć prawdopodobieństwo niepożądanych zdarzeń.

Ocena indywidualnego ryzyka sercowo- naczyniowego dla każdego pacjenta może być przeprowadzona za pomocą szeregu badań: laboratoryjnych, czynnościowych oraz z zastosowaniem narzędzi diagnostycznych np. karty ryzyka SCORE.[2] Następnie, na podstawie otrzymanych wyników pacjentowi przypisana zostaje kategoria ryzyka sercowo-naczyniowego. Zalecenia postępowania dla każdej kategorii znajdują swój wyraz w wytycznych Europejskiego Towarzystwa Kardiologicznego (ESC) oraz Europejskiego Towarzystwa Badań nad Miażdżycą (EAS). Na podstawie tych dokumentów istnieje możliwość wdrożenia odpowiednich działań z zakresu prewencji pierwotnej i wtórnej, co pozwala zmniejszyć całkowitą zachorowalność i śmiertelność.[3]

Poza klasycznymi czynnikami ryzyka sercowo- naczyniowego takimi jak m.in. nadciśnienie tętnicze, wiek powyżej 55 r.ż. u mężczyzn oraz powyżej 65. r.ż. u kobiet, palenie tytoniu, zaburzenia lipidowe, otyłość brzuszna, dodatni wywiad rodzinny w kierunku chorób układu krążenia, choroby współistniejące np. cukrzyca i niewydolność nerek, podwyższony poziom białka C- reaktywnego istnieje szereg dowodów wskazujących, że również czynniki psychospołeczne, stres, depresja oraz zaburzenia snu wpływają w sposób niezależny na

[1] Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J.* 2016;37(29):2315-2381.

[2] Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J.* 2003;24(11):987-1003.

[3] Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS), *European Heart J.* 2020; 41(1): 111–188.

zwiększenie ryzyka sercowo- naczyniowego. Pomocne w doprecyzowaniu ryzyka sercowo-naczyniowego są także biomarkery takie jak fibrynogen, kwas moczowy, homocysteina, fosfolipaza lipoproteinowa A2 i apolipoproteiny, a także ocena wskaźnika uwapnienia tętnic wieńcowych za pomocą tomografii komputerowej lub inne metody obrazowe, np. wykrywanie blaszek miażdżycowych w ultrasonografii tętnic szyjnych.[4] Należy jednak zaznaczyć, że kluczową rolę w oszacowaniu bezwzględnego ryzyka sercowo- naczyniowego odkrywają klasyczne czynniki ryzyka opisane w badanu Framingham.[5]

Zaburzenia snu takie jak zaburzenia oddychania podczas snu (np. obturacyjny bezdech senny) czy bezsenność zostały powiązane w licznych publikacjach ze wzrostem ryzyka sercowo- naczyniowego.[6] Brak jest jednak w literaturze jednoznacznych danych dotyczących związku bruksizmu sennego, jednego z najczęściej występujących zaburzeń snu z chorobami układu krążenia oraz zwiększonym ryzykiem sercowo- naczyniowym. Z tego powodu, sprawdzenie związku pomiędzy bruksizmem sennym a jego potencjalnymi implikacjami sercowo- naczyniowymi było głównym celem mojej pracy badawczej w ramach studiów doktoranckich.

Bruksizm senny to aktywność mięśni żwaczy podczas snu polegająca na zgrzytaniu zębami lub/i zaciskaniu ich. Wyróżnia się 3 typy elektromiograficzne bruksizmu sennego: fazowy, toniczny oraz mieszany. Typowe objawy bruksizmu to starcie powierzchni zębów, ból w obrębie żuchwy, silne bóle głowy oraz mięśni szyi i obręczy barkowej.[7] Bruksizm senny jest schorzeniem często występującym w populacji, zachorowalność w grupie osób dorosłych szacowana jest na 8-13%.[8] Dowiedziono, że nieprawidłowa funkcja neuroprzekaźników w ośrodkowym układzie nerwowym takich jak dopamina, serotonina i GABA oraz polimorfizmy genów kodujących receptory dla serotoniny i dopaminy mogą odgrywać podstawową rolę w

[4] Referowska M., Leśniak W.: Zapobieganie chorobom sercowo-naczyniowym w praktyce klinicznej. Podsumowanie wytycznych towarzystw europejskich 2016. Med. Prakt., 2016; 11: 12–33

[5] Andersson C, Johnson AD, Benjamin EJ, Levy D, Vasan RS. 70-year legacy of the Framingham Heart Study. *Nat Rev Cardiol*. 2019;16(11):687-698.

[6] Yacoub M, Youssef I, Salifu MO, McFarlane SI. Cardiovascular Disease Risk in Obstructive Sleep apnea: An Update. *J Sleep Disord Ther*. 2017;7(1):283.

[7] American Academy of Sleep Medicine. *International Classification of Sleep Disorders. 3rd ed.* Darien, IL, USA: American Academy of Sleep Medicine; 2014.

[8] Manfredini D, Serra-Negra J, Carboncini F, Lobbezoo F. Current concepts of bruxism. *Int J Prosthodont*. 2017;30(5):437–438.

patofizjologii bruksizmu sennego i stanowić przesłankę o jego genetycznym podłożu. Zaburzenia funkcji szlaków dopaminergicznego i serotoninergicznego związane są ze zwiększonym poziomem lęku, który pozostaje jednym z komponentów nasilających epizody bruksizmu sennego.[9] Przewlekły stres wpływa na homeostazę organizmu oraz aktywuje układ współczulny. Wzrost aktywności współczulnej wyrażający się wzrostem akcji serca i ciśnienia tętniczego oraz mikrowzbudzeniami ze snu obecnymi w zapisie elektroencefalograficznym jest nieodłącznym elementem patogenezy bruksizmu sennego.[10] Zwiększenie aktywności współczulnej powoduje aktywację procesu zapalnego oraz zwiększa ryzyko wystąpienia dysfunkcji śródbłonka naczyniowego i rozwoju chorób układu krążenia.

Celem niniejszej pracy doktorskiej była ocena wpływu bruksizmu sennego na wybrane czynniki ryzyka sercowo- naczyniowego takie jak: markery zapalne (CRP, fibrynogen, leukocytoza), wartości glikemii i insulinooporność ocenianą za pomocą wskaźnika HOMA, wartości ciśnienia tętniczego ocenianego metodą ABPM (ambulatory blood pressure monitoring; ambulatoryjny monitoring ciśnienia tętniczego) oraz ocena związku wybranych zaburzeń oddychania podczas snu z RMMA (rytmic musculatory muscle activity; rytmiczną aktywnością mięśni żwaczy). Ponadto, celem podsumowania dotychczasowych badań nad implikacjami sercowo- naczyniowymi bruksizmu dokonano przeglądu systematycznego dostępnej literatury naukowej.

Projektując badania będące składowymi publikacji wchodzących w skład niniejszej rozprawy postanowiłam eksplorować potencjalny związek bruksizmu sennego z poszczególnymi, wybranymi czynnikami ryzyka sercowo- naczyniowego oraz zaburzeniami oddychania podczas snu w grupie relatywnie młodych i zdrowych pacjentów. Celem mojego badania było sprawdzenie hipotezy, czy bruksizm senny- jako często występujący i uważany za łagodne schorzenie- może mieć potencjalnie poważne następstwa zdrowotne.

W pracy zatytułowanej *„Determination of Inflammatory Markers, Hormonal Disturbances, and Sleepiness Associated with Sleep Bruxism Among Adults."* zbadałam zaburzenia gospodarki węglowodanowej i hormonalnej u pacjentów z bruksizmem sennym. W grupie badanej stwierdzono podwyższone stężenie 17- hydroksysterydów w dobowej zbiórce

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[9] Wieckiewicz M, Bogunia-Kubik K, Mazur G, et al. Genetic basis of sleep bruxism and sleep apnea—response to a medical puzzle. *Sci Rep.* 2020;10(1):1–14.

[10] Lavigne, G.J.; Huynh, N.; Kato, T.; Okura, K.; Adachi, K.; Yao, D.; Sessle, B. Genesis of sleep bruxism: Motor and autonomic- cardiac interactions. *Arch. Oral Biol.* 2007, *52*, 381–384.

moczu oraz znamiennie podwyższone markery stanu zapalnego: CRP i fibrynogenu w surowicy krwi. Co ważne, było to pierwsze doniesienie w literaturze wykazujące związek pomiędzy wskaźnikiem BEI (bruxism episode index, indeks epizodów bruksizmu przypadających na godzinę snu) a podwyższonymi wykładnikami stanu zapalnego po wykluczeniu innych możliwych przyczyn, w tym bezdechu sennego. Przypuszczalnie, w badanej grupie pacjentów z bruksizmem sennym statystycznie istotne wyższe stężenie wykładników stanu zapalnego w surowicy krwi bez innej przyczyny może być traktowane jako czynnik zwiększający ryzyko sercowo- naczyniowe. Dalsze badania nad potencjalnym mechanizmem prozapalnym bruksizmu sennego może przynieść istotne korzyści w praktyce klinicznej oraz pozwoli oszacować ryzyko kardiowaskularne w tej grupie chorych. Ponadto, w badanej grupie stwierdziłam zaburzenia gospodarki węglowodanowej. Insulinooporność wyrażona wskaźnikiem HOMA-IR była zdiagnozowana u 23% pacjentów, przy czym średni indeks masy ciała (BMI) w tej grupie był prawidłowy (22.71 ± 3.83 kg/m2). Dotychczas w licznych doniesieniach naukowych łączono zaburzenia metabolizmu glukozy i rozwój insulinooporności z zaburzeniami oddychania podczas snu;[11] powiązanie zaburzeń metabolicznych z bruksizmem sennym wymaga pogłębienia badań. Przytoczona publikacja skłania do dalszego projektowania badań naukowych w tej dziedzinie.

Problematyka zaburzeń oddychania podczas snu postała poruszona w kolejnej pracy z cyklu pt. *„The Relationship between Simple Snoring and Sleep Bruxism: A Polysomnographic Study."* Przesłanką do zaprojektowania badania oceniającego chrapanie u pacjentów z bruksizmem sennym bez rozpoznanego bezdechu sennego był fakt, że większość autorów uznaje chrapanie jako wyraz wiotkości tkanek miękkich gardła- początek kontinuum- z obturacyjnym bezdechem sennym na końcu.[12] Ponadto, pomimo, że korelacje pomiędzy bruksizmem sennym a bezdechem sennym oraz pomiędzy bezdechem sennym a zwiększonym ryzykiem sercowo- naczyniowym zostały zbadane i szeroko przedstawione w literaturze międzynarodowej, zależność chrapania i bruksizmu sennego pozostawała niedostatecznie zbadana. Wyniki pracy pomogły sformułować kilka istotnych wniosków: natężenie głośności chrapania pozytywnie korelowało z bruksizmem fazowym, niezależnie od pozycji spania.

[11] Kent, B.D.; McNicholas, W.T.; Ryan, S. Insulin resistance, glucose intolerance and diabetes mellitus in obstructive sleep apnoea. *J. Thorac. Dis.* 2015, 7, 1343–1357.

[12] De Meyer, M.M.D.; Jacquet, W.; Vanderveken, O.M.; Marks, L.A.M. Systematic review of the different aspects of primary snoring. *Sleep Med. Rev.* 2019, 45, 88–94.

Ponadto pozycja spania wpływała zarówno na natężenie chrapania jak i zdarzeń bruksizmu. To istotne odkrycie pozwala potwierdzić hipotezę o ochronnym wpływie bruksizmu na zdarzenia związane z hipoksją oraz zachęca do prowadzenia dalszych szczegółowych badań w grupie osób bez stwierdzonego bezdechu sennego. Ponadto, wyniki badania wykazały negatywną korelację pomiędzy bruksizmem fazowym a akcją serca. Jak dyskutowałam w publikacji, bradykardia może być odpowiedzią samoregulacyjną wegetatywnego układu nerwowego na przyspieszoną akcję serca towarzyszącą mikrowzbudzeniom ze snu lub epizodom bruksizmu.

Klasycznym, dobrze zbadanym czynnikiem ryzyka sercowo- naczyniowego jest nadciśnienie tętnicze.[13] Podwyższona zmienność ciśnienia tętniczego w ciągu doby jest uznawana za jeden z czynników predysponujących do rozwoju nadciśnienia.[14] Ambulatoryjny pomiar ciśnienia tętniczego (ABPM) to prosty i nieinwazyjny sposób na ocenę kluczowych parametrów ciśnienia tętniczego- metoda ta została zastosowana w kolejnym badaniu, którego wyniki przedstawiłam w publikacji zatytułowanej *„Effect of Sleep Bruxism Intensity on Blood Pressure in Normotensives."* W badaniu uczestniczyło 65 pacjentów z podejrzeniem bruksizmu sennego. Charakterystyka grupy obejmowała pacjentów o średnim wieku 33.96 ± 11.22 lat z prawidłową masą ciała, bez rozpoznanego nadciśnienia tętniczego. W badaniu wykazałam, że częstość występowania epizodów bruksizmu (stopień ciężkości schorzenia) związana była ze zwiększoną zmiennością skurczowego ciśnienia tętniczego w czasie nocy. Wieloczynnikowa analiza regresji wykazała ponadto, że zmienność skurczowego ciśnienia tętniczego w okresie nocy była związana także z innymi niezależnymi czynnikami ryzyka: wyższym indeksem zdarzeń bruksizmu powiązanych z bezdechem, płcią męską, ciężkim bruksizmem sennym (BEI> 4/ godzinę), nadwagą, wyższym indeksem wybudzeń i krótszym czasem snu. Istotnym wnioskiem z badania jest nasuwająca się wskazówka kliniczna wnikliwego spojrzenia na bruksizm senny jako na schorzenie wpływające na zmienność ciśnienia tętniczego krwi, a co za tym idzie przypuszczalnie prowadzące do rozwoju nadciśnienia tętniczego w przyszłości.

Z uwagi na złożoną i niedostatecznie zbadaną etiopatogenezę bruksizmu sennego oraz szereg doniesień dotyczących możliwych następstw sercowo- naczyniowych tego częstego zaburzenia snu w publikacji pt. *„Cardiovascular Implications of Sleep Bruxism- A Systematic*

[13] Kannel WB. Blood Pressure as a Cardiovascular Risk Factor: Prevention and Treatment. *JAMA.* 1996;275(20):1571–1576.

[14] Parati, G.; Stergiou, G.S.; Dolan, E.; Bilo, G. Blood pressure variability: Clinical relevance and application. *J. Clin. Hypertens.* 2018, 20, 1133–1137.

Review with Narrative Summary and Future Perspectives." dokonałam przeglądu systematycznego i podsumowania aktualnego stanu wiedzy na ten temat. Stanowi ona jedyny dostępny w literaturze przekrojowy zbiór informacji dotyczący powiązania bruksizmu sennego z możliwymi następstwami sercowo- naczyniowymi. Praca przedstawia i systematyzuje heterogenne badania dotyczące związku pomiędzy bruksizmem sennym a potencjalnymi czynnikami ryzyka sercowo- naczyniowego, m.in. zwiększoną aktywnością współczulną, wzrostem akcji serca i ciśnienia krwi oraz markerami stanu zapalnego. W przytoczonej publikacji dokonałam oceny i podsumowania dotychczasowych osiągnięć badawczych w tej dziedzinie wskazując na potencjalne implikacje w praktyce klinicznej oraz sugerując konieczność dalszych badań. Podobnie jak w przytoczonych wcześniej pracach oryginalnych (*„The Relationship between Simple Snoring and Sleep Bruxism: A Polysomnographic Study."* oraz *„Effect of Sleep Bruxism Intensity on Blood Pressure in Normotensives."*), dyskutowana wzmożona aktywność współczulna wyrażona zarówno jako wzrost, jak i spadek częstości akcji serca, określana jako wyraz autonomicznej homeostazy organizmu, stanowi podłoże patofizjologiczne dalszych implikacji sercowo- naczyniowych.

Analiza parametrów snu we wszystkich przytoczonych pracach oryginalnych obejmowała badanie polisomnograficzne z rejestracją wideo wykonane w laboratorium snu. W istocie, prawidłowa ocena bruksizmu sennego powinna opierać się na polisomnografii z wideorejestracją ocenianej przez wykwalifikowanego polisomnografistę. Wykorzystanie tego narzędzia to złoty standard, a pełny opis badania, który obejmuje również ocenę czynności elektrycznej mózgu, zdarzeń oddechowych, napięcia mięśni oraz czynności elektrycznej serca może być niezwykle pomocny w pracy klinicystów różnych dziedzin medycyny. W odniesieniu do stratyfikacji ryzyka sercowo- naczyniowego, biorąc pod uwagę dotychczasowy stan wiedzy na temat jego składowych, multidyscyplinarne podejście w diagnostyce i leczeniu bruksizmu sennego jako schorzenia, którego podłożem jest wzmożona aktywność współczulna, wydaje się kluczowe. W toku realizacji projektu będącego podstawą niniejszej rozprawy wykazałam związek bruksizmu sennego z wieloma udokumentowanymi czynnikami ryzyka sercowo-naczyniowego: markerami stanu zapalnego (CRP, fibrynogenu), zmiennością ciśnienia tętniczego oraz zaburzeniami oddychania podczas snu. W związku z powyższym, zasadne wydaje się prowadzenie dalszych badań dotyczących związku bruksizmu sennego i jego implikacji sercowo- naczyniowych.

Podsumowując, aby dokonać dokładnej oceny ryzyka sercowo- naczyniowego u pacjentów, musimy wziąć pod uwagę szereg czynników wpływających na ostateczny wynik tej oceny, takich jak np. wiek, płeć, wyniki badań laboratoryjnych i czynnościowych. W

dotychczasowej praktyce klinicznej bruksizm senny traktowany był jako schorzenie typowo stomatologiczne, a jego związek z układem sercowo- naczyniowym odgrywał drugoplanową rolę. Wydaje się, że w kontekście przytoczonych badań wykonanych w ramach pracy doktorskiej oraz przeglądu systematycznego, stanowiących spójny ciąg tematyczny, bruksizm senny może stanowić przykład zaburzenia snu wpływającego na indywidualne ryzyko sercowo-naczyniowe. W związku z tym, zasadne wydaje się rozważenie przeprowadzenia oceny ryzyka sercowo- naczyniowego u pacjentów z bruksizmem sennym niezależnie od ich wieku i chorób współistniejących. Określenie roli bruksizmu sennego jako potencjalnie niezależnego czynnika podwyższonego ryzyka sercowo- naczyniowego wymaga dalszych szczegółowych badań.

4. PRACA 1

Determination of Inflammatory Markers, Hormonal Disturbances, and Sleepiness Associated with Sleep Bruxism Among Adults.

Nature and Science of Sleep

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ORIGINAL RESEARCH

Determination of Inflammatory Markers, Hormonal Disturbances, and Sleepiness Associated with Sleep Bruxism Among Adults

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Purpose: Sleep bruxism (SB) is characterized by repetitive phasic, tonic, or mixed masticatory muscle activity during sleep with multifactorial etiology. Previous studies have shown that the complex origin of SB can be related to the psychological features of the affected individual, consumption of caffeine and alcohol, smoking, obstructive sleep apnea, diabetes, increased body mass index, hypertension, thyroid diseases, and probable genetic vulnerability. This study aimed to investigate the inflammatory markers, hormonal disturbances, and sleepiness associated with SB, which have a potential effect on the total cardiovascular (CV) risk among relatively young and healthy patients.

Patients and Methods: A total of 74 individuals with probable SB were subjected to single-night polysomnography, followed by blood panel and 24-h urinary excretion tests. The level of daytime sleepiness was assessed in the participants using the Epworth Sleepiness Scale.

Results: SB was found in 78.4% of participants. The bruxism episode index (BEI) positively correlated with the concentrations of 17-hydroxycorticosteroids, C-reactive protein, and fibrinogen in the collected urine samples. A positive correlation was also found between phasic BEI and glucose concentration 2 h after the consumption of glucose solution. Sleep bruxers showed significantly increased sleepiness compared to nonbruxers ($p = 0.02$). The scores on sleepiness were positively correlated with mixed BEI, minimal oxygen saturation, and mean heart rate.

Conclusion: The results of this study revealed that participants with SB had metabolic and hormonal disturbances, probably due to stress and sympathetic activity. Moreover, it was found that young sleep bruxers potentially have a high CV risk due to the increased level of inflammatory and stress markers.

Keywords: sleep bruxism, obstructive sleep apnea, polysomnography, cardiovascular diseases, inflammatory markers

Introduction

Bruxism is a condition observed during sleep or wakefulness and has been estimated to be present in 8–31% of the population worldwide.[1] A widely accepted international consensus by Lobbezoo et al proposed two separate definitions for this condition,[2] which describes sleep bruxism (SB) as

> "a masticatory muscles activity during sleep that is characterized as rhythmic (phasic) or nonrhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals".[2]

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The consensus also proposed a grading system for categorizing bruxism: "possible"—grade based on a positive interview, "probable"—grade based on a clinical examination with or without a positive interview, and "definite"—grade based on a positive instrumental examination with or without a positive interview and/or positive clinical inspection.[2] SB is estimated to frequently occur in 13% of adults.[2] The American Academy of Sleep Medicine (AASM) defined bruxism as "a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible."[3] The International Classification of Sleep Disorders (ICDS-3) subsequently proposed the following criteria for the classification of SB: (A) regular or frequent tooth grinding sounds produced during sleep and (B) presence of one or more of the clinical signs that are pertinent to the aforementioned reports of tooth grinding during sleep: (1) abnormal tooth wear and (2) transient jaw-muscle pain or fatigue in the morning and/or temporal headache and/or jaw locking upon awakening.[4] The possible underlying causes of SB include dysfunction of the autonomic nervous system,[5,6] autonomic response to arousal, and impaired airway patency.[7] Lavigne et al reported that SB mostly occurs during cortical recovery associated with sympathetic activation manifested as an increased heart rate.[8,9] The international consensus[10] classified the causes of SB into three groups: biological, psychological, and external. The first group includes neurotransmission, cortical arousals, age, and genetic components of SB. The second group includes the important risk factors associated with the psychological features of the individual such as sensitivity to emotional stress[11] or anxiety disorders. The third group or external factors are constituted by caffeine consumption, smoking, alcohol intake, and drug use.[12] Furthermore, the multifactorial origin of bruxism involves medical conditions and disorders such as obstructive sleep apnea (OSA),[13,14] diabetes,[14] increased body mass index (BMI), hypertension,[15,16] thyroid diseases, sleepiness, and snoring.[17]

The contraction of cardiovascular diseases (CVDs) increases with age among patients with an established CVD and those at an increased risk of developing a CVD. Lifetime management of cardiovascular (CV) risk is important for patients of all ages, especially young and healthy ones and those who already have acquired comorbidities.[18] CVD prevention is described as a population-based strategy or targeted individual plan that focuses on eliminating or reducing CV morbidity and mortality as well as their related consequences.[19] Overall CV risk is contributed by multiple risk factors that may occur together and are specific for each patient. Hence, the CVD prevention plan should be customized to individuals based on their CV risk. Clinicians can assess the CV risk in an individual using many diagnostic tools, laboratory tests, and estimation systems such as the recommended Systematic Coronary Risk Evaluation (SCORE) scale.[20] These interventions can decrease the fatality of CVD.[21] A Cochrane review of randomized controlled trials revealed that modifying the CV risk by counseling or educating the general population did not reduce the overall CV mortality, but this intervention was effective in a distinct group of hypertensives or diabetics.[22] Psychosocial factors and chronic emotional stress are considered when assessing both the CV risk and SB etiology. In addition, depression and chronic stress affect homeostatic and autonomic functions and are associated with inflammatory processes and increased CV risk. The literature shows that sleep disturbances may be associated with increased CV risk.[23] It was previously indicated that increased sympathetic activity leads to inflammatory process[24] and is associated with SB.[6] Therefore, we hypothesized that SB may increase the CV risk by inducing the inflammatory process. This study aimed to determine sleepiness, hormonal disturbances, and inflammatory markers in individuals with SB, which might have a potential effect on their overall CV risk.

Participants and Methods

This study was conducted in the Sleep Laboratory of the Department of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at the Wroclaw Medical University, Poland. Patients who were suspected with primary bruxism were examined by qualified dentists in the Clinic of Prosthetic Dentistry in the Department of Prosthetic Dentistry at the Wroclaw Medical University, Poland. All the examined individuals were diagnosed with probable SB[2] based on a clinical investigation with or without a positive interview. Participants were recruited in the dental office, in accordance with the international consensus on the assessment of bruxism.[2] A physical extra- and intraoral examination was also conducted for a complex assessment of the teeth and oral soft tissue for each individual. The observed clinical symptoms included abnormal tooth wear and damage to the dental hard tissues (ie, cracked teeth), hypertrophy of masseter and temporalis muscles, tongue and lip indentations, injury to the inner

surface of the cheeks (linea alba), and repetitive damage of restorative work or prosthodontic constructions.[2]

Immature patients were excluded from the study group. In addition, the following exclusion criteria were applied: unwillingness to provide informed consent or undergo polysomnography; presence of secondary bruxism associated with neurological conditions; history of treatment with medications that can interfere with the functions of the nervous and muscular systems; presence of severe mental disorders, cognitive disability, or severe systemic diseases including active malignancy; presence of neurological disorders and/or neuropathic pain; coexistence of respiratory insufficiency or active inflammation; addiction to analgesics and/or drugs that can affect the muscles and breathing; or treatment with foregoing medications.

The protocol used for qualifying patients for the study is presented in Figure 1.

Daytime sleepiness was assessed in participants using the Epworth Sleepiness Scale (ESS), which is a simple, self-administered questionnaire consisting of eight items that measure a subject's habitual chance of dozing or falling asleep in common situations. The total score is obtained by adding up the scores of the individual items (rated on a scale of 0–3 for each item), and the maximum total score is 24. Scores above 10 were considered abnormal.[25] In addition, the participants were asked a series of questions about their symptoms and comorbidities, weight and height, age, and gender, with which their BMI (calculated as weight in kilograms divided by the square of height in meters) was determined.

Blood samples were collected from the participants by venipuncture and analyzed at the hospital's main laboratory at the University Clinical Hospital, Wroclaw, Poland. The levels of insulin and glucose in serum were determined after 12 h of overnight fasting. Insulin resistance (IR) was measured using the Homeostatic Model Assessment (HOMA) index. Based on fasting plasma levels of insulin and glucose, the HOMA index was calculated by dividing the values of fasting glucose (mmol/l) and fasting insulin (μU/l) by constant 22.5.

The polysomnographic examination was conducted at the Sleep Laboratory of the Department of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at the Wroclaw Medical University, Poland. All the patients were subjected to the standardized overnight, single-night polysomnography using the Nox-A1 (Nox Medical, Iceland) device. Polysomnograms (PSGs) were assessed in 30-s epochs. The outcomes of

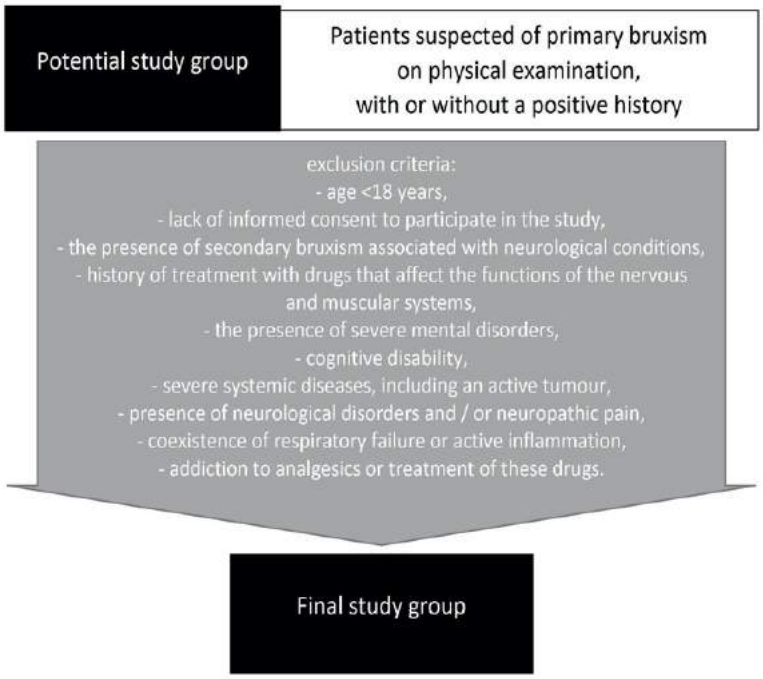

Figure 1 The protocol of qualifying patients for the study.

PSG included the following: sleep latency; total sleep time and sleep efficiency (%); the ratio of N1 (sleep stage 1), N2 (sleep stage 2), and N3 (sleep stage 3); and the stage of rapid eye movement sleep. Abnormal respiratory events were scored from the nasal pressure airflow signal. Apneas were defined as the absence of airflow for ≥10 s, while hypopneas were defined as a reduction in the breathing amplitude by ≥30% for ≥10 s with a ≥3% decline in blood oxygen saturation or followed by an arousal. Sleep scoring data and respiratory events were evaluated according to the standard criteria of the AASM 2013 Task Force.[26]

SB was assessed through the electromyographic (EMG) recordings of bilateral masseter muscle activity during sleep, supplemented by video and audio recordings. Following the AASM standards, the masticatory muscle activity events and bursts clustered in bruxism episodes were scored as phasic, tonic, or mixed. These standards recommend that the EMG outcome measures, such as peak amplitude, must be at least twice the basal EMG amplitude for confirming the diagnosis of SB. The interval between two EMG bursts should not be longer than 3 s to be considered as a part of the same episode. During the audiovisual scoring, a sustained burst in the EMG recording for a duration of 2 s was classified as tonic, three or more bursts or "twitches" for over 2 s were classified as phasic, and a mix of them was classified as a mixed episode. These episodes were summed up and expressed as bruxism events per hour of sleep or BEI (<2: irrelevant SB; 2–4: mild/moderate SB; >4: severe SB).[27]

Statistical analysis was performed using the statistical program "Dell Statistica 13" (Dell Inc., USA). For quantitative variables, arithmetic means and standard deviations in the studied groups were calculated. For quantitative independent variables with a normal distribution, the *t*-test or analysis of variance (ANOVA) was used for further statistical analysis. For quantitative independent variables with a distribution other than normal, the Mann–Whitney *U*-test or the nonparametric ANOVA Kruskal–Wallis test was used. The results for the qualitative variables are expressed as percentages. Chi-square test was used for further statistical analysis of independent qualitative variables. To determine the relationship between the studied variables, correlation and regression analyses were performed. For quantitative variables with a normal distribution, Pearson's *r* correlation coefficients were determined, and for those with a distribution other than normal, Spearman's *r* correlation coefficients were calculated. The model parameters in the regression analysis were estimated using the least-squares method. The results at the level of $p \leq 0.05$ were considered statistically significant.

This study was approved by the Ethics Committee of the Wroclaw Medical University (no. KB-195/2017) and was conducted in accordance with the guidelines of the Declaration of Helsinki. All the included patients gave written informed consent. The study was also registered in the international database for clinical studies (clinical trial registration: NCT03083405, WMU1/2017, https://clinicaltrials.gov/ct2/show/NCT03083405).

Results

The study group consisted of 74 Caucasian patients with probable SB (54 women and 20 men, mean age 34.24 ± 10.65 years, range 18–63 years). According to the commonly accepted BMI ranges, 6.8% (n = 5) of patients were diagnosed as underweight (BMI <18.5 kg/m^2), 63.5% (n = 47) had a normal weight (BMI 18.5–25 kg/m^2), 20.3% (n = 15) were identified as overweight (BMI 25–30 kg/m^2), and 6.8% (n = 5) were found as obese (BMI >30 kg/m^2). The demographic characteristics of the study group are presented in Table 1.

SB was diagnosed based on the polysomnographic findings. Almost three out of four (78.4%, n = 58) patients met the criteria required for the diagnosis of SB, while 36.5% were diagnosed with mild bruxism (n = 27) and 41.9% with severe bruxism (n = 31).

OSA was diagnosed in 23.0% (n = 17) of the examined patients. The condition was mild in 13.5% (n = 10), moderate in 5.4% (n = 4), and severe in 4.0% (n = 3). The results of the laboratory studies are presented in Table 2.

Plasma lipid measurements included mean total cholesterol level (195.76 ± 39.10 mg/dl), mean triglyceride level (112.01 ± 53.82 mg/dl), mean concentration of low-density lipoprotein cholesterol (LDL-C; 113.51 ± 32.71 mg/dl), and mean concentration of high-density lipoprotein cholesterol

Table 1 Demographic Characteristics of the Study Group

Age (Years)	34.24 ± 10.65
Body mass (kg)	65.73 ± 14.38
Height (m)	1.70 ± 0.09
BMI (kg/m^2)	22.71 ± 3.83
Men (%)	27.0 (n = 20)
Women (%)	73.0 (n = 54)
CAD (%)	0.0 (n = 0)
HT (%)	0.0 (n = 0)
IR (%)	22.9 (n = 17)

Abbreviations: BMI, body mass index (kg/m^2); CAD, coronary artery disease; HT, hypertension; IR, insulin resistance.

Table 2 Bruxism, Respiratory, and Laboratory Mean Indices in the Study Group

Polysomnography Parameter	Mean	SD	Laboratory Parameter	Mean	SD
BEI	4.56	3.54	ALT (U/l)	26.67	18.09
Phasic	1.56	2.08	AST (U/l)	24.78	8.39
Tonic	2.00	1.54	GGT (U/l)	20.78	10.58
Mixed	1.06	1.00	Creatinine (mg/dl)	0.94	0.13
AHI	5.02	8.50	Uric acid (mg/dl)	4.69	1.15
ODI	4.62	7.47	Urea (mg/dl)	24.39	6.66
Snore (%)	7.38	14.38	Magnessium (mg/dl)	2.06	0.12
OSA	0.36	1.75	Potassium (mmol/l)	4.23	0.39
MA	0.02	0.09	Sodium (mmol/l)	140.65	1.97
CA	0.26	0.45	Calcium (mg/dl)	9.18	0.22
Hypopnea	3.99	7.18	WBC (10^9/l)	5.92	1.62
Cheyne–Stokes	0.70	1.84	RBC (10^{12}/l)	4.71	4.00
Mean SpO_2 (%)	94.78	1.80	Hemoglobin (g/dl)	13.96	1.39
Min SpO_2 (%)	88.72	7.27	Platelets (10^9/l)	248.89	57.44
SpO_2 <90% (%)	1.16	3.45	Microalbuminuria (mg/g)	5.42	4.80
Mean heart rate	61.65	8.17	fT3 (pg/mL)	3.24	0.30
Max heart rate	97.66	15.24	fT4 (ng/dl)	1.21	0.21
Min heart rate	48.63	7.01	TSH (μU/mL)	1.91	1.42

Abbreviations: BEI, Bruxism Episode Index; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; OSA, obstructive sleep apnea; MA, mixed apnea; CA, central apnea; mean SpO_2, mean oxygen saturation (%); SpO_2 <90% (%), time with oxygen saturation <90% (% of total sleep time); ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyltransferase; WBC, white blood cells; RBC, red blood cells; fT3, free triiodothyronine; fT4, thyroxine; TSH, thyroid-stimulating hormone.

(HDL-C; 60.19 ± 14.61 mg/dl). The total cholesterol level was elevated (>200 mg/dl) in 43.2% (n = 32) of the patients. Increased triglyceride levels (>150 mg/dl) were observed in 18.9% (n = 14) of the cases, whereas elevated LDL-C (>135 mg/dl) was found in 18.9% (n = 14). Low HDL-C, classified as <40 mg/dl, was found in 5.4% (n=4) of the tested patients. No statistically significant differences were noted in any of these measurements between patients without SB (BEI <2) and those with severe SB (BEI >4). The mean concentration of LDL-C in patients with OSA (apnea–hypopnea index (AHI) ≥5) was significantly greater than that in those without OSA (126.81 ± 40.47 mg/dl vs 109.77 ± 29.54 mg/dl, $p = 0.047$). An increased mean triglyceride value was found in patients with severe OSA (AHI >30) as compared to those with AHI ≤30 (176.00 ± 133.29 mg/dl vs 109.19 ± 48.01 mg/dl, $p = 0.03$).

The mean ESS score of the diagnosed patients was 9.90 ± 4.96. Daytime sleepiness, which was identified with a sleepiness score ≥10 in the ESS, was observed in 48.6% (n = 36) of the participants. A significant difference in the ESS scores was noted between patients with SB (BEI ≥2) and those without SB (10.62 ± 4.72 and 7.07 ± 5.03, respectively, $p = 0.02$). The sleepiness scores were positively correlated with the following indices: mixed bruxism episodes, minimal oxygen saturation, and mean heart rate (correlation coefficients: 0.33, 0.25, and 0.24, respectively, $p < 0.05$).

The comparison of bruxism and respiratory indices between patients who reported daytime sleepiness (ESS ≥10) and those without sleepiness (ESS <10) is presented in Table 3.

The HOMA index was calculated based on the results obtained from the analysis of carbohydrate metabolism, the analysis of fasting glucose and insulin levels, and the analysis of glucose and insulin level 1 and 2 h after the intake of the glucose solution. In the entire study group, the mean levels of fasting glucose (mmol/l), glucose 2 h after consuming the glucose solution, fasting insulin (μU/mL), and insulin 1 and 2 h after consuming the glucose solution were determined as 5.10 ± 0.58 mmol/l, 4.90 ± 1.20 mmol/l, 8.04 ± 6.96 μU/mL, 51.77 ± 55.31 μU/mL, and 25.24 ± 28.98 μU/mL, respectively. An elevated level of fasting glucose (>5.5 mmol/l) was found in 12.2% (n = 9) of the examined patients. Based on the HOMA indices, 13.5% (n = 10) of patients were found to have early-stage IR (HOMA-IR >1.9), 9.5% (n = 7) had advanced IR (HOMA-IR >2.9), and 73.0% (n = 54) were normal. The levels of glucose measured 2 h after consuming the glucose solution were positively correlated with phasic bruxism episodes ($r = 0.26$, $p < 0.05$).

Table 3 Comparison of Bruxism and Respiratory Indices Based on the Sleepiness Scores

Parameter	ESS <10		ESS ≥10		p
	Mean	SD	Mean	SD	
BEI	**3.93**	**3.40**	**5.50**	**3.63**	**0.05**
Phasic	1.36	2.43	1.92	1.78	0.28
Tonic	1.82	1.47	2.27	1.64	0.23
Mixed	**0.76**	**0.82**	**1.43**	**1.07**	**0.00**
AHI	5.00	8.33	5.56	9.21	0.79
ODI	4.34	7.14	5.28	8.24	0.61
Snore (%)	7.69	11.01	8.10	17.67	0.91
TST (min)	417.57	56.53	424.73	64.62	0.63
SL (min)	20.41	15.76	25.47	26.91	0.35
REML (min)	**118.85**	**78.89**	**88.77**	**39.31**	**0.05**
OSA	0.13	0.50	0.61	2.45	0.27
MA	0.02	0.04	0.03	0.12	0.56
CA	0.26	0.39	0.28	0.53	0.88

Note: Statistically significant differences are marked in bold font ($p \leq 0.05$).
Abbreviations: BEI, Bruxism Episode Index; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; TST, total sleep time (minutes); SL, sleep latency (minutes); REML, rapid eye movement stage latency (minutes); OSA, obstructive sleep apnea; MA, mixed apnea; CA, central apnea; ESS, Epworth Sleepiness Scale.

Table 4 Correlation of Bruxism and Respiratory Indices with Laboratory Findings: 17-OHCS, CRP, and Fibrinogen

Parameter	17-OHCS (mg/24 h)	CRP (mg/l)	Fibrinogen (g/l)
BEI	**0.27**	**0.34**	**0.42**
Phasic	**0.26**	0.11	**0.33**
Tonic	0.22	**0.38**	**0.43**
Mixed	0.18	**0.39**	0.18
AHI	0.23	**0.36**	**0.26**
ODI	**0.27**	**0.48**	**0.33**
Snore (%)	**0.35**	**0.41**	0.21
OSA	0.18	0.18	0.13
MA	−0.06	−0.09	**0.35**
CA	0.1	−0.08	0.09
Hypopnea	**0.25**	**0.41**	**0.32**

Note: Correlation coefficients are marked in bold font, relevant with $p \leq 0.05$.
Abbreviations: 17-OHCS, 17-hydroxycorticosteroids; CRP, C-reactive protein; BEI, Bruxism Episode Index; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; OSA, obstructive sleep apnea; MA, mixed apnea; CA, central apnea.

The 24-h urinary excretion rates of 17-hydroxycorticosteroids (17-OHCS) were higher in 12.2% (n = 9) of patients, whereas 62.2% (n = 46) had normal ranges and 13.5% (n = 10) showed lower rates. The estimated mean value was 5.86 ± 3.14 mg/24 h. In patients with severe SB (BEI >4), the level of 17-OHCS was found as 6.94 ± 3.76 mg/24 h, which was significantly higher than that in patients without SB (5.05 ± 2.31 mg/24 h, $p = 0.02$). Student's *t*-test also revealed a statistically significant difference in the urinary levels of 17-OHCS between patients with OSA (AHI ≥5) and those without OSA (AHI <5) (8.36 ± 4.12 mg/24 h vs 5.18 ± 2.44 mg/dl, $p = 0.01$). Urinary 17-OHCS levels were positively correlated with the following indices: BEI, phasic bruxism episodes, oxygen desaturation index (ODI), snore, and hypopnea (correlation coefficients: 0.27, 0.26, 0.27, 0.35, and 0.25, respectively, $p < 0.05$) (Table 4).

The mean concentration of CRP in the blood plasma of the examined patients was 2.28 ± 5.15 mg/l, which was increased by 6.8% (n = 5) of the patients. A statistically significant difference was observed in BEI between patients with normal CRP values and those with increased values (4.39 ± 3.43 mg/l vs 7.88 ± 4.43 mg/l, respectively, $p = 0.042$). Student's *t*-test also revealed a significant difference between patients with severe OSA (AHI >30) and those with AHI ≤30 (15.57 ± 16.62 mg/l vs 1.69 ± 3.35 mg/l, respectively, $p = 0.01$). Patients with CRP values >5 mg/l exhibited a significantly increased level of tonic and mixed SB episodes compared to patients with normal CRP levels (3.70 ± 1.96 mg/l vs 1.88 ± 1.46 mg/l, respectively, $p = 0.01$ for tonic; 2.02 ± 1.49 mg/l vs 1.01 ± 0.94 mg/l, respectively, $p = 0.03$ for mixed). Plasma CRP levels were positively correlated with the following indices: BEI, tonic and mixed bruxism episodes, AHI, ODI, snore, and hypopnea (correlation coefficients: 0.34, 0.38, 0.39, 0.36, 0.48, 0.41, and 0.41, respectively, $p < 0.05$) (Table 4). In patients with elevated CRP values, sleep indicators such as AHI, ODI, snore percentage, hypopnea index, and mean desaturation drop were significantly higher as compared to those with a normal level of CRP (Table 5).

The mean fibrinogen concentration in the blood serum of the patients was 2.69 ± 0.57 g/l. With the normal fibrinogen range being 1.8–3.5 g/l, 1.3% (n = 1) of the patients had a below-normal range and 5.4% (n = 4) showed an above-normal range, while 82.4% (n = 61) of the patients exhibited the normal range. Fibrinogen concentration in patients with severe SB (BEI >4) was significantly increased to 2.86 ± 0.69 g/l, compared to those without SB (2.58 ± 0.45 g/l; $p = 0.046$). Serum fibrinogen levels were positively correlated with the following indices: BEI, phasic and tonic bruxism episodes, AHI, ODI, mixed apnea, and hypopnea (correlation coefficients: 0.42, 0.33, 0.43, 0.26, 0.33, 0.35, and 0.32, respectively, $p < 0.05$) (Table 4).

The multivariate regression analysis showed that the relationships between BEI and 17-OHCS, BEI and CRP,

Table 5 Differences in Bruxism and Respiratory Indices Based on CRP Level

Parameter	CRP 0–5 mg/l		CRP >5 mg/l		p
	Mean	SD	Mean	SD	
BEI	**4.39**	**3.43**	**7.88**	**4.43**	**0.04**
Phasic	1.57	2.07	2.26	2.65	0.48
Tonic	**1.88**	**1.46**	**3.70**	**1.96**	**0.01**
Mixed	**1.01**	**0.94**	**2.02**	**1.49**	**0.03**
AHI	**4.21**	**6.85**	**17.10**	**18.81**	**0.00**
ODI	**3.68**	**5.27**	**18.18**	**17.76**	**0.00**
Snore (%)	**5.83**	**11.7**	**25.42**	**30.59**	**0.00**
OSA	0.29	1.80	1.14	1.43	0.31
MA	0.02	0.09	0.00	0.00	0.60
CA	0.27	0.47	0.16	0.36	0.61
Hypopnea	**3.19**	**5.22**	**15.8**	**17.58**	**0.00**
SpO_2 <90% (%)	0.78	3.10	3.10	5.82	0.07
Mean desaturation drop (%)	**3.14**	**0.69**	**3.90**	**1.26**	**0.03**

Note: Statistically significant differences are marked in bold font ($p \leq 0.05$).
Abbreviations: BEI, Bruxism Episode Index; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; OSA, obstructive sleep apnea; MA, mixed apnea; CA, central apnea; SpO_2 <90% (%), time with oxygen saturation <90% (% of total sleep time).

Table 6 Results of the Regression Analysis in the Studied Group

Model for 17-OHCS (mg/24 h)				
A. The model of relationship between BEI, AHI, BMI (kg/m^2) and 17-OHCS (mg/24 h)				
	intercept	**BEI**	**AHI**	**BMI**
regression coefficient	− 2.43	**0.21**	0.02	**0.32**
SEM of Rc	2.29	**0.11**	0.04	**0.10**
p value	0.29	**0.04**	0.67	**0.01**
B. The model of relationship between BEI, AHI, BMI (kg/m^2) and CRP (mg/l)				
	intercept	**BEI**	**AHI**	**BMI**
regression coefficient	− 2.93	**0.39**	**0.16**	0.11
SEM of Rc	3.62	**0.17**	**0.07**	0.16
p value	0.42	**0.02**	**0.03**	0.48
C. The model of relationship between BEI, AHI, BMI (kg/m^2) and Fibrinogen (g/l)				
	intercept	**BEI**	**AHI**	**BMI**
regression coefficient	**1.57**	**0.06**	0.01	**0.04**
SEM of Rc	**0.40**	**0.02**	0.01	**0.02**
p value	**0.01**	**0.01**	0.55	**0.04**

Note: Statistically significant values are marked in bold font ($p \leq 0.05$).
Abbreviations: BEI, Bruxism Episode Index; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; BMI, body mass index (kg/m^2); 17-OHCS, 17-hydroxycorticosteroids; CRP, C-reactive protein; SEM of Rc, structural equation modeling of regression coefficient.

as well as BEI and fibrinogen were independent of AHI and BMI (Table 6). A higher BEI and a higher BMI were independently associated with a higher level of 17-OHCS (mg/24 h), as well as with a higher level of fibrinogen (g/l). Higher BEI and higher AHI were identified as independent predictors of higher CRP (mg/l).

Discussion

The positive correlation between the inflammatory parameters (CRP and fibrinogen) and BEI is one of the most interesting results, which has not been investigated by any study as shown by an extensive review of the available literature. Nevertheless, a large number of published studies have examined several risk factors for SB, including sensitivity to stress[11] or anxiety disorders, consumption of caffeine and alcohol, smoking,[12] OSA,[13,14] diabetes,[14] increased BMI, hypertension,[15] thyroid diseases, sleepiness, and snoring.[17] The association between many foregoing risk factors and inflammatory markers has been previously reported in the literature. However, to date, the association between SB and inflammation remains unclear, and hence, the present paper addresses the need for investigating the inflammatory features of SB in order to bridge the gaps in the scientific literature. The association between stress and inflammatory markers has been well documented,[28] which suggests that SB, linked with psychoemotional components (such as emotional stress),[11,29,30] may also have an inflammatory etiology.

Some authors have indicated that there is a lack of evidence on the association between SB and stress.[31] For instance, a recent study by Ohlmann et al[30] could not prove that SB is related to chronic stress and sleep quality. Instead, the available literature indicates that a high level of CRP is associated with an increased risk of adverse health outcomes such as diabetes and CVD.[32] This implies that chronic SB is associated with inflammatory markers (as shown by the current study), which leads to increased CV risk. However, several questions about the role of inflammatory markers in SB remain unanswered.

Furthermore, an increased level of CRP was correlated with AHI and other respiratory indices, and the relationship between SB and AHI has been explored in earlier studies,[14,33–35] but it is beyond the scope of the present study. A regression analysis was conducted in this study to compare between the SB and OSA subjects. Multivariate regression showed that the relationships between BEI and

17-OHCS, BEI and CRP, as well as BEI and fibrinogen were statistically significant, independent of AHI and BMI. A higher BEI and a higher BMI were independently associated with a higher level of 17-OHCS (mg/24 h), as well as a higher level of fibrinogen (g/l). Moreover, higher BEI and higher AHI were identified as independent predictors of higher CRP (mg/l).

In line with the previous studies,[36] an increased concentration of 17-OHCS was found to be a probable response to stress in patients with severe SB, which has been widely discussed in the literature.[30,35] In the study performed by Fluerașu et al, the levels of salivary cortisol were tested using the ELISA technique to investigate the impact of stress,[35] which were found to be higher in subjects with SB. Smardz et al[30] screened SB patients with Perceived Stress Scale-10 and reported that the intensity of SB was not statistically significantly correlated with self-reported perceived stress and depression. The present study was designed to test the urinary excretion rate of 17-OHCS in order to evaluate the stress response. The level of perceived stress reported by SB patients may contrast with the level of stress markers in the studied SB patients, which was confirmed by the results of the laboratory tests. In other words, misperceived stress does not mean a lack of metabolic stress.

This study also verified other potential CV risk factors such as the levels of HDL-C and LDL-C and glucose metabolism. The results showed no statistically significant differences in the plasma lipid measurements with respect to SB between the studied subjects. As relevant studies are not available in the literature, it can be assumed that SB does not affect these CV risk factors.

The analysis of the association between carbohydrate metabolism and SB revealed a positive correlation between phasic episodes and glucose concentration found 2 h after the glucose tolerance test. These results are an extension of the previous report of Martynowicz et al,[14] which showed that higher AHI, male gender, and diabetes were independent predictors of increased BEI. However, there is limited evidence on the association between diabetes and bruxism. The results of this study shed new light on phasic SB, which is considered to be predominant,[9,37,38] and diabetes. Previous research on the relationship between SB and OSA[14] demonstrated the association between hypoxia and SB. One of the interesting questions arising from this finding is: does hypoxia control the blood glucose level? Several theories have been proposed on the association between hyperglycemia and hypoxia in human and animal models, with some focusing on the increased ratio of reduced and oxidized free cytosolic NADc[37,39,40] and others analyzing the increased production of free radicals[41,42] or the paradoxical protective effects of diabetes and brief periods of hypoxia preceding severe hypoxia in order to attenuate organ damage.[43] Broox et al[44] also explored this relationship in their study and showed that glucose concentration did not vary in response to acute hypoxia after several hours. An increase in the glucose level due to chronic hypoxia occurred about 3 days later,[45] which returned to the normal level after acclimatization.

Another interesting result of the carbohydrate metabolism analysis is that IR (assessed based on the HOMA-IR factor) was diagnosed in 23% (n = 17) of the patients, whereas the mean BMI was normal (22.71 ± 3.83 kg/m^2). The risk of IR is significant in patients with a BMI ≥25, which is the cutoff point for the risk of being overweight according to the World Health Organization (WHO).[46] OSA, described as nocturnal intermittent hypoxia, has been associated with an increased risk of developing diabetes and IR. The recent study by Perantoni et al[45] showed that the mean desaturation duration was significantly associated with IR (r = 0.289, p = 0.047) as well as the total duration of SpO_2 desaturation (r = 0.322, p = 0.025). On the other hand, intermittent hypoxia/normoxia training was found to have a positive effect on the reduction of serum glucose concentration in prediabetic patients.[47]

There is no evidence on the association between SB, hypoxia, and glycemia, which requires additional studies. Apparently, IR is associated with respiratory indices other than SB.

Our results also demonstrated that sleep bruxers exhibited significantly increased sleepiness when assessed by ESS, which is considered as an independent prognostic factor of adverse outcome in patients with sleep disorders. Therefore, we considered this information significant for the assessment of CV risk. The findings observed are directly in line with previous research.[48,49] Elevated ESS scores were positively correlated with mixed bruxism episodes, minimal oxygen saturation, and mean heart rate. These support the evidence on the association between SB and autonomic sympathetic activity expressed by tachycardia, which usually precedes a bruxism episode.[5] The phasic SB, as a component of mixed episodes, was positively correlated with minimal $SatO_2$ (blood oxygen saturation) in

a previous study.[14] Hypoxia has been potentially linked with the onset of a bruxism episode, and the relationship between excessive daytime sleepiness, OSA, and hypoxia is well known. According to one of the hypotheses associating SB with OSA, SB restores airway flow during a respiratory event by the protrusion of the mandible.[50] As has been previously reported in the literature, patients with severe daytime sleepiness exhibited significantly lower baroreflex sensitivity and higher heart rate variability compared to those who did not show daytime sleepiness.[49]

Together, the results of this study revealed that daytime sleepiness is associated with an increased number of bruxism episodes and a higher heart rate. However, the extent to which SB can be attributed to autonomic sympathetic activity is unknown.

Overall CV risk is determined by many risk factors. Of these, genetics, family history, and comorbidity of atherosclerotic diseases are classified as modifiable, whereas smoking, high blood pressure, diabetes and IR, physical inactivity, emotional stress, being overweight, inflammatory markers, and high level of blood cholesterol are recognized as modifiable.

A lifetime approach to CVD prevention is to implement lifestyle changes and medical interventions. The associations between neuromodulatory pathways and SB etiology are not clearly described in the available literature, but a recent study by Wieckiewicz et al[50] revealed the possible contribution of genes encoding dopamine and serotonin receptors to the etiology of SB. Moreover, the single-nucleotide polymorphism (SNP) that affects both SB and OSA was investigated (HTR2A serotonin receptor-encoding gene, rs2770304 SNP). From this standpoint, the probability of genetic vulnerability to SB and the study's findings on inflammatory markers emphasize the role of SB in the etiology of unmodifiable and modifiable CV risk factors.

One of the limitations of the present study is the sex ratio. Firstly, there was no sex parity in the study group; women constituted 73% of the examined population. Secondly, to estimate the total CV risk, data on smoking and systolic blood pressure should be included, and a lack of these is an apparent limitation. In addition, children were not included in the study population. Therefore further research among children and adolescent population is needed. A third limitation of the study is that the findings are based only on single-night polysomnography.

However, it is worth mentioning that the study used polysomnography as a diagnostic tool, which is a gold standard for confirming the presence of SB. Moreover, this study is the first to analyze inflammatory markers in SB patients.

The findings of this study signal the need for additional research on the inflammatory features of SB. The aforementioned sympathetic modulatory activity of SB and the relatively young age of sleep bruxers indicate that it is necessary to explore the relationship between potentially increased CV risk and SB.

Conclusion

The present study showed that sleep bruxers exhibited increased sleepiness, as indicated by higher ESS scores. Moreover, patients with SB had metabolic and hormonal disturbances, which were manifested as increased levels of 17-OHCS, CRP, and fibrinogen, probably as a result of stress and sympathetic activity. Importantly, this is the first report to show the relationship between BEI and elevated inflammatory markers. Therefore, further research is needed to support the hypothesis that SB is associated with proinflammatory features or inflammatory etiology. The relationship between SB and disturbances in carbohydrate metabolism is still unclear. However, the results of this study indicated that young sleep bruxers potentially have an increased CV risk and therefore need special targeted prophylaxis and care.

Abbreviations

SB, sleep bruxism; CV risk, cardiovascular risk; BEI, Bruxism Episode Index; CRP, C-reactive protein; BMI, body mass index; CVD, cardiovascular disease; ESS, Epworth Sleepiness Scale; HOMA, Homeostatic Model Assessment; PSG, polysomnogram; EMG, electromyographic; CAD, coronary artery disease; HT, hypertension; IR, insulin resistance; AHI, Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; OSA, obstructive sleep apnea; MA, mixed apnea; CA, central apnea; $SatO_2$, blood oxygen saturation; mean SpO_2, mean oxygen saturation; SpO_2 <90%, time with oxygen saturation <90%; TST, total sleep time; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyltransferase; WBC, white blood cells; RBC, red blood cells; fT3, free triiodothyronine; fT4, thyroxine; TSH, thyroid-stimulating hormone; SL, sleep latency; REML, rapid eye movement stage latency.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author (MW), upon reasonable request.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed on the journal to which the article will be submitted; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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5. PRACA 2

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The Relationship between Simple Snoring and Sleep Bruxism: A Polysomnographic Study

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Abstract: Simple snoring is defined as the production of sound in the upper aerodigestive tract during sleep, not accompanied by other pathologies. Sleep bruxism (SB) refers to repetitive phasic, tonic, or mixed masticatory muscle activity during sleep. In this study, we investigated the relationship between simple snoring and SB in patients without obstructive sleep apnea (OSA). A total of 565 snoring subjects underwent polysomnography. After examination, individuals with OSA were excluded from the study group. Finally, 129 individuals were analyzed. The bruxism episode index was positively correlated with maximum snore intensity. Phasic bruxism was positively correlated with snore intensity in all sleep positions. Bruxers had a significantly decreased average and minimum heart rate compared with non-bruxers. Supine sleep position seemed to have a significant impact on snore intensity and SB. In summary, our study showed the relationship between SB, snore intensity, and body position. Phasic bruxism was positively correlated with snore intensity despite the body position, which is an interesting and novel finding.

Keywords: simple snoring; sleep bruxism; polysomnography

1. Introduction

Snoring is defined as the production of sound due to the vibration of respiratory structures in the upper aerodigestive tract during sleep. Simple snoring (SS) not accompanied by daytime sleepiness and fatigue or obstructive sleep apnea (OSA) is called primary snoring [1]. Simple snoring is also known as non-apneic snoring [2]. The risk factors for snoring include nasal congestion, obstruction/inflammation of the upper airways, increased body mass index (BMI), male gender, or intake of alcohol, drug, or tobacco [3]. The existing literature pertaining to physical implications of snoring associates this condition with mild symptoms such as dry mouth or irritated tissues and severe symptoms such as excessive daytime sleepiness [4], carotid artery atherosclerosis [5], stroke [6], cardiovascular diseases [7], metabolic syndrome [8], and increased all-cause mortality [9]. On the other hand, a previous study suggested that SS has no adverse effects on an individual [10]. According to the American Academy of Sleep Medicine (AASM), the International Classification of Sleep Disorders, 3rd Edition (ICSD-3) classifies SS as a sleep-related breathing disorder (SRBD) [11]. Some authors have suggested and

developed methods for the assessment of snoring. For instance, Lee et al. defined a snore sound as "an obvious deflection from background (with no minimum decibel threshold), which was in phase with inspiration and occurred during sleep" [5]. They considered three or more snore events in a 30 s epoch as a "snore epoch," and subsequently calculated the snore index. The criteria based on snore intensity with peak ≥40 dB for ≥30% sleep breaths were established by Guzman et al. [12]. The definition of snore trains is used to describe periods with multiple single-snore events [13]. The epidemiology of SS is not clearly explained in the literature but depending on the method of measurement and the population studied, its incidence varies between 2% and 85% [3]. Among the studies that focus on snoring, the Hungarian population survey by Torzsa et al. is worth mentioning as it is the largest study to analyze the prevalence of snoring, in which 37% of males and 21% of females reported loud snoring with breathing pauses [14].

Bruxism is a common phenomenon which is defined by the AASM as "repetitive masticatory muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible" [11]. This condition may be divided into two types: sleep bruxism (SB) and awake bruxism. According to the international consensus originated by Lobbezoo et al., sleep bruxism is defined as a masticatory muscle activity during sleep that is characterized as either rhythmic (phasic) or nonrhythmic (tonic) and should not be considered as a movement disorder or a sleep disorder in otherwise healthy individuals [15]. The estimated prevalence of sleep bruxism varies with age, ranging from 13% in young adults to 3% in the elderly [15,16]. The consensus proposed distinguishing the risk factors for SB into three groups: biological, psychological, and external. The multifactorial etiology of SB includes genetic vulnerability [17], age, synaptic transmission, disturbances in sleep architecture, perception of stress and anxiety, intake of alcohol and drug, smoking, and comorbidities [16]. Previous studies have acknowledged the following medical conditions as coexisting with SB: OSA [18–20], diabetes [19], gastroesophageal reflux disorder [21,22], increased BMI, hypertension [23,24], excessive daytime sleepiness, and snoring [20].

The newest literature-based analysis of the global obstructive sleep apnea prevalence carried out by Benjafield et al. revealed that about "1 billion adults aged 30–69 years were estimated to have OSA, with and without symptoms" [25]. In some countries, the prevalence of OSA even exceeds 50%. Although the relationship between sleep bruxism and obstructive sleep apnea seems to be significant and has also been explored in prior studies, the data obtained are inconsistent. Several studies have confirmed the association between these two conditions [19,26–28], whereas some have failed to prove the link between them [29–31]. However, in our previous study, we demonstrated the association between OSA and SB [19] and showed a positive correlation among the sleep bruxers having mild or moderate OSA.

Sleep-related breathing disorders are classified based on the differences in the obstruction of the upper airways and in the degrees of alteration in gas exchange during the night. Simple snoring, classified as a separate entity in ICSD-3, is frequently reported by many individuals [32], but its definition and role is not clearly presented in literature. Simple snoring may indicate a slight obstruction in the upper respiratory tract which is a probable risk factor for the development of OSA. OSA is associated with significant morbidity (e.g., diabetes [33], hypertension [34], stroke [35], ischemic heart disease [36], and arrythmias [37–39]) as well as mortality [40].

An important question associated with simple snoring and sleep bruxism that remains to be answered is whether these phenomena can coexist and relate. Second, does sleep position impact SB or SS? Therefore, this study aimed to analyze the relationships between SS, SB, and sleep position in patients without OSA.

2. Materials and Methods

The study was performed in the Sleep Laboratory of the Department of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at the Wroclaw Medical University (Wroclaw, Poland). The number of n = 565 patients included in the study were admitted to the

department for polysomnographic examination from the outpatient clinic operating at the Department of Experimental Dentistry of the Wroclaw Medical University, as they reported snoring and were diagnosed with probable bruxism. All the participants provided informed consent to participate in the study. The study was approved by the Ethics Committee of the Wroclaw Medical University (ID KB-794/2019) and was conducted in accordance with the Declaration of Helsinki. Information regarding clinical trial registration is available at www.ClinicalTrials.gov (identifier NCT04214561). After conducting a single, full-night polysomnographic examination, individuals with OSA were excluded from the study. The final study group consisted of 129 individuals, including 38 men and 91 women, who had a mean age of 33.60 ± 9.89 years.

We included the individuals who declared their willingness to participate in the study and fulfilled the following criteria: Aged above 18 years and clinically suspected with SS and/or SB. All participants met ICSD III B 1 or 2 criteria for SB.

Patients who were less than 18 years of age and diagnosed with OSA were excluded from the study. Other exclusion criteria were as follows: inability to undergo polysomnography; secondary bruxism associated with neurological conditions; intake of medicines that affect the neuromuscular functioning; presence of severe mental disorders, active malignancy, neurological disorders, and/or neuropathic pain; coexistence of respiratory insufficiency or active inflammation; addiction to analgesic drugs and/or drugs that affect muscle and breathing functions; and presence of severe allergic symptoms.

SB was assessed according to the AASM standards. Bruxism episodes were qualified as phasic, tonic, or mixed based on the electromyographic (EMG) recording obtained from the masseter muscle region bilaterally, which was complemented by audio and video recording. Bruxism episode index (BEI) indicates the total number of bruxism episodes per hour. To confirm the bruxism episodes, an audiovisual assessment was performed and the EMG measures were taken. According to the AASM standards, the peak of the EMG amplitude during bruxism episode has to be at least twice the amplitude of the background EMG and should not be separated more than 3 s in order to be considered as a part of the same episode [41]. EMG activities were scored as phasic if the episode lasted 2 s with three or more bursts, or as tonic if the episode lasted more than 2 s with sustained bursts, or as mixed if the episode had a mix of them. SB can be confirmed if the value of BEI is at least 2. Based on BEI, we can assess the severity of SB as follows: BEI = 2–4, mild/moderate SB; BEI > 4, severe SB [11].

A full-night polysomnographic assessment was performed using Nox-A1 (Nox Medical, Reykjavik, Iceland) among all patients in the Sleep Laboratory of the Department of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at the Wroclaw Medical University (Wroclaw, Poland). Patient EEGs were recorded using the AASM recommended EEG montages during the PSG. The eight electroencephalographic (EEG) and electrooculographic (EOG) channels were used (F4-M1, C4-M1, O2-M1, F3-M2, C3-M2, O1-M2, E1-M2, E2-M2). The EEG electrode position was determined by an International 10-20 System. Three electrodes have been placed to record chin EMG in mental and submental positioning. Two channels of respiratory effort from respiratory inductance plethysmography (RIP) belts circulating the thorax and abdomen were used. A single modified electrocardiogram Lead II was used to assess ECG. Nasal pressure transducer was used to assess hypopnea. Oronasal thermal airflow sensor was used to assess apnea. Polysomnograms (PSGs) were scored in 30-s epochs. After an automatic analysis was conducted, a manual analysis was performed by certified polysomnographist. Epochs were classified based on the standard criteria for sleep by the AASM 2013 Task Force [42]. The PSG outcomes included the following: sleep latency (SL); rapid eye movement (REM) latency; total sleep time; sleep efficiency; and the ratio of N1 (sleep stage 1), N2 (sleep stage 2), N3 (sleep stage 3), and REM (REM sleep stage). Sleep position was determined automatically using position sensors.

Snoring was monitored using an acoustic sensor and a nasal pressure transducer. All the snore sounds that were in synchrony with breathing and protuberant from the background with an audible oscillatory component were considered as snore events. The Noxturnal software (Nox Medical, Reykjavik, Iceland) recorded a full audio signal with 8.000 Hz sampling. Then, the audio signal was derived and stored with 100 Hz, followed by a conversion with dBc weighting to receive an audio

envelop signal in dB. A period of multiple single snores was scored as a snore train. All the snore trains were automatically recorded [13]. Both inspiratory and expiratory snores were scored. Other non-snore sounds—i.e., coughing, groaning, bruxing, duvet, and movement noise, as well as large breathing sounds without any vibration—were excluded.

The statistical package "Dell Statistica 13.1" (Dell Inc., Round Rock, TX, USA) was used to perform statistical analysis. For the quantitative variables, arithmetic means and SDs of the estimated parameters were calculated. The distribution of variables was examined using Lilliefors and W-Shapiro–Wilk tests. For the independent quantitative variables with normal and other than normal distribution, we used Student's t-test and Mann–Whitney U-test, respectively. For the dependent quantitative variables with normal distribution, the t-test for linked variables was used. In the case of dependent quantitative variables showing the distribution distinct from normal, Wilcoxon's paired sequence test was applied. The results for qualitative variables were expressed as percentages. For dependent qualitative variables, McNemar's test or Cochran's test was used for statistical analysis. To determine the relationship between the analyzed variables, a correlation analysis was performed. The results at the level of $p < 0.05$ were considered statistically significant.

3. Results

A total of $n = 565$ patients were included in our study, then after one-night polysomnography patients with OSA (AHI ≥ 5) were excluded. Finally, study group estimated $n = 129$ individuals (mean age 33.60 ± 9.89 years; 38 men and 91 women). The study group had only sleep bruxers and/or snorers. Based on the BEI value calculated from the PSG findings, 98 individuals (75.97%) were diagnosed with SB; of them, 39 (30.23%) met the criteria for mild/moderate bruxism and 59 (69.77%) for severe bruxism.

The polysomnographic parameters calculated for the studied group are presented in Table 1. Among the participants, nine were diagnosed with hypertension, while no one met the criteria for coronary artery disease.

Table 1. Bruxism and respiratory parameters—polysomnographic characteristics of the study group.

Parameter	Mean	SD
BEI (*n*/h)	4.39	3.33
Phasic (*n*/h)	2.49	2.74
Tonic (*n*/h)	1.20	1.01
Mixed (*n*/h)	0.75	0.66
AHI (*n*/h)	2.00	1.33
ODI (*n*/h)	2.38	1.74
Snore (% of TST)	5.01	9.78
Snore index (*n*/h)	61.64	105.82
TST (min)	429.68	56.45
SL (min)	22.83	21.60
WASO (min)	35.17	36.57
SE (%)	86.71	10.36
N1 (% of TST)	3.52	4.02
N2 (% of TST)	48.3	8.46
N3 (% of TST)	24.22	8.00
REM (% of TST)	23.97	6.06
Arousals (*n*/h)	3.28	2.39
Mean SpO_2 (%)	94.86	1.58
Min SpO_2 (%)	89.56	5.29
$SpO_2 < 90\%$ (%)	0.70	3.20
Mean desaturation drop (%)	3.13	0.83
Mean heart rate (*n*/min)	61.26	9.84
Max heart rate (*n*/min)	99.29	19.11
Min heart rate (*n*/min)	48.69	7.21

BEI, bruxism episode index; AHI, apnea–hypopnea index; ODI, oxygen desaturation index; TST, total sleep time (min); SL, sleep latency; WASO, wake after sleep onset; SE, sleep efficiency; N1, sleep stage 1; N2, sleep stage 2; N3, sleep stage 3; REM, rapid eye movement sleep stage; mean SpO_2, mean oxygen saturation (%); $SpO_2 < 90\%$, time with oxygen saturation < 90% (% of TST).

Regarding the mean bruxism and snore parameters differentiated based on body position, BEI supine was higher than BEI non-supine. Phasic bruxism was found to be most frequent bruxism type independent of the sleep position. With respect to snore parameters, snore indexes were found to be higher in the supine position in all sleep stages (Table 2).

Table 2. Mean bruxism and snore parameters differentiated on the basis of body position.

Parameter	Mean	SD	Parameter	Mean	SD
BEI supine (*n*/h)	6.16	7.40	Snore index supine (*n*/h)	74.21	138.05
BEI mixed supine (*n*/h)	0.85	0.89	Snore index non-supine (*n*/h)	35.53	77.18
BEI phasic supine (*n*/h)	3.52	4.92	Snore index N1 (*n*/h)	67.97	84.82
BEI tonic supine (*n*/h)	1.43	1.54	Snore index N1 supine (*n*/h)	67.32	102.80
BEI non-supine (*n*/h)	3.99	12.88	Snore index N1 non-supine (*n*/h)	58.55	119.32
BEI mixed non-supine (*n*/h)	0.72	2.19	Snore index N2 (*n*/h)	60.28	108.25
BEI phasic non-supine (*n*/h)	2.61	10.77	Snore index N2 supine (*n*/h)	68.17	132.57
BEI tonic non-supine (*n*/h)	0.68	0.84	Snore index N2 non-supine (*n*/h)	35.40	82.84
Mean snore intensity (dB)	54.13	25.45	Snore index N3 (*n*/h)	90.06	168.28
Max snore intensity (dB)	65.38	31.23	Snore index N3 supine (*n*/h)	109.87	202.72
Min snore intensity (dB)	43.78	20.97	Snore index N3 non-supine (*n*/h)	38.36	122.04
Mean snore intensity supine (dB)	46.20	30.62	Snore index REM (*n*/h)	42.86	108.45
Max snore intensity supine (dB)	55.00	36.81	Snore index REM supine (*n*/h)	44.35	117.10
Min snore intensity supine (dB)	37.44	25.05	Snore index REM non-supine (*n*/h)	24.61	72.54
Mean snore intensity non-supine (dB)	31.88	32.81	Snore train supine (*n*/h)	6.36	13.18
Max snore intensity non-supine (dB)	37.99	39.28	Snore train non-supine (*n*/h)	2.72	7.36
Min snore intensity non-supine (dB)	26.81	27.76			

BEI, bruxism episode index; N1, sleep stage 1; N2, sleep stage 2; N3, sleep stage 3; REM, rapid eye movement sleep stage.

In the study group, we found statistically significant differences between severe bruxers (BEI > 4) and the remaining individuals. The maximum snore intensity was found to be significantly higher among the severe bruxers (BEI > 4) than in the group with BEI < 4 (70.83 ± 27.02 dB vs. 60.77 ± 33.88 dB, $p = 0.05$). The mean and maximum snore intensity in the supine position were also significantly higher in individuals with BEI > 4 compared with those with BEI < 4 (mean score intensity: 51.69 ± 27.86 dB vs. 41.57 ± 32.24 dB, $p = 0.04$; maximum snore intensity: 61.70 ± 33.59 dB vs. 49.35 ± 38.65 dB, $p = 0.05$). Furthermore, arousal frequency was observed to be statistically increased in severe bruxers compared with individuals with BEI < 4 (3.82 ± 2.82 *n*/h vs. 2.82 ± 1.87 *n*/h, $p = 0.02$).

To determine the relationship between bruxism, sleep position, polysomnographic parameters, and heart rate, a correlation analysis was subsequently performed (Table 3).

Table 3. Polysomnographic indices correlated with bruxism and the body position.

Body Position	Bruxism Indices	AHI (*n*/h)	ODI (*n*/h)	Snore (% of TST)	SL (min)	Arousals (*n*/h)	Mean Heart Rate (*n*/min)	Max Heart Rate (*n*/min)	Min Heart Rate (*n*/min)
Total	Average BEI (*n*/h)	0.08	0.09	−0.02	−0.00	**0.23**	−0.16	0.04	**−0.25**
	Phasic (*n*/h)	0.10	0.10	−0.01	0.00	0.10	−0.15	0.09	**−0.25**
	Tonic (*n*/h)	0.08	0.07	0.03	−0.05	**0.27**	−0.06	−0.11	−0.03
	Mixed (*n*/h)	−0.09	−0.06	−0.09	−0.01	**0.35**	−0.09	0.05	**−0.22**
Supine	Average BEI (*n*/h)	0.07	0.03	−0.07	−0.02	0.15	−0.08	−0.02	−0.12
	Phasic (*n*/h)	0.12	0.10	−0.06	0.01	0.04	−0.10	0.01	−0.17
	Tonic (*n*/h)	0.08	0.10	0.02	−0.03	**0.25**	−0.03	−0.11	−0.04
	Mixed (*n*/h)	0.12	0.10	−0.03	0.00	**0.36**	−0.14	−0.04	**−0.26**
Non-supine	Average BEI (*n*/h)	0.12	**0.29**	−0.05	**0.31**	−0.01	0.20	0.09	**0.21**
	Phasic (*n*/h)	0.13	**0.29**	−0.04	**0.30**	−0.02	0.20	0.09	**0.21**
	Tonic (*n*/h)	0.05	0.04	−0.09	0.03	0.09	−0.01	−0.05	0.02
	Mixed (*n*/h)	0.07	**0.25**	−0.08	0.32	−0.01	0.22	0.11	**0.23**

BEI, bruxism episode index; AHI, apnea–hypopnea index; ODI, oxygen desaturation index; TST, total sleep time (min); SL, sleep latency. The values in the table represent correlation coefficients. Statistically significant correlations are marked in bold ($p < 0.05$).

Regardless of bruxism severity, the mean and minimum heart rates were significantly decreased in patients with bruxism (Table 4).

Table 4. Results for heart rate in bruxers and non-bruxers, differentiated on the basis of bruxism severity.

Parameter	BEI < 2 (*n*/h)		BEI > 2 (*n*/h)			BEI < 4 (*n*/h)		BEI > 4 (*n*/h)		
	Mean	SD	Mean	SD	*p*	Mean	SD	Mean	SD	*p*
Mean heart rate (*n*/min)	64.47	11.25	60.25	9.18	0.04	62.95	9.88	59.26	9.49	0.03
Max heart rate (*n*/min)	101.90	18.41	98.47	19.34	0.39	99.46	19.25	99.10	19.09	0.92
Min heart rate (*n*/min)	51.00	8.36	47.96	6.69	0.04	49.87	8.05	47.29	5.84	0.04

BEI, bruxism episode index.

Snore intensity was positively correlated with phasic bruxism in all sleep positions (Table 5).

Table 5. Correlation between snore intensity parameters and bruxism episode index.

Parameter	BEI (*n*/h)	Phasic (*n*/h)	Tonic (*n*/h)	Mixed (*n*/h)
Snore index (*n*/h)	0.03	0.06	0.03	−0.12
Mean snore intensity (dB)	0.17	0.17	0.02	0.15
Max snore intensity (dB)	**0.21**	**0.22**	0.02	0.15
Min snore intensity (dB)	0.15	0.13	0.04	**0.18**
Mean snore intensity supine (dB)	**0.19**	**0.22**	0.01	0.09
Max snore intensity supine(dB)	**0.21**	**0.24**	0.03	0.09
Min snore intensity supine (dB)	**0.18**	**0.21**	0.02	0.10
Mean snore intensity non-supine (dB)	0.15	**0.21**	−0.08	0.03
Max snore intensity non-supine (dB)	0.17	**0.23**	−0.09	0.03
Min snore intensity non-supine (dB)	0.14	**0.19**	−0.09	0.04

BEI, bruxism episode index. The values in the table represent correlation coefficients. Statistically significant correlations are marked in bold ($p < 0.05$).

Based on the impact of body position on bruxism (Table 6), a statistically significant difference was found in BEI total and tonic rates between the supine and non-supine position. The incidence of mixed, phasic, and tonic bruxism episodes was observed more frequently in the supine than in the non-supine position, but a statistically significant difference was found only in the case of tonic bruxism.

Table 6. Impact of the body position on bruxism indices.

	Supine		Non-Supine		
BEI (*n*/h)	Mean	SD	Mean	SD	*p*
Total	**6.16**	**7.04**	**3.99**	**12.88**	**0.04**
Mixed	0.85	0.89	0.72	2.19	0.53
Phasic	3.52	**4.92**	2.61	10.77	0.37
Tonic	**1.43**	**1.54**	**0.68**	**0.84**	**0.00**

BEI, bruxism episode index. Statistically significant differences are marked in bold ($p < 0.05$).

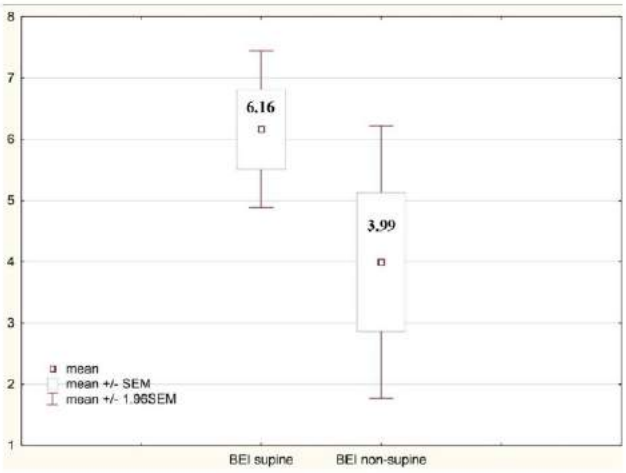
Assessing the impact of body position on snoring, snore indices were found to be significantly higher in the supine position compared with the non-supine position (Table 7).

Table 7. Impact of the body position on snore indices.

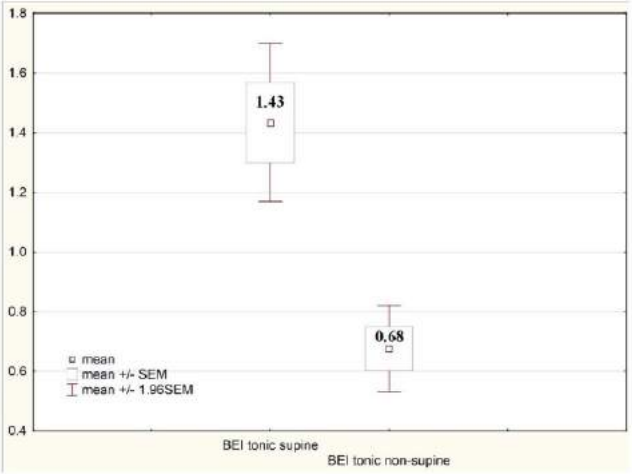
	Supine		Non-Supine		
Parameter	**Mean**	**SD**	**Mean**	**SD**	***p***
Snore index total (*n*/h)	**74.21**	**138.05**	**35.53**	**77.18**	**0.00**
Snore index N1 (*n*/h)	67.32	102.80	58.55	119.32	0.52
Snore index N2 (*n*/h)	**68.17**	**132.57**	**35.4**	**82.84**	**0.01**
Snore index N3 (*n*/h)	**109.87**	**202.72**	**38.36**	**122.04**	**0.00**
Snore index REM (*n*/h)	44.35	117.10	24.61	72.54	0.10
Snore train (*n*/h)	**6.36**	**13.18**	**2.72**	**7.36**	**0.00**
Mean snore intensity (dB)	**46.20**	**30.62**	**31.88**	**32.81**	**0.00**
Max snore intensity (dB)	**55.00**	**36.81**	**37.99**	**39.28**	**0.00**
Min snore intensity (dB)	**37.44**	**25.05**	**26.81**	**27.76**	**0.00**

N1, sleep stage 1; N2, sleep stage 2; N3, sleep stage 3; REM, rapid eye movement sleep stage. Statistically significant differences are marked in bold ($p < 0.05$).

The statistically significant differences from Tables 6 and 7 have been presented in Figures 1 and 2.

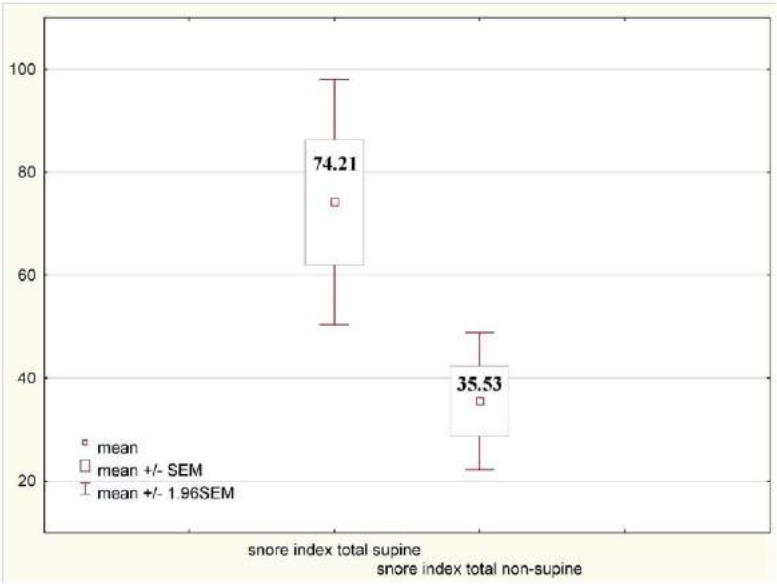


(**a**) BEI total (*n*/h).

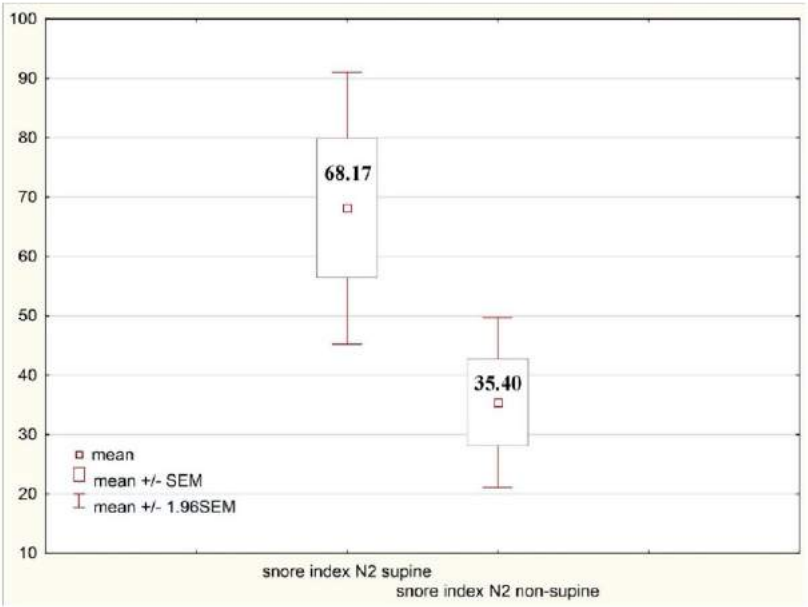


(**b**) BEI tonic (*n*/h).

Figure 1. Impact of the body position on bruxism indices.

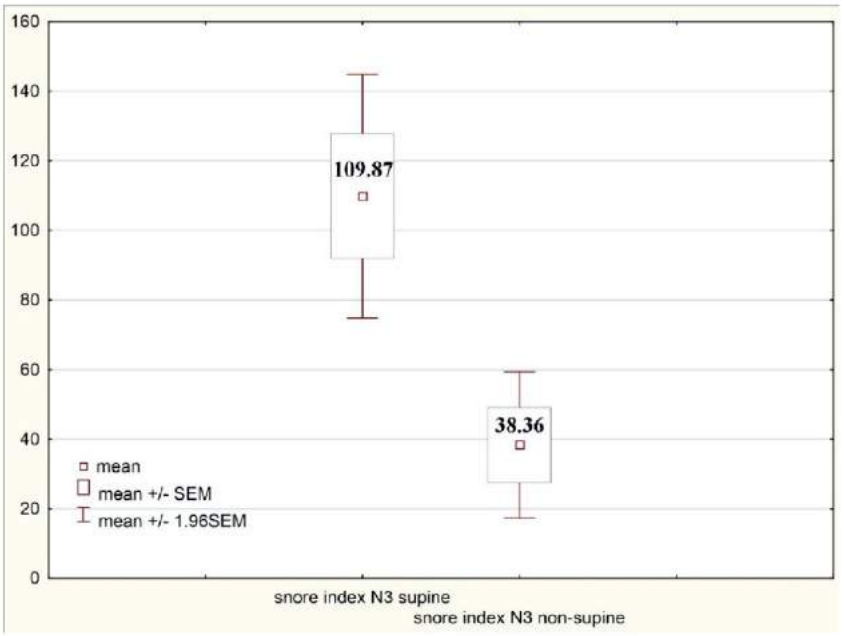


(a) snore index total (*n*/h).

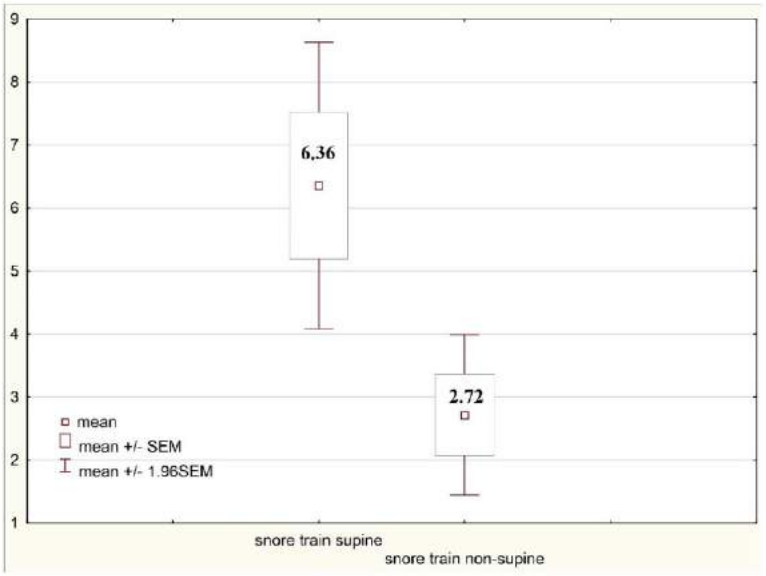


(**b**) snore index N2 (*n*/h).

Figure 2. *Cont.*

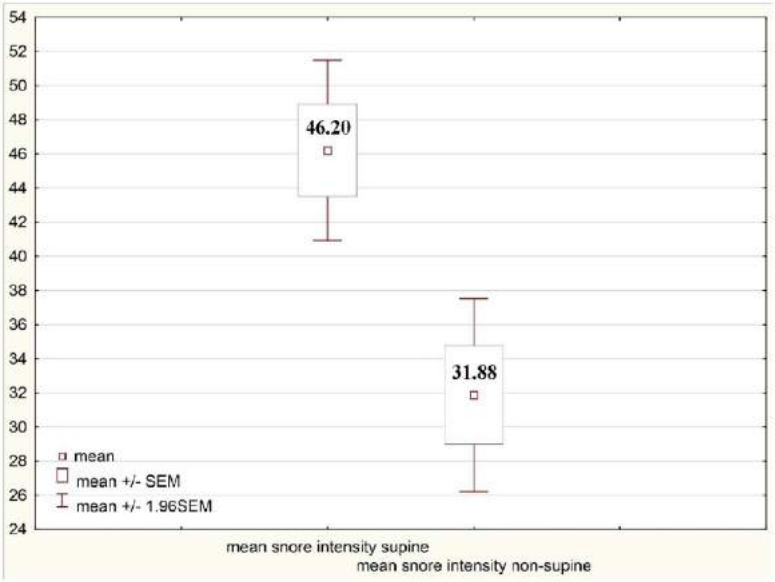


(c) snore index N3 (*n*/h).

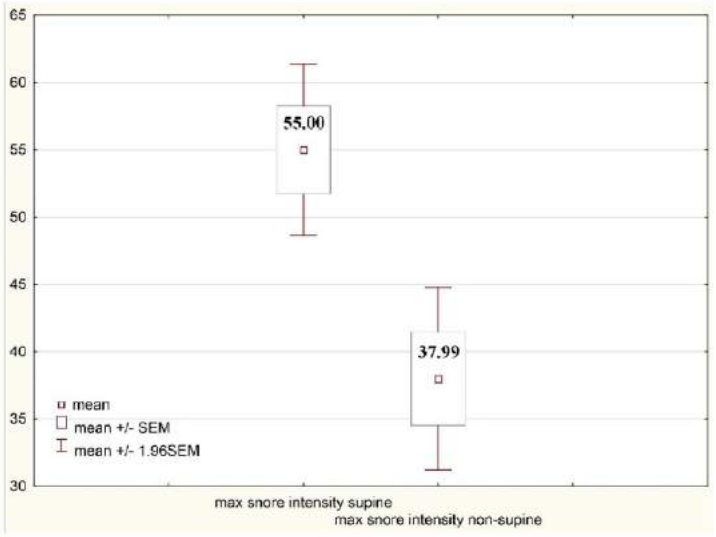


(d) snore train (*n*/h).

Figure 2. *Cont.*

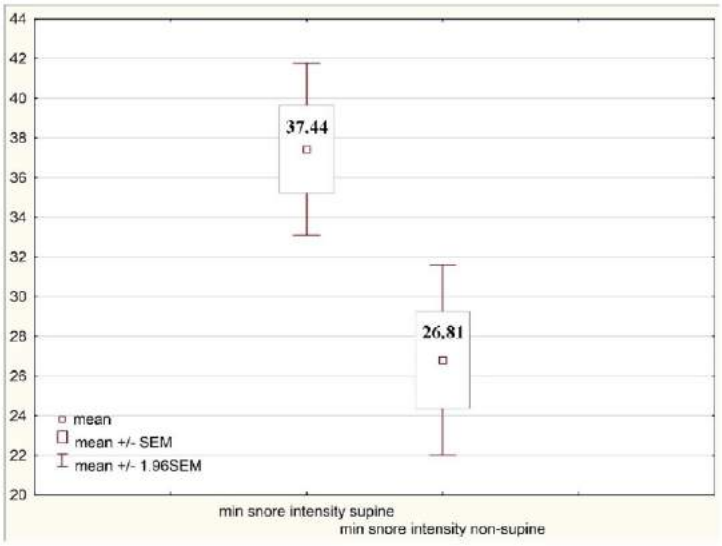


(e) mean snore intensity (dB).



(f) max snore intensity (dB).

Figure 2. *Cont.*



(g) min snore intensity (dB).

Figure 2. Impact of the body position on snore indices.

In order to verify the independence of the obtained relationships between snore intensity parameters and BEI, regression analysis was performed, obtaining the following models:

Maximum snore intensity = 1.83 BEI + 0.51 N3 + 8.20 mean desaturation drop +0.19 maximum heart rate;

Mean snore intensity supine = 1.51 BEI + 5.09 AHI + 1.77 sleep stage N3 + 1.33 sleep stage REM;

Maximum snore intensity supine = 1.82 BEI + 5.81 AHI + 4.69 sleep stage N3 − 4.27 mean SpO_2 + 0.37 maximum heart rate;

Minimum snore intensity supine = 1.45 sleep stage N3 + 1.16 sleep stage REM − 1.10 mean SpO_2.

Regression analysis showed that the relationship between snore intensity parameters and BEI is independent for maximum snore intensity, mean snore intensity supine, and maximum snore intensity supine. Higher BEI, higher percentage of N3 sleep stage, higher mean desaturation drop, and higher maximum heart rate are independently associated with higher maximum snore intensity. Higher mean snore intensity supine is independently influenced by higher BEI, higher AHI, higher percentage of N3 sleep stage, and higher percentage of REM sleep stage. Higher maximum snore intensity supine is the result of higher BEI, higher AHI, higher percentage of N3 sleep stage, lower mean SpO_2, and higher maximum heart rate, independently of each other.

Regression analysis also showed that BEI is not an independent predictor of minimum snore intensity supine. Independent factors associated with higher minimum snore intensity supine are higher percentage of N3 sleep stage, higher percentage of REM sleep stage and lower mean SpO_2.

4. Discussion

The findings of the present study demonstrate the common coexistence of sleep bruxism and simple snoring. Sleep bruxism is classified by the ICSD-3 as a sleep-related movement disorder [41] and confirmed by several studies as decreasing the quality of life [43,44] and increasing the risk of negative consequences for oral health [15,45] and general health condition [18–20,23,24]. The consensus authors, Lobbezoo et al., suggested that bruxism is only a risk factor that increases the probability of a harmful effect but does not guarantee it [15,46]. Sometimes, bruxism may have a protective effect; for example, in a study by Ohmure et al., the episodes of rhythmic masticatory muscle activity (RMMA) were significantly higher in the 20-min period after acidic infusion causing salivation that protects

against chemical tooth wear which occurs in patients with gastroesophageal reflux [47]. Similarly, the role of snoring, especially among people without sleep apnea, remains unclear. Some authors have demonstrated that snoring causes a number of severe physical implications such as excessive daytime sleepiness [4], carotid artery atherosclerosis [5], stroke [6], cardiovascular diseases [7], metabolic syndrome [8], and increased all-cause mortality [9]. Most of these are exactly in line with the consequences of sleep bruxism. Although studies on simple snoring and sleep bruxism have been conducted by many authors, their implications are still insufficiently explored and it remains unclear as to what extent these conditions can be attributed to severe health conditions. However, it is worth noting that SB and SS commonly coexist.

The results of our study confirm the statistically significant correlation between SB and SS. Snore intensity (loudness) in supine sleep position was found to be positively correlated with BEI total and phasic. Such a correlation was also found in the non-supine position for phasic bruxism and snoring, but as far as we know, no previous research has investigated this relationship. Palinkas et al. suggested that individuals with SB experience an increased amount of habitual snoring during sleep. The authors recorded the number of inspiratory, expiratory, and mixed snores but did not evaluate the loudness of snores [48]. In the current study, we examined the relationship between SS and SB and their parameters (intensity, frequency, types, and sleep position). Snore intensity was positively correlated with phasic bruxism subtype. Phasic bruxism was previously linked with hypoxic events due to its probable protective features [19]. Thus, the presence of positive correlation between phasic bruxism and snore intensity in current non-apneic study group suggest that simple snoring may have adverse effect on oxygen metabolism and intensive snoring could serve as a marker of mild obstruction. Therefore, the relationship between the simple snoring and sleep bruxism is investigated in the current work. Most earlier studies of our research team focused on the relationship between sleep bruxism and obstructive sleep apnea. For example, we confirmed the association between SB and mild and moderate stages of OSA [19]. Recently, our team showed that the single-nucleotide polymorphism (SNP) genetically affects the relationship between SB and OSA (HTR2A serotonin receptor encoding gene, rs2770304 SNP) [17]. SB and SS are considered as risk factors for negative health consequences [3,15] therefore the coexistence of them warrants further research by clinicians.

In this study, we showed that sleep position affects both snoring and bruxism indices. Statistically significant differences were found when comparing snore index, snore intensity, and the frequency of snore trains in supine and non-supine positions, and snoring was observed to be more frequent in the supine position. This result complies well with a previous study by Nakano et al. which demonstrated that most of the non-apneic snorers snored less in the lateral sleep position [49]. Taking under consideration, risk factors for snoring and obstructive sleep apnea are similar and include nasal congestion, obstruction of the upper airways, increased BMI, intake of alcohol, drug, or tobacco, and male gender [3]. Moreover, lateral sleep position was associated with OSA severity by many authors [50]. That gives the hypothesis, that supine sleep position in non-apneic patients which is associated with increased snore intensity could lead at least to development of OSA as a part of the continuum of disease predilection [3].

This paper also reports the impact of sleep position on SB, which has not been explained in the literature. SB was statistically more frequent in the supine position, but this was true only in the case of total and tonic bruxism. The difference between the prevalence of phasic bruxism in supine and non-supine positions was irrelevant. On the other hand, phasic bruxism was more frequent in the non-supine position, associated with desaturation. These findings go beyond previous reports that described the relationship between the sleep position and the severity of bruxism. In one of them, bruxism severity was estimated from the frequency of RMMA episodes [51], and the results showed that patients who were suffering from SB had 74% of RMMA and swallowing events in the supine position compared with 23% in the lateral decubitus position. An apparent limitation of the aforementioned research is a small study group (nine patients with SB and seven normal individuals in the control group). In another study by Phillips et al., bruxism activity was found

to be higher in individuals with increased AHI, which indicated a correlation between clenching index and AHI. In addition, it was observed that clenching index and AHI were higher in the supine position than in the lateral decubitus position [27]. This study also involved a small population (consisting of 24 individuals). In both studies, the patients underwent polysomnography. The findings of the present study also support the hypothesis that the phasic and tonic types of bruxism exhibit different features and roles. Phasic bruxism was linked with sleep-related breathing disorders by some authors. Tan et al. indicated the predominant role of phasic bruxism in OSA patients and suggested that RMMA possibly had a protective effect against respiratory-related arousals [52]. Similar findings were shown in the study by Hosoya et al., in which phasic SB correlated positively with OSA, microarousals, and oxygen desaturation [28]. Our analysis proved that phasic bruxism contributed to oxygen desaturation events, independent of sleep position. Generally, SB events were more frequently observed in the supine position and, hence, the positive correlation of phasic SB with ODI confirms its predominant role in desaturation events. The role of tonic SB in SRBDs was emphasized in a study by Smardz et al., which showed a significant relationship between the tonic EMG pathways in SB episodes and SRBDs [53]. However, this issue should be further explored.

An interesting result of our study is the positive correlation between ODI and BEI in the non-supine position (total, mixed, and phasic), while the correlation of ODI with tonic bruxism was irrelevant. The positive correlation between phasic bruxism and ODI was demonstrated in our prior research [19], in which mild and moderate obstructive sleep apnea was linked with sleep bruxism. To investigate the relationship between sleep bruxism and non-apneic hypoxia, we designed the current research. Our study group involved only individuals without obstructive sleep apnea, and thus the increased BEI observed in the subjects can be considered as a physiological response to low blood oxygen level (expressed as increased ODI). It is worth noting that this positive correlation was only observed for the non-supine sleep position, whereas total and tonic bruxism was predominant in the supine position with respect to BEI and sleep position association in total. This result suggests the protective effect of SB against hypoxia independent of sleep position. The association between these two conditions in the absence of sleep-disordered breathing was also investigated by Dumais et al. Their results suggested that transient hypoxia was probably a factor linked with the onset of RMMA, regardless of concomitant sleep arousal or body movements [54]. However, there were some limitations in the study such as insufficient sample size (22 participants) and the use of ambulatory, home PSG.

Regarding sleep latency, a positive correlation was found between BEI non-supine and the two phenotypes of sleep bruxism: mixed and phasic non-supine. The presence of a long SL, frequent awakenings, or prolonged WASO is considered as evidence of insomnia [55], so our findings signal the need for additional studies to understand more about this relationship. Bruxism episodes are more frequent during light sleep and are associated with arousals [56–58]; therefore, prolonged SL, as an element of sleep architecture with wake/N1 sleep stage transition [59], may provoke bruxism events. Our results are consistent with other studies indicating insomnia as a risk factor for bruxism. For instance, a study conducted by Ahlberg et al. investigated self-reported bruxism and perceived sleep difficulties [60]. An apparent limitation of this survey-based research was the lack of objective assessment of the reported complaints. Furthermore, a statistically significant relationship was demonstrated by Maluly et al. This population-sampled study showed a positive association between SB and insomnia, higher degree of schooling, and a normal/overweight BMI [58]. On the other hand, in the study by Kishi et al., sleep latency was shorter in bruxers compared with controls [61]. These suggest that further research with the instrumental approach is needed to confirm our novel findings.

Our research indicated a negative correlation between BEI total, phasic, and mixed subtypes and minimum heart rate. Moreover, based on sleep position, positive correlations were observed between mean and minimum heart rate, and BEI total, mixed, and phasic in the non-supine position. Individuals suffering from SB had significantly decreased mean and minimum heart rate than others, independent of bruxism severity. These results are identical to that of a previous study by Haraki et al.,

which also demonstrated that mean heart rate during sleep was lower in individuals with high-RMMA (BEI > 5.7 *n*/h) frequency, but the heart rate variability did not differ between the SB group and controls [62]. The authors implicated that these findings may suggest that a more recuperative function occurs to maintain normal sleep in young individuals or that the arousals related to SB events are neither frequent nor intense enough to cause any change in the sleep macrostructure. In an original study by Huynh et al., the association between the incidence of RMMA and autonomic cardiac activity across sleep cycles was demonstrated; the authors showed that in moderate-to-severe sleep bruxism, increase in sympathetic activity precedes the onset of SB [63]. A review paper by Lavigne et al. also indicated this relationship [64]. Furthermore, it has been previously reported in the literature that SB is linked with increased sympathetic tone and heart rate variability [65].

The results of our study suggest that the sympathovagal balance in SB subjects is expressed by a significantly decreased heart rate, probably as the response to the increase in heart rate preceding microarousal or an SB episode. Having low heart rate in patients with SB is the implication of this self- regulating mechanism and could lead to insufficient blood flow, fatigue, and other bradycardia consequences.

Regression analysis has showed that BEI, increase of N3 sleep, and hypoxia expressed as higher mean desaturation drop are independently associated with snore intensity, whereas supine snore intensity is influenced by BEI, AHI, increase of N3 sleep, higher heart rate, and lower oxygen saturation, all independent of one another. Summarizing, sleep bruxism, hypoxia, and sleep architecture may influence snore intensity in non-apneic adults.

One of the strengths of our study was that full-night polysomnography was performed to diagnose SS, SB, and respiratory events in the participants. To our knowledge, this study is the only study to investigate the association between BEI, sleep position, and snoring in patients without OSA. These findings include probable key component in future attempts to lower snoring by treating SB or influencing risk for OSA by modifying SB and SS intensity. Moreover, a large, heterogenous group was analyzed in the study, which increased the research relevance. However, the study had some limitations. First, lack of parity (38 men and 91 women) and a narrow age range of participants restricted study interpretation. The features displayed by younger SB patients differed from those of the elderly. Apparently, sample bias of the study group involved lack of probability sampling. We have decided to include in our study only patients with reported snoring and/or probable bruxism. Moreover, hypertension, diabetes, increased BMI, neck circumference, and the Mallampati Score that are known as risk factors for simple snoring and/or sleep bruxism were not evaluated and included in the exclusion criteria. Second, prior research studies on the topic are limited and the theoretical foundation is poor. However, we considered this limitation as an opportunity to identify new gaps in the prior literature and highlight the need for further development in this area of study. Third, for bruxism assessment, electrode leads were inserted into EMG inputs of the Nox A1 device. The same inputs are used for leg EMG, thus device construction limited ability to conduct an analysis of periodic limb movement.

5. Conclusions

Overall, our results showed the association between sleep bruxism and simple snoring. Snore intensity was positively correlated with phasic bruxism, both in supine and non-supine sleep positions, which is an important and novel finding. In addition, body position affects the intensity of both snoring and bruxism. Results of current study provided evidence for the relationship between hypoxia and sleep bruxism in individuals with simple snoring. Moreover, data also indicated a negative correlation between phasic bruxism and minimum heart rate, as the effect of sympathovagal homeostasis. Looking forward, further research is needed to assess clinical implications of both sleep bruxism and simple snoring for patients without obstructive sleep apnea.

Author Contributions: H.M. and M.M.-Z. created the research concept, analyzed the data, and wrote the manuscript. P.M. prepared original draft. J.S., H.M., M.M.-Z., M.W., and A.W. recruited patients for the study. H.M. and M.W. edited the manuscript. R.P. and P.G. made the statistical analysis. A.W. collected the data and references.

G.M. revised the paper before submission. M.W. evaluated the content, edited the manuscript, and finally revised it before submission. All authors have read and agreed to the published version of the manuscript.

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6. PRACA 3

Effect of Sleep Bruxism Intensity on Blood Pressure in Normotensives.

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Effect of Sleep Bruxism Intensity on Blood Pressure in Normotensives

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Abstract: The present research aimed to investigate the influence of sleep bruxism (SB) intensity on blood pressure parameters in normotensive subjects by using an ambulatory blood pressure device. The study group included 65 normotensive individuals suspected of having SB. All participants underwent one-night video-polysomnography, and ambulatory blood pressure monitoring was performed the next day; 86.15% of them were diagnosed with SB. Statistical analysis included correlation and regression analysis. The obtained results showed that systolic blood pressure variability during sleep significantly increased in individuals with BEI > 4 (bruxism episodes index; episodes/hour) compared to those with BEI $\leq$ 4 (8.81 $\pm$ 3.36 versus 10.57 $\pm$ 3.39, $p = 0.05$). Multivariable regression analysis showed that systolic blood pressure variability at nighttime was also associated with the following independent risk factors: higher apnea-to-bruxism index, male gender, BEI > 4 episodes/hour, body mass index (BMI) $\geq$ 25 kg/m^2, higher arousal index, and shorter total sleep time. In summary, sleep bruxism intensity was associated with increased systolic blood pressure variability during sleep. Coincidental apnea, male gender, severe sleep bruxism (SB intensity with BEI > 4/hour), excess weight and obesity, higher arousal index, and shorter sleep time seem to be the main determinants that influence blood pressure in normotensive sleep bruxers.

Keywords: sleep bruxism; ambulatory blood pressure monitoring; polysomnography

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1. Introduction

Nocturnal drop in blood pressure (BP) is a physiological component of circadian rhythm. [1] The dipping of BP at nighttime is an effect of sympathetic tone decrease during sleep. Absent or diminished decrease in BP during sleep is associated with increased cardiovascular mortality and morbidity [2,3]. Arterial hypertension (HTA) has been reported to be linked with a large number of sleep disturbances: short sleep duration [4], insomnia [5], restless leg syndrome [6], and obstructive sleep apnea (OSA) [7].

Sleep bruxism (SB) is a common sleep-related disorder. The etiology of SB is multifactorial and is still insufficiently explored. Several theories on sleep bruxism etiology and pathophysiology have been proposed; some of these theories focus on a genetic basis and neurotransmission [8], while others focus on psychological risk factors or sympathetic hyperreactivity. The prevalence of SB in adults is estimated between 3% and 8% [9,10]. Clinical manifestations of SB include tooth grinding and/or jaw clenching, abnormal tooth wear, and jaw muscle pain due to the fact of jaw muscle activity (rhythmic masticatory mus-

cle activity (RMMA)) during sleep and are classified in the 3rd edition of the International Classification of Sleep Disorders [11].

As shown in the literature, SB commonly coexists with obstructive sleep apnea (OSA) [12]. A recent systematic review by Van Ryswyk et al. [12] examined a large number of epidemiological studies on the relationship between sleep-related breathing disorders and hypertension. As explored in a cross-sectional, multicenter Sleep Heart Health Study (SHHS), the odds ratio increased and was estimated to be 1.37 (95% confidence interval (CI), 1.03–1.83) for hypertension for subjects with severe OSA compared to that in individuals without OSA [13]. The relationship between OSA and HTA was also confirmed by the Wisconsin Study [14] and the Zaragoza Sleep Cohort Study [15]. The pathomechanism linking increased mortality in apneic patients with HTA refers to BP variability (BPV), with a gradual rise in BP at the beginning of an apneic/hypopneic event and then abrupt fall in BP after the respiratory event [16]. Recurrent episodes of hypoxic events cause increased cardiovascular morbidity and mortality due to the oxidative stress [17].

Previous studies have emphasized the role of increased sympathetic activity preceding the SB event [18]. A repetitive surge in sympathetic activity expressed as increased heart rate followed by an increase in electroencephalography (EEG) frequency (microarousal) precedes RMMA [19]. Correspondingly, an autonomic sympathetic activation is a key component of pathophysiological repercussions of HTA, for example, vascular, cardiac, renal, metabolic, and immune-related abnormalities [20].

As previously reported in the literature, HTA is correlated with sleep bruxism. A seminal contribution has been made by Nashed et al. [21], who revealed that BP fluctuations during sleep were associated with RMMA. In another study by Martynowicz et al. [22], bruxism intensity was found to be increased in hypertensives. It is worth noting that the design of this study was focused on the assessment of intensity (frequency) and prevalence of SB in patients with HTA compared to that in non-hypertensive subjects.

To date, only a few studies have investigated the association of SB with hypertension. To fill this gap in the literature, the current descriptive study aimed to assess the relationship between ambulatory blood pressure measurements and SB intensity in individuals without HTA.

2. Materials and Methods

Sixty-five subjects suspected of having SB were admitted to the Department of Internal Medicine, Occupational Diseases, Hypertension, and Clinical Oncology at the Wroclaw Medical University in Poland. Before admission, all participants underwent complex dental examination at the Clinic of Prosthetic Dentistry at Wroclaw Medical University. The dental examination involved physical examination (focusing on clinical indicators of bruxism [23]) and a medical interview. Individuals who met the criteria for the presence of probable SB according to an international consensus on the assessment of bruxism were included in the study group [24].

The inclusion criteria for the study were as follows: age above 18 years, diagnosis of probable SB based on dental examination, and willingness to participate in the study. The exclusion criteria were diagnosis of HTA or use of anti-hypertensive medications; use of medicines affecting the nervous and muscular systems; cognitive disabilities and inability to provide informed consent; inability to undergo polysomnography (PSG) or measurement with an ambulatory blood pressure monitoring (ABPM) device; severe physical and mental conditions; presence of diabetes, coronary artery disease, active malignancy, or inflammation.

All participants signed a consent form and voluntarily underwent examination. The study was approved by the local Ethics Committee (no. KB-195/2017) and was conducted by adopting the principles of the Declaration of Helsinki. This clinical trial was also registered in Clinical Trials Database (www.ClinicalTrials.gov, accessed on: 20 March 2021): identifier NCT03083405, WMU1/2017.

Polysomnographic examinations were conducted in the sleep laboratory at the Department of Internal Medicine, Occupational Diseases, Hypertension, and Clinical Oncology at the Wroclaw Medical University in Poland. The PSG data were collected using a Nox-A1 (Nox Medical, Reykjavík, Iceland) device for one-night video-PSG. Recordings included sleep, bruxism, and respiratory data as follows: sleep latency, total sleep time, and sleep efficiency (%); the ratio of N1 (sleep stage 1), N2 (sleep stage 2), N3 (sleep stage 3), and the stage of REM (rapid eye-movement sleep); electromyographic (EMG) recordings of bilateral masseter muscle activity during sleep; video and audio recordings; respiratory events recorded by a nasal pressure transducer; and arterial oxygen saturation (SpO_2) measured by a finger pulse oximeter.

After conducting an automatic analysis, 30 s epochs of polysomnograms were evaluated by a certified polysomnographist according to the gold standard criteria of the American Academy of Sleep Medicine (AASM) task force [25]. Respiratory events were scored as follows: the absence of airflow for ≥10 s was scored as an apneic event, while a reduction in the amplitude of breathing by ≥30% for ≥10 s with a ≥3% decline in blood oxygen saturation or arousal was scored as hypopnea. Sleep bruxism was assessed audiovisually from EMG measurements supplemented by audio and video recordings. The increase in EMG amplitude that was at least twice that of the background EMG was considered as a bruxism episode. Electromyographic bursts within 3 s were considered to be the part of the same episode. The bruxism episode index (BEI) was determined as the number of bruxism events per hour of sleep, and the SB intensity was classified as insignificant (BEI < 2), mild or moderate (BEI = 2–4), or severe (BEI > 4) [23]. The apnea-to-bruxism index refers to a bruxism event secondary to a respiratory event. Temporal association between SB and respiratory events were demonstrated and evaluated previously, suggesting that SB events were secondary to apneic–hypopneic events [26]. As there are no reference values, the authors assumed an apnea-to-bruxism index of <1 as normal, concluding that an apnea-to-bruxism index greater than 1 may suggest other etiology of bruxism events, e.g., primary bruxism or against-hypoxia protective features of SB.

The study group consisted of normotensive individuals. Normotension was defined as the lack of use of any antihypertensive medications in medical history and was based on the office BP measurements. According to European guidelines for the management of HTA, individuals with BP values of at least 140/90 mmHg were considered as normotensive [27]. All patients included in the study had an office BP measurement in the normal range at the day of admission to internal ward. On the first night, individuals underwent full-night video-polysomnography. Blood pressure measurements were conducted the next day. After conducting PSG, in the morning, patients received ABPM for 24 h home use as a mandatory requirement for the diagnosis of hypertension. The ABPM devices were attached by a qualified technician, and the measurement was performed according to recommendations of European Society of Hypertension [28]. First, the technician measured the circumference of the upper arm and selected the appropriate cuff. Next, all participants were instructed about the correct position during BP measurement, and the technicians read through the instruction paper together with the patient before 24 h measurements and explained the possible hazards in detail on the basis of the warnings included in the instructions. The ABPMs were conducted with validated Spacelabs OnTrak Ambulatory Blood Pressure Monitor appliances. The measurement intervals estimated were 15 and 20 min during daytime and nighttime periods, respectively. Daytime was recorded as the period between the time of attachment of the device by the patient and the time when the patient went to bed. Nighttime was registered as the period between the time when the patient went to bed and the time when the patient woke up in the morning. Subsequently, the devices were collected from patients on the following day. The ABPM measurements were scored according to the cut off values in the ESH/ESC (the European Society of Hypertension and the European Society of Cardiology) guidelines for 2018 [27] and extrapolated with findings from PSG.

Statistical analyses were performed using Dell Statistica 13.1 statistical package (Dell Inc., Round Rock, TX, USA). The distribution of variables was assessed with the W-Shapiro–Wilk test. For independent quantitative variables with normal distribution, the *t*-test was used for further statistical analysis. For variables with non-normal distribution, the Mann–Whitney U test was used. Correlation and regression analyses were performed to determine the relationship between the studied variables. The model parameters obtained in the regression analysis were estimated using the least squares method. The results at the level of $p < 0.05$ were considered to be statistically significant.

3. Results

The study group consisted of 65 normotensive individuals; the mean age of the participants was 33.96 ± 11.22 years, and 20 (30.77%) were men and 45 (69.23%) were women. The average body mass estimated was 65.12 ± 13.22 kg, the mean height was 1.70 ± 0.08 m, and the average body mass index (BMI) (calculated as weight in kilogram divided by square of height in meters) was 22.48 ± 3.87 kg/m^2. According to BMI, three subjects were identified to be underweight (BMI < 18.5 kg/m^2), 33 had normal weight (BMI = 18.5–25 kg/m^2), nine were overweight (BMI = 25–30 kg/m^2), and three were obese (BMI > 30 kg/m^2).

After one-night PSG, 56 (86.15%) participants met the criteria for SB, of which 25 were diagnosed with mild/moderate SB (BEI = 2–4 events/h) and 31 had severe SB (BEI > 4 events/h). On the basis of the apnea–hypopnea index (AHI), 14 (21.54%) participants were diagnosed to have OSA, including eight (12.31%) with mild OSA (AHI = 5–15 events/h), three (4.62%) with moderate OSA (AHI = 15–30 events/h), and three (4.2%) with severe OSA (AHI > 30 events/h).

None of the patients in the study group met the criteria for accompanying diseases such as hypertension, diabetes mellitus, or coronary artery disease. The polysomnographic and ABPM parameters in the studied group are presented in Tables 1 and 2.

Table 1. Polysomnographic characteristics of the study group.

Parameter	Mean	SD
AHI (*n*/h)	5.07	8.62
ODI (*n*/h)	4.76	7.48
Snore (% of TST)	7.35	14.74
TST (min)	428.00	65.50
SL (min)	22.76	21.91
REML (min)	100.03	62.31
WASO (min)	31.12	31.19
SE (%)	86.30	10.60
N1 (% of TST)	4.48	3.75
N2 (% of TST)	49.92	7.59
N3 (% of TST)	22.65	7.02
REM (% of TST)	22.95	5.26
Arousals (n/h)	5.04	3.92
Mean SpO_2 (%)	94.65	1.80
Min SpO_2 (%)	88.62	6.16
SpO_2 < 90% (%)	1.48	4.74
Mean desaturation drop (%)	3.23	0.60
Mean heart rate (beats/min)	60.67	6.84
Max heart rate (beats/min)	95.97	11.79
Min heart rate (beats/min)	48.52	5.98
BEI (*n*/h)	5.06	3.54
Phasic (*n*/h)	3.86	7.27
Tonic (*n*/h)	2.34	2.29
Mixed (*n*/h)	1.30	1.59
Apnea-to-bruxism index	1.09	1.99

AHI, apnea–hypopnea index; ODI, oxygen desaturation index; TST, total sleep time (min); SL, sleep latency; REML, REM latency; WASO, wake after sleep onset; SE, sleep efficiency; N1, sleep stage 1; N2, sleep stage 2; N3, sleep stage 3; REM, rapid eye-movement sleep stage; mean SpO_2, mean oxygen saturation (%); SpO_2 < 90%, time with oxygen saturation < 90% (% of TST); BEI, bruxism episode index.

Table 2. Ambulatory BP characteristics of the study group (values are shown as mean ± SD).

	Variable	24 h Mean	Daytime	Nighttime
SBP	Average (mmHg)	110.56 ± 7.91	114.03 ± 8.78	101.68 ± 7.94
	Variability (mmHg)	12.61 ± 2.99	11.09 ± 2.68	9.66 ± 3.46
	Minimum (mmHg)	84.75 ± 7.43	90.59 ± 9.46	85.55 ± 8.05
	Maximum (mmHg)	141.88 ± 14.10	141.67 ± 14.07	121.75 ± 12.92
	Decline (%)	10.67 ± 6.06		
DBP	Average (mmHg)	68.83 ± 6.08	72.31 ± 7.12	60.60 ± 6.55
	Variability (mmHg)	11.19 ± 2.65	9.98 ± 2.89	8.48 ± 3.00
	Minimum (mmHg)	46.81 ± 6.58	51.73 ± 8.08	47.15 ± 6.42
	Maximum (mmHg)	99.64 ± 15.29	99.09 ± 14.91	78.25 ± 12.26
	Decline (%)	15.75 ± 7.24		
MAP	Average (mmHg)	83.16 ± 6.11	86.13 ± 6.82	75.37 ± 6.37
	Variability (mmHg)	10.79 ± 2.42	9.74 ±2.53	8.07 ± 2.99
	Minimum (mmHg)	61.56 ± 6.49	65.61 ± 7.47	62.17 ± 6.63
	Maximum (mmHg)	113.28 ± 14.07	112.39 ± 13.87	91.97 ± 12.33
	Decline (%)	12.49 ± 6.00		
PP	Average (mmHg)	41.77 ± 4.97	42.02 ± 5.21	41.03 ± 5.03
	Variability (mmHg)	7.24 ± 1.95	7.45 ± 2.07	5.88 ± 1.81
	Minimum (mmHg)	23.80 ± 3.23	24.47 ± 4.16	29.35 ± 5.13
	Maximum (mmHg)	61.86 ± 9.97	61.00 ± 10.01	53.62 ± 8.31
HR	Average (beats/min)	72.09 ± 6.60	75.31 ± 7.24	63.35 ± 6.35
	Variability (beats/min)	12.82 ± 3.27	12.42 ± 3.69	7.20 ± 3.46
	Minimum (beats/min)	52.88 ± 5.98	55.39 ± 7.30	54.07 ± 5.32
	Maximum (beats/min)	112.55 ± 20.49	111.77 ± 20.10	83.62 ± 15.87

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate.

The difference in the ambulatory BP data among participants with BEI < 2 and those with BEI > 2 was nonsignificant, but the group of non-bruxers was relatively small (n = 9). However, significant differences in ABPM findings were observed between severe bruxers and the remaining study group (Table 3).

Table 3. Ambulatory BP characteristics of patients with and without severe bruxism (BEI > 4 per hour).

	Variable		BEI ≤ 4	BEI > 4	p
SBP (mmHg)	24 h mean	Average	111.55 ± 8.42	109.52 ± 7.31	0.31
		Variability	12.59 ± 3.27	12.62 ± 2.71	0.97
		Minimum	86.39 ± 7.39	83.00 ± 7.19	0.07
		Maximum	143.97 ± 15.21	139.65 ± 12.67	0.22
		Decline (%)	10.87 ± 7.15	10.46 ± 4.75	0.80
	Daytime	Average	115.18 ± 9.54	112.81 ± 7.85	0.28
		Variability	10.86 ± 2.79	11.32 ± 2.58	0.50
		Minimum	92.21 ± 10.59	88.87 ± 8.04	0.16
		Maximum	143.97 ± 15.21	139.23 ± 12.52	0.18
	Nighttime	Average	102.45 ± 7.98	100.86 ± 7.95	0.44
		Variability	**8.81 ± 3.36**	**10.57 ± 3.39**	**0.05**
		Minimum	**88.13 ± 8.43**	**82.79 ± 6.72**	**0.01**
		Maximum	121.10 ± 13.04	122.45 ± 12.98	0.69

Table 3. *Cont.*

Variable			BEI ≤ 4	BEI > 4	p
DBP (mmHg)	24 h mean	Average	68.97 ± 6.44	68.68 ± 5.78	0.85
		Variability	11.21 ± 2.76	11.17 ± 2.56	0.95
		Minimum	47.91 ± 6.78	45.65 ± 6.25	0.17
		Maximum	102.24 ± 15.98	96.87 ± 14.26	0.16
		Decline (%)	15.79 ± 8.88	15.71 ± 5.11	0.96
	Daytime	Average	72.09 ± 7.29	72.55 ± 7.04	0.80
		Variability	10.06 ± 3.01	9.91 ± 2.79	0.84
		Minimum	52.48 ± 8.19	50.94 ± 8.02	0.45
		Maximum	102.21 ± 16.00	95.77 ± 13.09	0.08
	Nighttime	Average	60.77 ± 7.13	60.41 ± 5.99	0.83
		Variability	7.99 ± 3.13	9.00 ± 2.82	0.20
		Minimum	48.52 ± 6.99	45.69 ± 5.50	0.09
		Maximum	77.71 ± 11.89	78.83 ± 12.83	0.73
MAP (mmHg)	24 h mean	Average	83.64 ± 6.35	82.65 ± 5.90	0.52
		Variability	10.86 ± 2.53	10.71 ± 2.34	0.80
		Minimum	62.33 ± 6.87	60.74 ± 6.07	0.33
		Maximum	116.09 ± 15.04	110.29 ± 12.50	0.10
		Decline (%)	12.62 ± 7.24	12.35 ± 4.45	0.87
	Daytime	Average	86.58 ± 7.37	85.65 ± 6.26	0.59
		Variability	9.83 ± 2.61	9.64 ± 2.49	0.76
		Minimum	66.24 ± 8.46	64.94 ± 6.32	0.49
		Maximum	**115.79 ± 15.04**	**108.77 ± 11.68**	**0.04**
	Nighttime	Average	75.81 ± 6.71	74.90 ± 6.07	0.58
		Variability	7.58 ± 2.92	8.59 ± 3.03	0.20
		Minimum	63.74 ± 7.16	60.48 ± 5.66	0.06
		Maximum	91.48 ± 12.28	92.48 ± 12.57	0.76
PP (mmHg)	24 h mean	Average	42.73 ± 5.37	40.74 ± 4.35	0.11
		Variability	7.36 ± 2.08	7.12 ± 1.82	0.63
		Minimum	24.00 ± 2.85	23.58 ± 3.62	0.61
		Maximum	62.97 ± 10.35	60.68 ± 9.57	0.36
	Daytime	Average	43.06 ± 5.65	40.90 ± 4.52	0.10
		Variability	7.61 ± 2.26	7.28 ± 1.87	0.53
		Minimum	24.73 ± 4.31	24.19±4.05	0.61
		Maximum	62.52 ± 10.64	59.39 ± 9.19	0.21
	Nighttime	Average	41.65 ± 5.24	40.38 ± 4.81	0.33
		Variability	5.58 ± 1.72	6.20 ± 1.89	0.19
		Minimum	30.48 ± 5.39	28.14 ± 4.63	0.08
		Maximum	52.87 ± 7.83	54.41 ± 8.87	0.48
HR (beats/min)	24 h mean	Average	72.24 ± 6.56	71.94 ± 6.76	0.85
		Variability	**13.64 ± 3.67**	**11.95 ± 2.57**	**0.04**
		Minimum	53.24 ± 6.17	52.48 ± 5.85	0.62
		Maximum	**117.82 ± 23.15**	**106.94 ± 15.70**	**0.03**
	Daytime	Average	75.45 ± 6.96	75.16 ± 7.65	0.87
		Variability	**13.33 ± 4.25**	**11.45 ± 2.72**	**0.04**
		Minimum	55.82 ± 7.68	54.94 ± 6.98	0.63
		Maximum	**116.76 ± 22.42**	**106.45 ± 15.99**	**0.04**
	Nighttime	Average	64.03 ± 7.17	62.62 ± 5.36	0.39
		Variability	7.65 ± 4.18	6.71 ± 2.44	0.30
		Minimum	54.77 ± 5.46	53.31 ± 5.15	0.29
		Maximum	**87.84 ± 18.84**	**79.10 ± 10.46**	**0.03**

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; values are shown as mean ± SD, statistically significant differences marked as bold ($p < 0.05$).

Differences in the ambulatory BP data between individuals with an apnea-to-bruxism index < 1 and those with an apnea-to-bruxism index ≥ 1 was statistically significant (Table 4).

Table 4. Comparison of ambulatory BP data among study groups with apnea-to-bruxism indexes < 1 and apnea-to-bruxism indexes ≥ 1.

Variable			Apnea-to-Bruxism < 1	Apnea-to-Bruxism ≥ 1	*p*
SBP (mmHg)	24 h mean	Average	**109.28 ± 7.16**	**113.83 ± 8.95**	**0.04**
		Variability	**12.13 ± 2.92**	**13.82 ± 2.91**	**0.04**
		Minimum	84.96 ± 7.54	84.22 ± 7.34	0.73
		Maximum	139.74 ± 12.92	147.33 ± 15.83	0.05
		Decline (%)	10.45 ± 6.39	11.22 ± 5.26	0.66
	Daytime	Average	**112.57 ± 7.97**	**117.78 ± 9.84**	**0.03**
		Variability	10.74 ± 2.36	11.98 ± 3.28	0.10
		Minimum	89.87 ± 9.11	92.44 ± 10.36	0.33
		Maximum	139.74 ± 12.92	146.61 ± 15.99	0.08
	Nighttime	Average	100.53 ± 7.54	104.59 ± 8.41	0.07
		Variability	**8.88 ± 3.24**	**11.64 ± 3.30**	**0.00**
		Minimum	86.02 ± 8.38	84.35 ± 7.25	0.47
		Maximum	**119.37 ± 10.80**	**127.76 ± 15.97**	**0.02**
DBP (mmHg)	24 h mean	Average	67.93 ± 5.81	71.11 ± 6.34	0.06
		Variability	10.94 ± 2.50	11.82 ± 2.97	0.24
		Minimum	47.20 ± 6.97	45.83 ± 5.51	0.46
		Maximum	98.22 ± 13.87	103.28 ± 18.39	0.24
		Decline (%)	15.78 ± 7.97	15.69 ± 5.16	0.97
	Daytime	Average	**70.96 ± 6.40**	**75.78 ± 7.68**	**0.01**
		Variability	9.94 ± 2.56	10.10 ± 3.68	0.84
		Minimum	51.04 ± 7.49	53.50 ± 9.44	0.28
		Maximum	98.13 ± 13.97	101.56 ± 17.25	0.41
	Nighttime	Average	59.70 ± 6.64	62.88 ± 5.89	0.09
		Variability	**7.92 ± 2.85**	**9.87 ± 3.00**	**0.02**
		Minimum	47.53 ± 6.81	46.18 ± 5.39	0.47
		Maximum	**75.98 ± 8.69**	**84.00 ± 17.54**	**0.02**
MAP (mmHg)	24 h mean	Average	**82.15 ± 5.63**	**85.72 ± 6.69**	**0.03**
		Variability	10.52 ± 2.33	11.48 ± 2.58	0.16
		Minimum	61.50 ± 6.59	61.72 ± 6.42	0.90
		Maximum	111.83 ± 13.01	117.00 ± 16.27	0.19
		Decline (%)	12.49 ± 6.48	12.49 ± 4.75	1.00
	Daytime	Average	**84.98 ± 6.29**	**89.06 ± 7.39**	**0.03**
		Variability	9.62 ± 2.21	10.02 ± 3.27	0.57
		Minimum	64.74 ± 6.89	67.83 ± 8.60	0.14
		Maximum	111.61 ± 12.94	114.39 ± 16.24	0.48
	Nighttime	Average	74.40 ± 6.09	77.82 ± 6.58	0.06
		Variability	**7.48 ± 2.82**	**9.57 ± 2.97**	**0.01**
		Minimum	62.26 ± 6.81	61.94 ± 6.35	0.87
		Maximum	**89.58 ± 9.60**	**98.00 ± 16.26**	**0.02**

Table 4. *Cont.*

Variable			Apnea-to-Bruxism < 1	Apnea-to-Bruxism ≥ 1	*p*
PP (mmHg)	24 h mean	Average	41.41 ± 4.97	42.67 ± 4.97	0.37
		Variability	7.02 ± 1.83	7.82 ± 2.17	0.14
		Minimum	23.65 ± 2.62	24.17 ± 4.50	0.57
		Maximum	61.28 ± 9.94	63.33 ± 10.17	0.46
	Daytime	Average	41.61 ± 5.14	43.06 ± 5.40	0.32
		Variability	7.25 ± 1.98	7.95 ± 2.26	0.23
		Minimum	24.17 ± 3.84	25.22 ± 4.93	0.37
		Maximum	60.52 ± 10.08	62.22 ± 10.01	0.55
	Nighttime	Average	40.86 ± 5.04	41.47 ± 5.15	0.68
		Variability	**5.50 ± 1.52**	**6.84 ± 2.16**	**0.01**
		Minimum	29.86 ± 4.95	28.06 ± 5.51	0.22
		Maximum	**52.16 ± 7.92**	**57.29 ± 8.39**	**0.03**
HR (beats/min)	24 h mean	Average	72.74 ± 5.63	70.44 ± 8.58	0.21
		Variability	**13.39 ± 3.04**	**11.34 ± 3.48**	**0.02**
		Minimum	53.30 ± 5.70	51.78 ± 6.68	0.36
		Maximum	**116.00 ± 20.41**	**103.72 ± 18.40**	**0.03**
	Daytime	Average	75.89 ± 6.06	73.83 ± 9.69	0.31
		Variability	**13.06 ± 3.47**	**10.77 ± 3.82**	**0.02**
		Minimum	56.02 ± 6.60	53.78 ± 8.85	0.27
		Maximum	**115.24 ± 19.75**	**102.89 ± 18.67**	**0.03**
	Nighttime	Average	64.14 ± 6.16	61.35 ± 6.56	0.13
		Variability	7.67 ± 3.68	5.99 ± 2.53	0.09
		Minimum	54.44 ± 5.29	53.12 ± 5.43	0.39
		Maximum	**86.56 ± 16.42**	**76.18 ± 11.78**	**0.02**

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; values are shown as mean ± SD, statistically significant differences marked as bold ($p < 0.05$).

Regression analysis was performed to determine the factors independently associated with mean arterial pressure (MAP) (average from the 24 h mean of APBM and daytime measurements) and systolic blood pressure (SBP) variability during sleep period. In the regression model, we used all potentially independent variables: apnea-to-bruxism index, male gender, BMI, age, BEI > 4, BMI ≥ 25, arousal index, and total sleep time (TST).

The regression model showed that a higher apnea-to-bruxism index and higher BMI were independently associated with the increased average of 24 h mean of MAP (Table 5).

Table 5. Results of estimation for the final model obtained on multivariate regression analysis. model for average MAP (24 h Mean).

Parameter	Model for Average MAP (24 h Mean)		
	Rc	SEM of RC	*p*
Intercept	**68.31**	**4.72**	**0.000**
Apnea-to-bruxism index	**0.44**	**0.23**	**0.045**
Male gender	0.66	1.62	0.685
BMI	**0.53**	**0.26**	**0.041**
Age	0.06	0.09	0.472

MAP, mean arterial pressure (mmHg); BMI, body mass index (kg/m^2); Rc, regression coefficient; SEM, standard error of mean; statistically significant differences are marked as bold ($p < 0.05$).

This finding confirmed that a higher apnea-to-bruxism index and higher BMI were independent predictors of the increased average MAP during daytime in the studied group (Table 6).

Table 6. Results of the estimation for the final model obtained on multivariate regression analysis. Model for average daytime MAP.

Parameter	Model for Average MAP (Daytime)		
	Rc	SEM of RC	*p*
Intercept	**69.01**	**5.14**	**0.000**
Apnea-to-bruxism index	**0.72**	**0.30**	**0.048**
Male gender	1.28	1.76	0.468
BMI	**0.59**	**0.28**	**0.036**
Age	0.08	0.10	0.424

MAP, mean arterial pressure (mmHg); BMI, body mass index (kg/m^2); Rc, regression coefficient; SEM, standard error of mean; statistically significant differences are marked as bold ($p < 0.05$).

The regression analysis also indicated that a higher apnea-to-bruxism index, male gender, BEI > 4, BMI $\geq$ 25 kg/m^2, higher arousal index, and shorter TST were the independent risk factors for increased SBP variability during sleep period (Tables 7 and 8).

Table 7. Results of the estimation for the final model obtained on multivariate regression analysis. Model for nighttime SBP variability and anthropometric and polysomnographic characteristics.

Parameter	Model for SBP Variability (Nighttime)		
	Rc	SEM of RC	*p*
Intercept	**8.49**	**2.64**	**0.002**
Apnea-to-bruxism index	**0.33**	**0.11**	**0.040**
Male gender	**2.08**	**0.90**	**0.025**
BMI	−0.05	0.14	0.724
Age	0.04	0.05	0.434

SBP, systolic blood pressure (mmHg); BMI, body mass index (kg/m^2); Rc, regression coefficient; SEM, standard error of mean; statistically significant differences are marked as bold ($p < 0.05$).

Table 8. Results of the estimation for the final model obtained on multivariate regression analysis. Model for nighttime SBP variability and anthropometric, bruxism, and polysomnographic indices.

Parameter	Model for SBP Variability (Nighttime)		
	Rc	SEM of RC	*p*
Intercept	**11.48**	**3.76**	**0.004**
BEI > 4	**1.57**	**0.63**	**0.039**
BMI $\geq$ 25	**2.03**	**1.00**	**0.042**
Arousals	**0.18**	**0.09**	**0.044**
TST	**−0.01**	**0.01**	**0.026**

SBP, systolic blood pressure (mmHg); BEI, bruxism episode index (*n*/hour); BMI, body mass index (kg/m^2); TST, total sleep time; Rc, regression coefficient; SEM, standard error of mean; statistically significant differences are marked as bold ($p < 0.05$).

4. Discussion

The results of the current study showed an association between SB intensity and blood pressure fluctuations. The results demonstrate that SB affects BP. The SBP variability at nighttime significantly increased in severe sleep bruxers as compared to those in the remaining study group. Blood pressure variability (BPV) reflects dynamic changes in BP caused by physical, emotional, and environmental factors. The clinical importance of BPV is broadly discussed as follows. BPV is considered a risk factor for cardiovascular events [29,30] and is associated with organ complications and cardiovascular mortality [29,31] independent from mean 24 h BP values. Therefore, cardiovascular reactivity and BP fluctuations promote an individual's risk of developing hypertension and can be considered to be equivalent to the traditional determinants of hypertension. Thus, the implications of the current findings involve serious risk of hypertension development in severe sleep bruxers

without the actual diagnosis of hypertension. Moreover, regression analysis demonstrated that SB intensity was associated with increased SBP variability independently from anthropometric and polysomnographic parameters such as age, gender, BMI, and apnea events. Importantly, the current findings show a novel association between SB intensity and SBP variability independent from OSA. Lower minimal values of SBP at nighttime in severe sleep bruxers as compared to that in the remaining study group may be considered due to the sympathetic tone balance as argued previously [32,33].

This result highlights that little is known about the implications of SB for general health. Metabolic and hormonal disturbances related to the increased level of inflammatory and stress markers were found in young sleep bruxers in a prior study by our research team [34]. Several existing studies in the broader literature have examined clinical implications of SB on oral health and sleep-related disorders [9,23,35]. Seminal contributions to more comprehensive perspectives have been made by Huynh and Lavigne [18,19,36] who investigated the role of autonomic cardiac activation in SB events. Finally, the authors demonstrated the co-occurrence of RMMA events, arousal, and respiratory events in patients with SB [37,38].

The literature on the relationship between SB and hypertension confirmed our results. For instance, Nashed et al. [21] demonstrated that RMMA is associated with BP fluctuations during sleep. The methods were based on nocturnal beat-to-beat BP measurements. Although the study was well conducted and designed, the study group consisted of only 10 participants, whereas the control group had nine individuals. In a previous study by our research team, Martynowicz et al. [22] demonstrated that hypertension was an independent risk factor for SB. The lack of objective diagnosis of hypertension was the most important limitation of this previous study; hence, we designed the current study to diagnose hypertension and assess cardiovascular risk in bruxing, normotensive healthy patients by using ABPM.

It is also important to highlight the genetic basis of SB. The influence of neurotransmitters involved in sleep regulation, such as acetylcholine, noradrenaline, dopamine, and serotonin, on the genesis of SB has been insufficiently explored [39,40]. Wieckiewicz et al. [8] suggested that the genetic basis of primary bruxism is associated with the rs686 G variant of the dopamine receptor DRD1 encoding gene and the rs2770304 and rs6313 polymorphisms of the serotonin receptor HRT2A encoding gene. Their study also revealed a possible genetic association between SB and OSA, wherein a statistically significant correlation was observed within a group of HTR2A rs2770304 polymorphism TT homozygous cases. The serotonin receptor HRT2A has been linked previously with stress-induced response and anxiety-level mediation [41]. Serotoninergic mechanisms seem to play a crucial role in SB pathogenesis [8]. Therefore, the potential mechanism that causes decrease and variability in SBP in severe sleep bruxers could reflect the regulating effect of serotonin on the autonomic system activity [42]. Serotonin is also related to vasoconstriction and vasodilatation functions [43]. The results of the current study support this fact by showing that severe sleep bruxers had lower MAP in daytime. This finding is consistent with the assumption that nocturnal BP fluctuations cause dysregulations of the cardiovascular system.

A further relevant result is the correlation between BP measurements and SB events related to apnea. The study group included relatively young, normotensive subjects (mean age 33.96 $\pm$ 11.22 years) without severe comorbidities; therefore, the prevalence of OSA in this study group was considered to be a surprising finding. It is difficult to explain this result within the context of the normal weight of the study group (average BMI: 22.48 $\pm$ 3.87 kg/m^2). Obesity is the major risk factor for OSA [44]. The remaining risk factors for OSA are well documented and include a family history of OSA, retrognathia, resistant hypertension, congestive heart failure, atrial fibrillation, stroke, and type 2 diabetes [45]. None of the participants from the study group met these criteria (risk factors). Thus, the high prevalence of OSA (21.54%) in the study group without classical risk factors for OSA may suggest a secondary SB related to apneic events. This relationship was previously observed by Hosoya et al., Martynowicz et al., and Tan et al. All these authors

have highlighted the protective features of SB against hypoxic event [46–48]. Moreover, the literature on SB has established sympathetic activity as the underlying reason for its consequences such as heart rate variability, hypertension, OSA, and hormonal and metabolic disturbances. A significant difference in the ABPM data between participants with an apnea-to-bruxism index < 1 and those with an apnea-to-bruxism index ≥ 1 supports this hypothesis. In the group with higher number of SB events related to apnea, increased BP values were found. Bruxism related to apnea events influenced both daytime and nighttime measurements of the increased BP values. In contrast, heart rate significantly decreased in the study group with an apnea-to-bruxism index ≥ 1. A recent study of our research team provided some information related to the background of this issue and reported heart rate variability as an expression of sympathetic tone in SB and its consequences. [33] A significant decrease in heart rate was considered as a consequence of autonomic homeostasis in response to increased cardiac activity. Xu et al. demonstrated that in a study group with severe OSA, nocturnal and awake BP values were associated with the duration of hypoxia during sleep and BP fluctuations. In contrast to our present study design, BP was assessed in this study by measuring pulse transmit time (PTT) [49].

The broad implication of the present research is that SB in young patients with increased sympathetic tone favors the development of BP fluctuations [21] and subsequently hypertension. Sympathetic activity is modulated by an increased level of stress and anxiety, which are the major determinants of SB. Subsequently, contributory risk factors, such as age, gender, and weight gain, influence and determine OSA and hypertension progression, which are associated with SB. [47] The very basis of this positive feedback loop is sympathetic activity. The cause-and-effect relationship between increased sympathetic activity and blood pressure fluctuations in sleep bruxers suggest association between SB and increased risk of cardiovascular complications. Despite previous and current study are preliminary, authors suggest assessing cardiovascular and respiratory implications of SB in bruxing patients. Further studies should aim to provide more information about this health prevention concern.

The present study had some limitations. First, the results are specific to young, healthy, normotensive adult subjects, and we did not diagnose elderly patients or children. It could also be argued whether BP fluctuations in sleep bruxers could affect co-existing cardiovascular conditions. Further studies on comparison between SB patients with cardiovascular diseases and controls are needed to determine whether SB affects BP alterations and worsens CVD. Future studies should aim to replicate the results in vulnerable individuals. Second, there was a lack of parity in the study group, and women constituted 69.23% of the study participants. This apparent limitation could influence our findings, as has been revealed in a recent study by Smardz et al. [50] where age and gender were found to influence SB. Last but not least, the participants underwent one-night PSG without an adaptation due to the presence of technical issues.

To summarize, the results of our present study shed new light on SB comorbidity, especially BP fluctuations and warrants a change in the clinical approach to patients with SB.

5. Conclusions

1. SB intensity is associated with increased SBP variability at nighttime (sleep period);
2. Coexisting apnea is considered to be the main determinant that influences BP in normotensive sleep bruxers;
3. A future approach should consider the potential risk of hypertension or abnormalities in BP regulation and other cardiovascular risk factors in sleep bruxers more carefully as potentially significant implications for health.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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7. PRACA 4

Cardiovascular Implications of Sleep Bruxism- A Systematic Review with Narrative Summary and Future Perspectives.

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Review

Cardiovascular Implications of Sleep Bruxism—A Systematic Review with Narrative Summary and Future Perspectives

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Abstract: Sleep bruxism is a common sleep-related behavior characterized as repetitive masticatory muscle activity. Genetic vulnerability to stress and anxiety is considered a basal component in the pathogenesis of bruxism events. Dysfunction of the autonomic nervous system related with an arousal during sleep is considered an underlying cause of the cardiovascular implications of sleep bruxism. Increased cardiovascular risk was previously linked with sleep conditions: for example, obstructive sleep apnea and insomnia, and sleep bruxism. The aim of present systematic review was to evaluate the current arguments on the relationship between sleep bruxism and cardiovascular diseases according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We have reviewed the Embase, PubMed (Medline) and Scopus databases to identify applicable articles (1994–2021). A total of 127 records in English language were identified, then after screening and exclusion of nonrelevant records, 19 full-text articles were evaluated. Finally, we included 12 studies for synthesis. Due to the heterogeneity of the compared studies, only a qualitative comparison and narrative summary were performed. In the majority of studies, increased sympathetic activity was successfully established to escalate heart rate variability, the inflammatory process, oxidative stress, endothelial remodeling and hormonal disturbances, leading to hypertension and other cardiovascular complications.

Keywords: sleep bruxism; RMMA, rhythmic masticatory muscle activity; cardiovascular risk; cardiovascular disease; arterial hypertension

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1. Introduction

One of the major topics investigated in the field of sleep conditions is sleep bruxism (SB). The widely adopted definition of bruxism constitutes that sleep bruxism is a rhythmic (phasic) or non-rhythmic (tonic) masticatory muscle activity during sleep and it is not a movement disorder or a sleep disorder in otherwise healthy subjects [1]. Clinical symptoms of SB are classified in the 3rd edition of International Classification of Sleep Disorders and involve regular or frequent bruxism events during sleep and the presence of abnormal tooth wear or incidents of jaw muscle pain or fatigue [2]. Most of the theories of bruxism etiology are focused on genetic and psychologic vulnerability to stress or anxiety [3], the role of neurotransmitters serotonin, dopamine, gamma aminobutyric acid (GABA) and noradrenaline [4], autonomic nervous system modulation [5] and exposure to exogenous risk factors, e.g., tobacco, alcohol or drugs and comorbidities [6]. The prevalence of sleep bruxism in the adult population is estimated to be about 8% [7,8] up to 13% [9]; however, it varies depending on age group. Widely accepted and used diagnostic criteria for sleep bruxism were proposed by the American Academy of Sleep Medicine (AASM) [10] and

international consensus by Lobbezoo et al. [11], but polysomnography remains the gold standard [12].

Although sleep bruxism is considered a sleep behavior rather than sleep disorder, previous studies have emphasized its coexistence with sleep-related disorders, for example, obstructive sleep apnea. Most SB events are preceded by brain and cardiovascular activity. Thus, there are some questions that naturally arise from the link between SB and OSA. Cardiovascular implications of both sleep bruxism and sleep-related disorders are widely investigated. Furthermore, a considerable body of literature showed the association between sleep-related disorders and cardiovascular complications. For example, studies have provided evidence for the relationship between obstructive sleep apnea and stroke [13,14], resistant hypertension [15,16], cardiac arrythmias [17] and diabetes [18]. As has also been previously reported, insomnia and sleep deprivation are associated with substantial impairments, e.g., heart failure [19] and hypertension [20]. Primary and secondary restless leg syndrome (RLS) was also discussed as associated with increased risk of cardiovascular disease (CVD). Van Den Eeden et al. [21] demonstrated that primary RLS was linked with increased risk of hypertension, whereas secondary RLS was associated with coronary artery disease (CAD) and hypertension.

This review investigates a relatively new area which has emerged from the pathophysiology of sleep bruxism, establishing that increased sympathetic activity is a core of the causal chain with an initial increase in heart rate and microarousal accompanied by rhythmic masticatory muscle activity (RMMA). The key contribution of autonomic-cardiac network hyperreactivity can be described as homeostasis maintenance in response to cortical activation and an arousal [5]. The increased sympathetic activity may provide significant cardiovascular implications and it is considered as the main subject of this review.

2. Objectives—The Aim of the Systematic Review

The main objective of the present systematic review was to investigate the current arguments on the relationship between sleep bruxism and cardiovascular diseases according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We focused on the critical revision of evidence for cardiovascular risk and increased sympathetic activity in available original articles in the field of sleep bruxism. The authors also intended to evaluate the strengths and weaknesses of reviewed reports and, therefore, to develop a new approach to sleep bruxism consequences.

Our PICO question was as follows: Are patients with diagnosed sleep bruxism (P, I) at increased cardiovascular risk (O) compared with non-bruxing patients (C)?

3. Methods

This systematic review's authors followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Checklist [22,23]. Only studies involving human adult sleep bruxers published in English language were included. The literature screening procedure was conducted with PRISMA guidelines; details are presented in the PRISMA flowchart in Figure 1. For the current systematic review, the search strategy included search terms as follows: sleep bruxism and (cardiovascular or sympathetic activity). The literature review was performed by three authors (M.M.-Z., H.M. and M.W.) who reviewed the Embase, PubMed (MEDLINE) and Scopus databases (access date 15 April 2021). A total number of 127 reports were found. Search results estimated 22 records in the Scopus database, 76 in Embase and 29 results in PubMed. Subsequently, duplicates were removed, and thorough screening of the titles and abstracts of the remaining articles was performed. The remaining 19 full-text records were analyzed for eligibility by two authors (M.M.-Z. and H.M.) independently. Finally, 12 manuscripts were included in the synthesis (see Table 1).

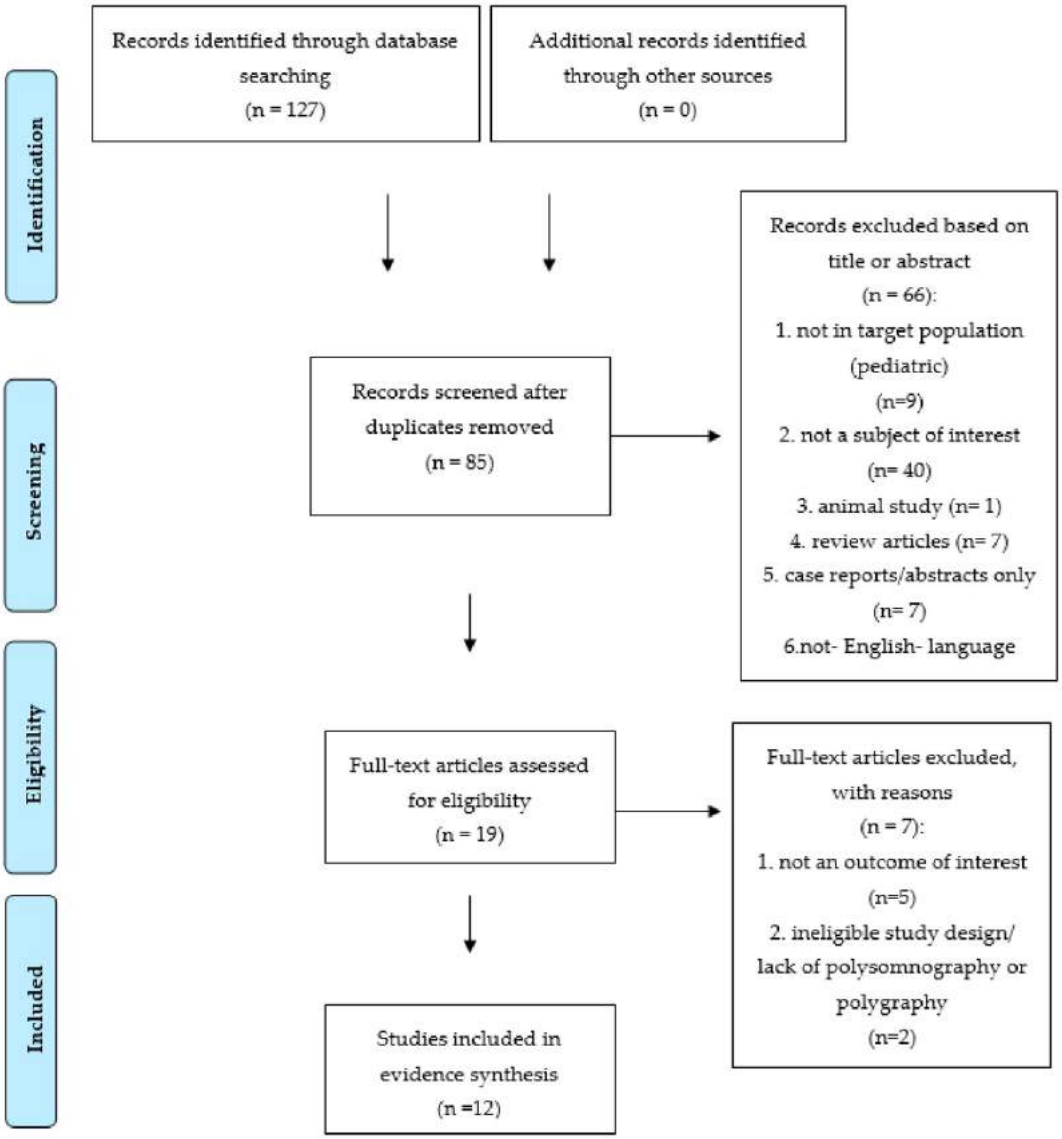

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart of the review protocol.

Table 1. The main characteristics of the revised studies.

Author and Year	Study Design	Study Population (Cases/Controls)	Compared Groups	Study Type *	Aim of the Study	Comments
Okeson et al., 1994 [24]	observational	20	none	I	to collect normative data on "nocturnal bruxing events"	none
Sjoholm et al., 1995 [25]	observational	11	none	I	to examine autonomic function in "nocturnal toothgrinders"	none
Kato et al., 2001 [26]	case–control	20 (10/10)	SB patients vs. normal	I	to evaluate association among autonomic-cardiac, cortical, and jaw muscle activities, to determine a sequence of events associated with RMMA and bruxism during sleep	none
Huynh et al., 2006 [27]	case–control	60 (40/20, see comments)	moderate to high SB vs. low SB vs. control subjects	III	to assess: (1) the distribution of RMMA referring to sleep stage and sleep cycles; (2) the time correlation between RMMA and microarousals referring to SWA dynamics over sleep cycles in three study groups; (3) the time correlation between SB activity and autonomic cardiac activity	2 study groups: moderate to severe SB $n = 20$ patients; low SB $n = 20$ patients; control group $n = 20$ subjects
Huynh et al., 2006 [28]	randomized control trial	25 (see comments)	propranolol vs. clonidine	III	to examine whether (1) propranolol or clonidine may reduce the occurrence of SB; (2) may prevent the rise in autonomic sympathetic activity preceding the onset of SB	Study with propranolol n = 10 subjects; study with clonidine n = 16 subjects; 1 patient participated in both studies
Nashed et al., 2012 [29]	case–control	24 (10/9 active subjects)	SB patients vs. normal	I	to determine association between BP surges and SB events in SB subjects in relation to arousals and/or body movements	5 of the 14 recordings in control group had technical difficulties; $n = 9$
Martynowicz et al., 2018 [30]	case–control	70 (35/35)	hypertensives vs. normal	III	to examine SB severity in hypertensives compared to normotensives	none
Nukazawa et al., 2018 [31]	case–control	11	none	I	to investigate the relationship between SB and AN system activity	none
Martynowicz et al., 2019 [32]	observational	87	see comments	I	to assess the relationship between SB intensity and serum renalase concentration	SB patients vs. normal; hypertensives vs. normotensives; selected according to results of the study
Zhong et al., 2020 [33]	case–control	21 (10/11)	SB patients vs. normal	I	to evaluate HRV in relation to: SB types, RMMAs + LMs and isolated LMs in sleep bruxers	none
Michalek-Zrabkowska et al., 2020 [34]	observational	74	none	I	to diagnose sleepiness, hormonal changes and inflammatory markers (CRP, fibrinogen) in SB patients	none
Michalek-Zrabkowska et al., 2021 [35]	observational	65	none	I	to assess the association between ambulatory blood pressure measurements and SB intensity in normotensive individuals	none

* study type according to AASM criteria [36]; SB, sleep bruxism; SWA, slow wave activity; RMMA, rhythmic masticatory activity; BP, blood pressure; AN, autonomic nervous system; LM, limb movement; CRP, C-reactive protein.

We have evaluated the quality of the evidence according to the GRADE system (Grading of Recommendations Assessment, Development and Evaluation) [37]. Results of the assessment are presented in Table 2. Most of the studies included in our systematic review (n = 10 from 12) demonstrated a statistically significant relationship between sleep bruxism and cardiovascular implications; others also revealed an association, but without statistical power due to poor analysis.

Table 2. Quality of the evidence of the included studies.

Outcome Significance	Author and Year	Quality of the Evidence (GRADE System)
non-significant	Okeson et al., 1994 [24]	+— very low due to high risk of bias, imprecision
non-significant	Sjoholm et al., 1995 [25]	+— very low due to high risk of bias, imprecision
significant	Kato et al., 2001 [26]	++– low due to risk of bias, imprecision
significant	Huynh et al., 2006 [27]	+++- moderate due to large effect
significant	Huynh et al., 2006 [28]	++– low due to risk of bias, imprecision
significant	Nashed et al., 2012 [29]	++– low due to risk of bias, imprecision
significant	Martynowicz et al., 2018 [30]	+++- moderate due to large effect
significant	Nukazawa et al., 2018 [31]	++– low due to risk of bias, imprecision
significant	Martynowicz et al., 2019 [32]	+++- moderate due to large effect
significant	Zhong et al., 2020 [33]	++– low due to risk of bias, imprecision
significant	Michalek-Zrabkowska et al., 2020 [34]	+++- moderate due to large effect
significant	Michalek-Zrabkowska et al., 2021 [35]	+++- moderate due to large effect

GRADE scores: +++- (moderate), ++– (low), +— (very low).

The most common quality of evidence score was low; 11 out of 12 studies were observational studies/case–controls. In 4 studies, we upgraded the result due to the large effect of the presented findings. On the other hand, a common cause of decreased grade was imprecision. One of the studies was designed as a randomized control trial [28].

4. Results

Most of the revised papers investigated bruxism events during sleep with polysomnography [24–26,29,32–35], three studies collected data using polygraphy devices [27,28,30] and one employed a sleep bruxism monitoring system composed of two accelerometers, an infrared camera, electroencephalography, electromyography and electrocardiography devices [31].

The investigated papers differed in terms of explored domain. Through analysis, we identified publications on autonomic function in bruxers [25,27,31]. Some studies focused on blood pressure in the context of sleep bruxism [29,30,32,35]; others evaluated changes in heart rate (heart rate variability, HRV) [24,26,28,33] in sleep bruxers. One study determined inflammatory markers and hormonal disturbances as cardiovascular risk factors [34].

Together, the findings of the presented studies confirm the association between sleep bruxism and cardiovascular response. The results of the research carried out by Sjöholm et al. [25] suggested that sympathetic vasoconstrictor function examined with cardiovascular reflex tests was disturbed in bruxers; however, tests were performed in waking state in relatively small sample size. Huynh et al. [27] separated three groups of patients: moderate to high SB, low SB and control. Then, a correlation analysis between sleep, RMMA events and HRV was performed. The authors concluded that an increase in sympathetic activity precedes SB onset in moderate to severe sleep bruxers [27]. Results of a recent study by Nukazawa et al. [31] demonstrated two things. First, they confirmed the association between autonomic nervous system activity and sleep bruxism events. Second, sympathetic nerve (SN) activity was correlated with SB event length, whereas parasympathetic nerve

(PSN) activity was correlated with muscle activity (% maximum voluntary contraction). It is worth discussing the interesting fact that 93.3% of SB events ($p < 0.01$) demonstrated a pattern where SN activation was followed by beginning of SB activity and finished with PSN tone [31].

The literature pertaining to blood pressure surges in sleep bruxism strongly suggests this correlation. As has been previously reported by Nashed et al. [29], RMMA events were associated with blood pressure fluctuations. Moreover, the study concluded that arousals and body movements accompanying SB events can impact BP changes. BP recordings were based on beat-to-beat measures using finger cuffs [29]. The publication by Martynowicz et al. [32] presented some information about the background of renalase involvement in hypertension pathogenesis and indicated that there is an association between renalase concentration and sleep bruxism severity. The next study by Martynowicz et al. [30] was designed to evaluate the intensity of SB in a hypertensive group of patients compared with normotensives. Hypertension was found as an independent risk factor for increased bruxism episode index (BEI). A recent publication by Michalek-Zrabkowska et al. [35] revealed that systolic blood pressure variability during nighttime was significantly increased in severe bruxers (with BEI > 4/h) compared to individuals with BEI ≤ 4/h.

According to heart rate variability, seminal contributions have been made by Okeson et al., who aimed to collect a normative data on sleep bruxism. Results of this study revealed a cardiovascular response to bruxing event, with an increase in heart rate of 16.6% on average [24]. Zhong et al. [33] examined patients with polysomnography and then extracted three types of movements associated with heart rate increase: RMMA, RMMA+ limb movements and separate limb movements. Data of increased heart rate associated with RMMA events suggested autonomic activation to cortical arousal forasmuch as increased HR in response to different types of movements and RMMA related to respiratory events. Another interesting finding was revealed by Kato et al. [26] The study reported quantitative analysis of sequential changes observed in cortical electroencephalographic activity and sympathetic tone related to arousal and RMMA. A significant increase in heart rate reflecting autonomic-cardiac activation was observed in SB patients compared to the control group. Huynh et al. [28] employed an experimental randomized controlled study methodology which prescribes the use of two sympatholytic medications—propranolol and clonidine in sleep bruxers. Both medications decreased sympathetic tone, whereas only clonidine reduced sleep bruxism frequency (by 61%). These findings support the hypothesis of sympathetic activity in sleep bruxism.

The study of increased inflammatory markers in sleep bruxers introduced by our research team has the advantage that, to our knowledge, it is the first research of this type in this field. Michalek-Zrabkowska et al. [34] demonstrated that the bruxism episode index positively correlated with the concentrations of plasma C-reactive protein and fibrinogen and 17-hydroxycorticosteroids in the collected urine samples independently of AHI and BMI. Escalated inflammatory markers are associated with increased risk of diabetes and cardiovascular diseases; thus, this aspect of the research suggests increased CV risk associated with SB.

The reviewed literature was also heterogeneous with respect to SB diagnostic criteria. Five recent studies [30,32–35] defined RMMA/SB events depending on EMG recordings in line with AASM standards [10]. On the other hand, Nashed et al. [29], Huynh et al. [27,28] and Kato et al. [26] diagnosed SB according to validated research criteria demonstrated by Lavigne et al. [38]. Sjoholm et al. [25] examined and counted episodes of masseter contractions per hour of sleep, whereas Okeson et al. [24] defined a bruxing event as "activity of the masseter muscle exceeding 40% of the maximum clench of the muscle and lasting for 2 s or longer". One study used different SB determination methods such as the original evaluating system by Yoshimi et al. [39] based on the criteria of EMG threshold level and event duration.

5. Discussion

Our systematic review has addressed the issue of the cardiovascular implications of sleep bruxism; however, it also reveals a number of gaps and shortcomings. The findings of most studies are still initial and insufficient. An apparent limitation of most studies was small sample size (see Table 1) and variability among subjects, which reduce the significance level. As has been demonstrated in Table 2, according to the GRADE system for assessing the quality of evidence, the majority of studies were low quality due to risk of biases and imprecision. Future studies should aim to replicate results in a larger, randomly assigned population.

Sleep bruxism is a common sleep-related behavior, but it is still insufficiently explored and underdiagnosed [40]. SB was previously linked with many consequences for oral and overall health as primary and secondary factor to different disorders, e.g., sleep disordered breathing, insomnia, headache, temporomandibular disorders or mental dysfunctions as increased anxiety/risk of depression [41]. From the review above, key findings reveal an association between sleep bruxism and increased sympathetic tone, thus increasing blood pressure fluctuations and heart rate variability. They are important cofactors associated with potential cardiovascular consequences of sleep bruxism for general health. The possibility of CV complications warrants changing the current clinical approach in this field.

On the basis of the reviewed articles, we conclude that autonomic function in sleep bruxers is disturbed, introducing a whole range of adverse effects. According to the literature regarding sympathetic hyperreactivity, all three studies confirmed an association between sleep bruxism and sympathovagal balance in relatively young and healthy subjects [25,27,31]. Three studies focused on temporal coincidence between heart rate changes and SB events [24,26,33]. Despite the heterogeneity of revised papers in terms of methodology and study population, the relationship between sleep bruxism and autonomic dysfunction was observed.

Sympathetic dominance in sleep bruxers was also investigated by using two sympatholytic medications—propranolol and clonidine. Clonidine affected sympathetic tone influencing HRV preceding SB onset. On the other hand, propranolol did not affect HRV related with SB events. A broad explanation is that propranolol and clonidine have various properties in terms of pharmacokinetics and pharmacodynamics; clonidine is considered as a more potent medication in sympathetic modulation, due to its impact on alfa-2 adrenergic and imidazoline 1 receptors in the central nervous system [42]. Moreover, clonidine was also linked with silencing modulation in dopaminergic pathways. Importantly, individual response variability in the study group with clonidine was observed [28].

The broad implication of autonomic nervous system stimulation is vasoconstriction. Increased risk of hypertension was previously linked with insomnia, sleep-related breathing disorders and restless leg syndrome [43]. Multiple control systems are involved in blood pressure regulation, but neurogenic dysfunction is considered a crucial component of blood pressure fluctuations in sleep bruxism. Blood pressure dynamics depends on circadian modulation with the influence of environmental, autonomic, emotional and physical factors. As has been established, blood pressure variability is linked with increased risk of organ damage and cardiovascular mortality. It is an important equivalent of hypertension and therefore, overall cardiovascular risk [44]. We identified four studies contributing to blood pressure: the study by Nashed et al. [29] confirmed an association between BP surges and SB events, the study by Michalek-Zrabkowska et al. [35] demonstrated the association between blood pressure variability during nighttime and sleep bruxism intensity in normotensive patients, whereas two studies by Martynowicz et al. [30,32] evaluated the statistically significant relationship between hypertension and sleep bruxism intensity. Future research should further develop and confirm these initial findings.

The majority of prior studies have focused on sympathetic hyperactivity and the cardiovascular complications of sleep bruxism. A recent study by Michalek-Zrabkowska et al. [34] concluded that sleep bruxers may be at increased CV risk due to hormonal disturbances and inflammatory process. As far as we know, no previous research has

investigated the relationship between SB and inflammatory response; however, the existing literature confirms the harmful effect of inflammatory mediators to cardiovascular system structures [45,46].

The reviewed studies have varied in terms of study design and methodology. In most studies, sleep bruxism diagnosis was based on polysomnography, the gold standard for SB diagnosis [47]; however, type I polysomnography with video and audio recordings was performed only in five studies [26,29,32,34,35]. Nonetheless, the next three studies consisted of PSGs supplemented with video recordings [24,31,33]. The risk of overestimation related to absence of audio/video recordings was raised by Carra et al. [48] and evaluated up to 25%. The risk of low specificity related to SB event overscoring is increased in level II and III polysomnographic systems and level I PSG without camera recordings. In consonance with Table 1, 3 out of 12 publications were based on the II or III study type according to AASM [27,28,30], but 2 of them had supplementary audio and video recordings [27,28], whereas 1 polysomnographic study was poor in terms of video and audio data [25].

Despite having a number of limitations, these findings provide a potential mechanism for the cardiovascular implications of sleep bruxism. Increased sympathetic activity can be considered as a basic pathomechanism in SB, likely leading to dysfunction of the cardiovascular system. As has previously been shown, sleep bruxism events are associated with microarousals and increase in sympathetic tone [49]. Moreover, Kato et al. [50] demonstrated that experimentally induced arousals were also related with sleep bruxism episodes. Cardiac-autonomic activation influences cortical pathways and induces microarousal and increase in heart rate with subsequent RMMA episode in the end. Moreover, SB events are frequently accompanied by respiratory events. Alternatively, increased sympathetic tone related to SB event could simply be a part of physiological reaction to arousal without an impact on general health.

Although the concept of the genetic heritability of primary sleep bruxism has been discussed by a great number of authors in the literature [5], many questions on the genetic basis of sleep bruxism have remained unanswered for years. Wieckiewicz et al. [3] investigated the possible genetic contribution to the etiology of sleep bruxism and its relationship with obstructive sleep apnea. Taking into consideration theories on serotonin and dopamine pathways' roles in SB and OSA, researchers investigated the association of selected single-nucleotide polymorphisms (SNPs) within serotonin and dopamine genes. Together, the findings confirmed a possible genetic predisposition to sleep bruxism and its relationship with obstructive sleep apnea [3]. The broad implication of the aforementioned study is that sleep bruxism may be considered an important predisposing factor for severe health conditions such as obstructive sleep apnea. Hence, sympathetic hyperactivity and oxidative stress cause cardiovascular diseases and death. Sleep disturbances accompanied by the chronic inflammatory process increase cardiovascular risk. The proposed cause and effect relationship is presented in Figure 2.

Overall, on the basis of the results of the current review, we speculate that environmental factors and genetic vulnerability to stress and anxiety may constitute the origin of the vicious cycle. Subsequently, the central nervous system is activated in response to chronic stress, affecting neurotransmission and hormonal regulation. Increased autonomic nervous system tone influences sleep architecture, leading to arousals and subsequent RMMA events. Sustained dysregulation and sleep reduction promote the production of free radicals, sympathetic activity, and subsequently, endothelial dysfunction and its consequences: heart rate variability, blood pressure fluctuations and metabolic disturbances. These may constitute risk factors for cardiovascular and metabolic diseases in the future: cardiac arrythmias, hypertension, coronary artery disease, insulin resistance or diabetes. The potential effect on general health condition may also include risk of obesity and metabolic syndrome, so-called civilization diseases. This component of a positive feedback loop accelerates CV disease development. Taking into consideration this domino effect, this is an interesting topic for new multidisciplinary approaches.

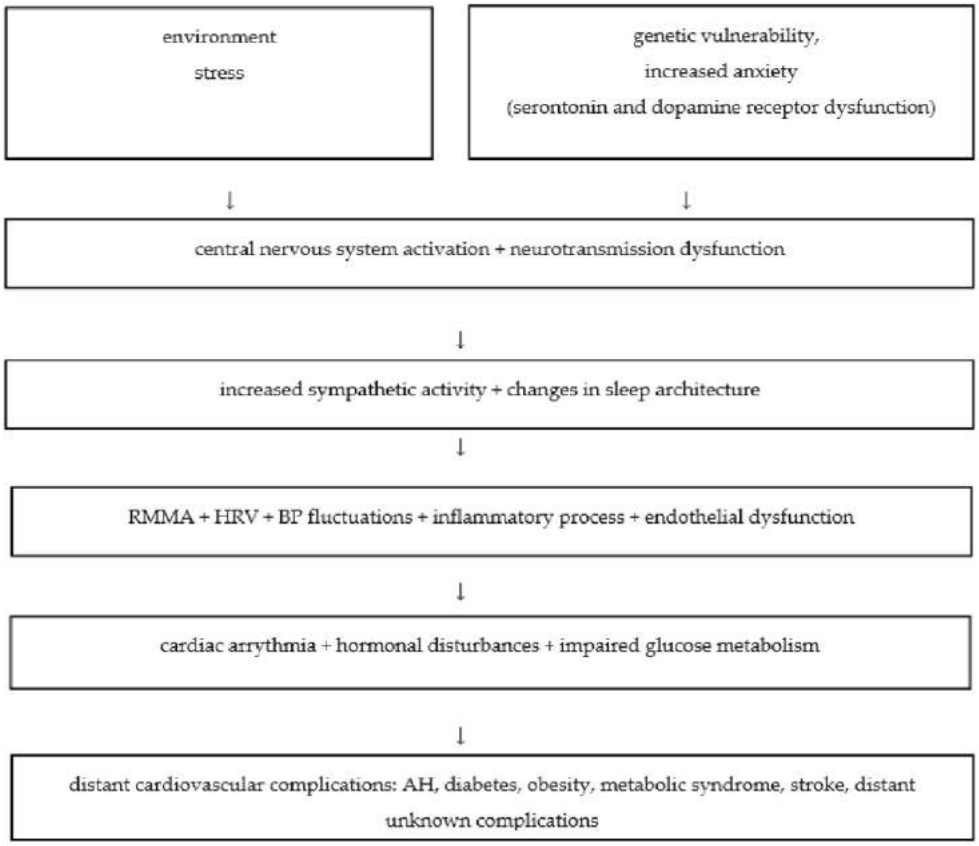

Figure 2. A possible cause-and-effect diagram of local and overall cardiovascular consequences of sleep bruxism. RMMA, rhythmic masticatory muscles activity; HRV, heart rate variability; BP, blood pressure; AH, arterial hypertension.

According to the PICO question, the broadly translated findings of the current review indicate that sleep bruxism can be considered as a predisposing condition to increased cardiovascular risk. Ideally, these findings should be replicated in a study investigating cardiovascular risk with validated scoring systems, e.g., the SCORE scale or The Framingham Risk Score.

A challenging problem which arises in the domain of sleep bruxism is its treatment, due to its multifactorial etiology and insufficiently determined consequences. A large number of alternative approaches have been developed over the last two decades to manage sleep bruxism: physio- and psychotherapy [51], oral appliances [52,53], CPAP [54], sleep hygiene [55], injections of botulinum toxin or medicaments [6]. However, we acknowledge that there are still considerable discussions among researchers about possible therapeutic paths in sleep bruxism. Several studies have been addressed on the clinical effectiveness of pharmacotherapy, some focusing on beta-blockers or dopamine agents, others on antidepressants. As we have presented in the current review, Huynh et al. [28] evaluated the impact of two sympatholytic medications: propranolol, a nonselective adrenergic β-blocker and clonidine, a selective α2-agonist, indicating that only clonidine influenced sympathetic tone and reduced the sleep bruxism index. Nonetheless, small sample size and morning symptomatic hypotension were apparent and serious study limitations. A recent study by Wieckiewicz et al. [56] concluded that opipramol, an atypical tricyclic antidepressant, reduced the amount of SB events (decreased BEI) in 78.95% of severe bruxers. Although the results appear promising, they suffer from study limitations, e.g., lack of control group,

small study sample and lack of longitudinal observation to estimate the side-effects of the applied pharmacotherapy. The possibility of severe cardiovascular implications of sleep bruxism warrants further investigation of targeted therapies.

Collectively, a number of proposed recommendations for future research and clinical approaches are given in Table 3.

Table 3. Practice points and research agenda proposed by authors.

No.	Practice Points	Future Research
1	Prior publications have suggested the role of increased sympathetic activity in sleep bruxism and its link with cardiovascular implications.	Further research is certainly required to determine distant effects of sleep bruxism on cardiovascular system and general health.
2	Studies on the relationship between SB and most common sleep-related disorders are well documented; for example, the association between sleep bruxism and obstructive sleep apnea or insomnia.	Future studies should aim to investigate the association between SB and civilization diseases: obesity, diabetes and hypertension.
3	A number of authors have documented CV implications in SB subjects as heart rate variability or blood pressure fluctuations.	Future studies should aim to replicate results in a larger population.
4	The existing literature suggests an association between SB intensity and increased CV risk.	Therefore, future research should be conducted in respect to standards and guidelines for clinical trials to obtain statistical power.
5	A more comprehensive description of increased sympathetic tone in SB assumes that genetic vulnerability and exposure to stress induces a cascade of reactions in the central and autonomic nervous systems with broad implications for overall health.	The sleep and bruxism data should be investigated with level 1 polysomnography, supplemented with audio and video recordings to avoid overestimation of bruxism events.
6	Cardiovascular implications of sleep bruxism have rarely been studied directly.	We propose that SB events should be evaluated according to the criteria of the American Academy of Sleep Medicine.
7	Previous studies on this subject cannot be considered as conclusive because of lack in statistical power and limitations.	The possibility of the cardiovascular implications of sleep bruxism warrants further longitudinal investigation.

SB, sleep bruxism; CV, cardiovascular.

Overall, the results of the current systematic review strongly suggest an association between sleep bruxism and its cardiovascular implications. Evidence synthesis demonstrated a reliable pathomechanism linking SB and sympathetic hyperactivity, and subsequently, potential increased CV risk in sleep bruxers. The main concern about the findings of the present research were the limitations of the presented studies. Most studies have relied on a small sample size and observational design. Moreover, the heterogeneity of the discussed papers in terms of studied population, study design, polysomnographic study type, SB diagnostic criteria and, last but not least, aim of the study foreclose a more profound synthesis of investigated issue. Although the results of the aforementioned publications are inconclusive, further attempts could prove quite beneficial not only for oral, but also the general health of sleep bruxers.

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9. STRESZCZENIE

Bruksizm senny to jedno z najczęstszych zaburzeń snu- to aktywność mięśni żwaczy w trakcie snu, która polega na zgrzytaniu zębami lub zaciskaniu ich. W konsekwencji, głównymi objawami bruksizmu sennego są starcie powierzchni zębów, ubytki klinowe szkliwa, uszkodzenie błony śluzowej policzków i języka, ból i uczucie napięcia w obrębie twarzoczaszki i głowy oraz silne bóle szyi i obręczy barkowej.

W etiopatogenezie bruksizmu sennego główną rolę odgrywa wzmożona aktywność autonomicznego układu współczulnego związana z nieprawidłową funkcją neuroprzekaźników w ośrodkowym układzie nerwowym oraz genetycznymi uwarunkowaniami funkcji receptorów serotoniny i dopaminy. Ponadto, środowiskowe narażenie na stres sprzyja wzmożonemu napięciu współczulnemu, co w konsekwencji doprowadza do mikrowzbudzeń ze snu, nasilenia epizodów bruksizmu i szeregu konsekwencji sercowo- naczyniowych: wzrostu akcji serca i zwyżki ciśnienia krwi, rozwoju procesu zapalnego oraz zaburzenia metabolizmu glukozy, co może prowadzić do dalszego rozwoju chorób układu krążenia.

W literaturze istnieje szereg doniesień dotyczących związku zaburzeń snu takich jak bezdech senny czy bezsenność ze zwiększonym ryzykiem sercowo- naczyniowym i licznymi chorobami układu krążenia. Pomimo, że zaburzenia homeostazy autonomicznego układu nerwowego zostały powiązane z bruksizmem sennym, dotychczas brak w literaturze jednoznacznych publikacji syntetyzujących wiedzę w tym temacie w kontekście wpływu na układ krążenia. Z uwagi, że choroby układu krążenia są główną przyczyną umieralności w krajach wysokorozwiniętych, w tym w Polsce, dokonanie próby oceny wpływu bruksizmu sennego na wybrane czynniki ryzyka sercowo- naczyniowego zostało nadrzędnym celem niniejszej pracy doktorskiej.

W praktyce klinicznej dokładna ocena czynników ryzyka sercowo- naczyniowego u pacjenta ma kluczowe znaczenie, ponieważ pozwala oszacować z dużym prawdopodobieństwem, czy w ciągu najbliższych 10 lat wystąpią groźne powikłania chorób sercowo- naczyniowych, w tym zgon. W tym celu wykonuje się szereg badań: laboratoryjnych, czynnościowych oraz z zastosowaniem narzędzi diagnostycznych np. karty ryzyka SCORE. Pomimo, że zachorowalność na choroby układu krążenia wzrasta z wiekiem, profilaktyka i wczesne wykrycie czynników ryzyka sercowo- naczyniowego są kluczowe by zredukować ryzyko niepożądanych zdarzeń poprzez zastosowanie działań z zakresu prewencji pierwotnej i wtórnej.

Do klasycznych i dobrze poznanych czynników ryzyka sercowo- naczyniowego możemy zaliczyć m.in. nadciśnienie tętnicze, wiek (powyżej 55 r.ż. u mężczyzn, 65. r.ż. u kobiet), płeć, palenie tytoniu, nieprawidłowe żywienie, zaburzenia lipidowe, nadwaga lub otyłość, dodatni wywiad rodzinny w kierunku chorób układu krążenia, choroby współistniejące np. cukrzyca i niewydolność nerek, podwyższony poziom białka C- reaktywnego (CRP). Czynniki te możemy podzielić na podlegające oraz nie podlegające modyfikacji. Ponadto, istnieje szereg dowodów naukowych oraz przesłanek klinicznych wskazujących, że również inne czynniki wpływają w sposób niezależny na wzrost ryzyka sercowo- naczyniowego (np. czynniki psychospołeczne, stres, depresja oraz zaburzenia snu) lub modulują już istniejące ryzyko (markery biochemiczne takie jak fibrynogen, kwas moczowy, homocysteina, fosfolipaza lipoproteinowa A2 i apolipoproteiny a także uwapnienie tętnic wieńcowych lub obecność blaszek miażdżycowych w tętnicach szyjnych oceniane za pomocą tomografii komputerowej lub ultrasonografii).

W cyklu prac składających się na niniejszą rozprawę doktorską w 3 pierwszych pracach oryginalnych oceniłam wpływ bruksizmu sennego na wybrane czynniki ryzyka sercowo-naczyniowego, w tym na markery zapalne takie jak CRP i fibrynogen, wartości glikemii i wskaźnik insulinooporności HOMA-IR, wartości ciśnienia tętniczego ocenianego metodą ABPM a także dokonałam oceny związku wybranych zaburzeń oddychania podczas snu z epizodami bruksizmu. Celem dokonania syntezy dotychczasowych doniesień w tej dziedzinie opracowałam przegląd systematyczny dostępnej literatury uwzględniając szerokie spektrum implikacji sercowo- naczyniowych bruksizmu. W pierwszej pracy z cyklu publikacji wykazano, że u pacjentów z bruksizmem sennym występuje szereg zaburzeń metabolicznych, hormonalnych oraz aktywny proces zapalny najprawdopodobniej w przebiegu nasilonego stresu aktywującego układ współczulny. Wyniki drugiej publikacji potwierdziły związek bruksizmu sennego z chrapaniem oraz przypuszczalnie hipoksją u pacjentów bez rozpoznanego bezdechu sennego. Ostatnia praca oryginalna wchodząca w skład rozprawy zademonstrowała wyższą zmienność skurczowego ciśnienia tętniczego w trakcie nocy związaną z epizodami bruksizmu u pacjentów bez rozpoznanego nadciśnienia tętniczego. Wyniki tej pracy sugerują zwiększone ryzyko rozwoju nadciśnienia tętniczego u pacjentów z bruksizmem sennym.

Podsumowując, uzyskane w toku pracy doktorskiej wyniki pozwalają zidentyfikować możliwe sercowo- naczyniowe implikacje kliniczne bruksizmu sennego, skłaniają do dokładnej oceny ryzyka sercowo- naczyniowego w tej grupie pacjentów oraz dalszych badań w tym obszarze.

10. SUMMARY

Sleep bruxism is considered as one of the most common sleep disorders. It is jaw muscles activity during sleep and can be described as mandible clenching or tooth grinding. Clinical symptoms of sleep bruxism are as follow: tooth wear, enamel erosion, injury to the inner surface of the cheeks, orofacial pain and neck and shoulder pain.

Increased sympathetic activity related to neurotransmitters dysfunction in central nervous system and serotonin and dopamine receptors genetics is considered to play a crucial role in etiopathogenesis of sleep bruxism. Moreover, environmental stress exposure induces increased sympathetic tone, microarousals and bruxism episodes with number of cardiovascular consequences: increased heart rate, hypertension, inflammatory process, and glucose metabolism dysfunction with cardiovascular disorders in the end.

There exist a considerable body of literature on relationship between sleep- related disorders as obstructive sleep apnea or insomnia with increased cardiovascular risk and circulatory system disorders. However, the relationship between sleep bruxism and autonomic nervous system dysfunction and its cardiovascular implications has rarely been studied directly. In Poland and other highly developed countries circulatory system disorders are the most common cause of dead. For this study, it was of interest to investigate the impact of sleep bruxism on selected factors of cardiovascular risk.

Accurate clinical assessment of individual's cardiovascular risk is crucial for calculate an estimate for 10-year cardiovascular risk, including risk of death. We first identify risk factors, based on the history, physical examination, laboratory tests and validated scales, e.g., SCORE. Even though cardiovascular diseases morbidity increases with age, early prophylaxis and detection of cardiovascular risk factors play a crucial role in primary and secondary prevention.

Classical modifiable and nonmodifiable risk factors for increased cardiovascular risk include high blood pressure, age (above 55 y.o. in men, 65 y.o. in women), gender, tobacco smoking, hypercholesterolemia, obesity, family history of cardiovascular disease, diabetes mellitus, renal disease, or inflammatory process with elevated C- reactive protein (CRP). Over time, the literature strongly suggests that there are many alternative risk factors influencing independently cardiovascular risk (e.g., psychosocial factors, stress, depression, and sleep disorders) or modulating it (biomarkers as follows: fibrinogen, uric acid, homocysteine, lipoprotein associated phospholipase A2, apolipoproteins but also coronary arteries

calcification or atherosclerotic plaques in carotid arteries diagnosed by computer tomography or ultrasonography).

In my doctoral dissertation, in 3 original papers I have assessed the impact of sleep bruxism on several cardiovascular risk factors including inflammatory markers (CRP and fibrinogen), glycemia and index of insulin resistance (HOMA- IR), blood pressure measured with ABPM and the relationship between selected respiratory and sleep bruxism events. Subsequently, to summarize the information about cardiovascular implications of sleep bruxism, systematic review with narrative summary was performed. The results demonstrated in first research paper indicated that patients with sleep bruxism had inflammatory, metabolic, and hormonal disturbances probably because of stress and increased sympathetic activity. In the second original paper of this dissertation provided evidence for the relationship between sleep bruxism and simple snoring, therefore hypoxia in patients without obstructive sleep apnea. The last original paper revealed that increased systolic blood pressure variability during nighttime was associated with sleep bruxism in normotensive patients. These findings cast a new light on potential risk of hypertension in patients with sleep bruxism.

The results of this doctoral study found support for the existence of cardiovascular implications of sleep bruxism. Current findings strongly suggest that cardiovascular risk assessment could prove quite beneficial for sleep bruxers. This provides a good starting point for further research.

11. ZGODA KOMISJI BIOETYCZNEJ

KOMISJA BIOETYCZNA
przy
Uniwersytecie Medycznym
we Wrocławiu
ul. Pasteura 1; 50-367 WROCŁAW

OPINIA KOMISJI BIOETYCZNEJ Nr KB – 195/2017

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 78/XV R/2014 z dnia 26 listopada 2014 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 28 z 1997 r. poz. 152 z późniejszymi zmianami) w składzie:

prof. dr hab. Maciej Bagłaj (chirurgia, pediatria)
prof. dr hab. Karol Bal (filozofia)
dr hab. Jacek Daroszewski (endokrynologia, diabetologia)
prof. dr hab. Krzysztof Grabowski (chirurgia)
dr Henryk Kaczkowski (chirurgia szczękowa, chirurgia stomatologiczna)
mgr Irena Knabel-Krzyszowska (farmacja)
prof. dr hab. Jerzy Liebhart (choroby wewnętrzne, alergologia)
ks. dr hab. Piotr Mrzygłód (duchowny)
mgr Luiza Müller (prawo)
prof. dr hab. Krystyna Orzechowska-Juzwenko (farmakologia kliniczna, choroby wewnętrzne)
prof. dr hab. Zbigniew Rudkowski (pediatria)
dr hab. Sławomir Sidorowicz (psychiatria)
Danuta Tarkowska (położnictwo)
dr hab. Andrzej Wojnar (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)

pod przewodnictwem
prof. dr hab. Jana Kornafela (ginekologia i położnictwo, onkologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z projektem badawczym pt.

„Ocena jakości snu, funkcji śródbłonka naczyniowego, ryzyka sercowo-naczyniowego, czynności tarczycy, funkcji mięśni narządu żucia oraz stanu psychoemocjonalnego u pacjentów z bruksizmem"

zgłoszonym przez **dr Heleny Martynowicz** zatrudnioną w Katedrze i Klinice Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii Klinicznej Uniwersytetu Medycznego we Wrocławiu oraz złożonymi wraz z wnioskiem dokumentami, w tajnym głosowaniu postanowiła wyrazić zgodę na przeprowadzenie badania w Katedrze i Klinice Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii Klinicznej UM **pod warunkiem zachowania anonimowości uzyskanych danych.**

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu

Opinia powyższa dotyczy: projektów badawczych realizowanych poza działalnością statutową

Wrocław, dnia 26 kwietnia 2017 r.

BW

Wrocław, dn. 21.08.2021

dr hab. n. med. Helena Martynowicz, prof. UMW

Katedra i Klinika Chorób Wewnętrznych, Zawodowych,
Nadciśnienia Tętniczego i Onkologii Klinicznej
Uniwersytetu Medycznego we Wrocławiu
ul. Borowska 213
55- 556 Wrocław

Zaświadczenie

Zaświadczam, że doktorantka Monika Michałek- Zrąbkowska samodzielnie realizowała projekt badawczy dotyczący badań ujętych w rozprawie doktorskiej, a będący częścią badania „Ocena jakości snu, funkcji śródbłonka naczyniowego, ryzyka sercowo-naczyniowego, czynności tarczycy, funkcji mięśni narządu żucia oraz stanu psychoemocjonalnego u pacjentów z bruksizmem". Doktorantka przestrzegała zachowania zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, będąc pod stałym nadzorem dr hab. n. med. Heleny Martynowicz.

Zaświadczenie dotyczy zgody Komisji Bioetycznej przy Uniwersytecie Medycznym we Wrocławiu nr KB 195/2017 dot. projektu badawczego pt. „Ocena jakości snu, funkcji śródbłonka naczyniowego, ryzyka sercowo- naczyniowego, czynności tarczycy, funkcji mięśni narządu żucia oraz stanu psychoemocjonalnego u pacjentów z bruksizmem", za którego realizację odpowiadała dr hab. n.med. Helena Martynowicz.

dr hab. n. med. Helena Martynowicz, prof. UMW
specjalista chorób wewnętrznych
HIPERTENSJOLOG
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