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ROZPRAWA DOKTORSKA

KOMPLEKSOWA OCENA ELEKTROKARDIOGRAFICZNYCH PARAMETRÓW OKRESU REPOLARYZACJI ORAZ DOTYCZĄCYCH ZAŁAMKA P U DOROSŁYCH Z NADWAGĄ I OTYŁOŚCIĄ I ICH POWIĄZANIA Z WYSTĘPOWANIEM ZABURZEŃ RYTMU W RÓŻNYCH GRUPACH WIEKOWYCH

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SPIS TREŚCI

WYKAZ PUBLIKACJI WŁĄCZONYCH DO ROZPRAWY

1. **Environmental factors of obesity before and after COVID-19 pandemic: a review**
   Wolińska IA, Kraik K, Poręba R, Gać P, Poręba M. *Front Public Health*. 2023;11:1213033. Published 2023 Dec 18. doi:10.3389/fpubh.2023.1213033. 100 punktów. IF(3).

2. **The effect of obesity on repolarization and other ECG parameters**
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WYKAZ SKRÓTÓW

BMI – *Body Mass Index* – wskaźnik masy ciała

WHR – *Waist to Hip Ratio* – wskaźnik biodro-talia

WHO – *World Health Organization* – Światowa Organizacja Zdrowia

GUS – Główny Urząd Statystyczny

EKG – elektrokardiogram

SCD - *Sudden Cardiac Death* - nagła śmierć sercowa

HRV – *Heart Rate Variability* – zmienność akcji serca

ns – *not statistically significant* ($p > 0,05$) – nieistotne statystycznie ($p > 0,05$)

PVB – *premature ventricular beat* – komorowe pobudzenie dodatkowe

SPB – *supraventricular premature beat* – nadkomorowe pobudzenie dodatkowe

WPROWADZENIE

Nadwaga i otyłość, charakteryzujące się nieprawidłowym i nadmiernym odkładaniem się tkanki tłuszczowej w organizmie, są obecnie jednymi z najpoważniejszych problemów opieki zdrowotnej na świecie [1]. W ramach diagnostyki nadwagi i otyłości do praktyki klinicznej wprowadzono wiele wskaźników diagnostycznych. Jednymi z najpopularniejszych są BMI i WHR. BMI – *body mass index* – wskaźnik masy ciała – jest markerem opierającym się ilorazie masy ciała i wzrostu. Badacze i lekarze stosują BMI do klasyfikacji otyłości od lat ze względu szybkość i łatwość jego użycia. Nadwagą nazywamy stan, w którym wskaźnik BMI osoby dorosłej mieści się w przedziale 25,0–29,9 kg/m^2, natomiast otyłością, gdy BMI wynosi 30 kg/m^2 lub jest większy. WHR – *waist to hip ratio* – wskaźnik talia – biodra określa rozkład tkanki tłuszczowej w organizmie.

Według Światowej Organizacji Zdrowia (WHO) w 2022 r. populacja z nadwagą i otyłością osiągnęła 2,5 miliarda osób na świecie [1]. Około 43% wszystkich dorosłych na świecie zostało sklasyfikowanych jako osoby z nadwagą, a 16% jako osoby otyłe. Wg danych Eurostat osoby z BMI >25 kg/m^2 stanowiły 53% łącznej populacji dorosłych w Unii Europejskiej, Norwegii, Serbii i Turcji. Zauważalny był również związek między wzrostem odsetka populacji z nadwagą wraz z wiekiem [2]. Według danych opublikowanych w 2021 r. przez GUS, w Polsce w 2019 r., 57% dorosłych miało nieprawidłową masę ciała. Odsetek dorosłych cierpiących na otyłość w Polsce, w ciągu ostatnich kilku lat, systematycznie wzrasta [3]. Szacuje się, że do 2025 r. w Polsce 26% kobiet i 30% mężczyzn zostanie sklasyfikowanych jako osoby otyłe.

Warto zwrócić uwagę, że nadwaga i otyłość nie są tylko problemem zdrowotnym, ale również pogarszają jakość życia. Liczne czynniki mogą zwiększać ryzyko rozwoju nadwagi i otyłości, w tym uwarunkowania genetyczne, środowiskowe, behawioralne, biologiczne, społeczne i psychogenne [4]. Na przestrzeni ostatnich lat, wśród nich, znalazł się również wirus SARS-CoV-2, wywołujący infekcję COVID-19. Pandemia COVID-19, w jej efekcie międzynarodowy lockdown, wpłynęły na codzienne czynności, w tym nawyki żywieniowe i aktywność fizyczną. Zdalna praca i edukacja zamknęły miliony ludzi w domach na wiele miesięcy. Zmiany zachowania, wywołane lockdownem w rezultacie mogły również przyczynić się do wzrostu częstości występowania nadwagi i otyłości, które są stanami związanymi z większym

ryzykiem wystąpienia choroby niedokrwiennej serca, cukrzycy typu 2 i ciężkiego przebiegu infekcji COVID-19– głównych przyczyn zgonów na świecie w 2021 wg raportu WHO [5,6].

Choroby układu krążenia należą do najważniejszych i narastających problemów opieki zdrowotnej. Związek chorób układu sercowo-naczyniowego i otyłości jest niepodważalny. Badania jednoznacznie wykazują, że nadmierna masa ciała stanowi istotny czynnik ryzyka śmiertelności i zachorowalności, w tym nagłej śmierci sercowej. Każde zwiększenie BMI o 1 kg/m^2 prowadzi do 5–7% wzrostu częstości występowania choroby niedokrwiennej serca [7]. Zależność pomiędzy zwiększoną masą ciała a występowaniem zaburzeń rymu serca jest złożona. W konsekwencji epidemii otyłości zrozumienie mechanizmów leżących u podstaw, które łączą otyłość i zaburzenia rytmu serca, stało się konieczne, zarówno w sferze wysiłków klinicznych, jak i badawczych.

Nadmierna ilość tkanki tłuszczowej wpływa na organizm poprzez dysfunkcję układu autonomicznego, przewlekły stan zapalny, zaburzenia metaboliczne, przebudowę strukturalną i czynnościową, adaptację neurohormonalną i choroby towarzyszące. Prowadzi ona w konsekwencji do zmiany geometrii lewej komory i powiększenia lewego przedsionka. Tkanka tłuszczowa, ze względu na swoją wysoką aktywność metaboliczną, wpływa na wiele szlaków biochemicznych. Odpowiedzialna jest za zwiększone wydzielanie cytokin prozapalnych, indukujących hiperglikemię i zaburzenia gospodarki węglowodanowej [8-10].

Neurohormonalna adaptacja, związana z przestrojeniem równowagi układu autonomicznego, prowadzi do zmian w zakresie zmienności rytmu serca (HRV; *heart rate variability*), oceniającej w sposób nieinwazyjny funkcję układu autonomicznego. Wpływa również na aktywację układu renina-angiotensyna-aldosteron. W konsekwencji może powadzić do przerostu lewej komory serca, zwłóknienia mięśnia sercowego, dysfunkcji rozkurczowej i skurczowej lewej komory, ważnych czynników występowania zaburzeń rytmu serca [9].

Z powodu otyłości zmiany w elektrofizjologii komórkowej serca mogą prowadzić do zmian aktywności kanałów jonowych I_{Na}, $I_{Ca,L}$ i K_{ATP}. W zwierzęcych modelach otyłości ekspresja prądu potasowego do wewnątrz wyraźnie spadała i powodowała wydłużenie potencjału czynnościowego [8].

Elektrokardiografia jest metodą diagnostyczną, wykorzystywaną do oceny występowania zaburzeń rytmu serca. Jest to technika, która służy do wizualizacji i oceny aktywności elektrycznej serca. Informacje uzyskane za jej pomocą są wykorzystywane w diagnostyce chorób układu

krążenia. Elektrokardiografia może być również przydatna w wykrywaniu bezobjawowych zaburzeń rytmu serca. Ma również zastosowanie w stratyfikacji ryzyka i monitorowaniu leczenia chorób układu krążenia. EKG wyróżnia się, spośród innych badań diagnostycznych, przede wszystkim ze względu na swoje bezpieczeństwo, nieinwazyjny charakter, łatwość i szybkość wykonania oraz niski koszt badania.

Analiza zapisu EKG pozwoliła wyodrębnić liczne markery, które odzwierciedlają różne fazy pracy serca. Wśród nich istnieje potrzeba poszukiwania nowych wskaźników, oceniających fazę depolaryzacji i repolaryzacji mięśnia sercowego, związanych ze zwiększonym ryzykiem występowania złośliwych, komorowych zaburzeń rytmu serca, które mogłyby przewidywać nagłą śmierć sercową (SCD – *Sudden Cardiac Death*) [11]. Niektóre z tych parametrów, np. odstęp QT, a zwłaszcza skorygowany odstęp QT (QTc), są powszechnie stosowane do określania ryzyka złośliwych, komorowych zaburzeń rytmu serca. Inne, nowe elektrokardiograficzne wskaźniki, takie jak Tpeak-Tend i jego pochodne, nadal nie są wykorzystywane w rutynowej diagnostyce. Wskaźnik Tpeak-Tend może być potencjalnym predyktorem śmiertelności u chorych z niewydolnością serca [12,13], niekorzystnych zdarzeń sercowych w zespole wydłużonego odstępu QT [14-16]. Zwiększona wartość wskaźnika Tpeak-Tend może być wykorzystana jako marker ryzyka komorowych zaburzeń rytmu serca u chorych z zawałem serca po przezskórnych interwencjach wieńcowych [17,18].

Nowe wskaźniki oceniające fazę repolaryzacji obejmują także dyspersję Tpeak-Tend oraz współczynniki JTpeak/JT, Tpeak-Tend/JTpeak i Tpeak/JT [19]. Wskaźnik JTpeak odzwierciedla fazę wczesnej repolaryzacji, podczas gdy wskaźnik Tpeak-Tend odzwierciedla fazę późnej repolaryzacji. Pomimo licznych badań nadal istnieje niepewność, co do zastosowania nowych wskaźników w codziennej praktyce klinicznej. Nie określono również wartości referencyjnych dla tych markerów, dlatego ważne jest dalsze prowadzenie badań w ocenie ich zastosowania w praktyce klinicznej [20].

ZAŁOŻENIA I CEL PRACY

Ze względu na konieczność poszukiwania nowych, elektrokardiograficznych wskaźników ryzyka występowania zaburzeń rytmu serca w populacji chorych z nadwagą i otyłością przeprowadzono badania, których celem była:

1. Ocena elektrokardiograficzna wskaźników okresu repolaryzacji oraz dotyczących załamka P u osób z nadwagą i otyłością i ich powiązania z występowaniem zaburzeń rytmu serca.
2. Analiza zapisów 24-godzinnych EKG wykonanych metodą Holtera z oceną czasowych parametrów zmienności rytmu serca, w tym również określenie rozpowszechnienia nadkomorowych i komorowych zaburzeń rytmu serca oraz innych zmian w EKG u chorych z nadwagą i otyłością.
3. Ocena zależności pomiędzy wybranymi czynnikami ryzyka chorób sercowo-naczyniowych a wskaźnikami okresu repolaryzacji oraz dotyczącymi załamka P.

W dwóch pracach poglądowych, wchodzących w skład niniejszej dysertacji doktorskiej, omówiono z kolei aktualny stan wiedzy na temat epidemiologii otyłości i nadwagi, przed i po pandemii COVID-19 oraz dokonano przeglądu piśmiennictwa określającego związek pomiędzy wskaźnikiem Tpeak-Tend a chorobami układu krążenia.

METODYKA

Badania będące tematem rozprawy doktorskiej były przeprowadzone w latach 2020-2023. Projekt badawczy otrzymał zgodę Komisji Bioetycznej Uniwersytetu Medycznego we Wrocławiu (nr KB 710/2020) i został przeprowadzony zgodnie z Deklaracją Helsińską.

Do badania zakwalifikowano 250 osób, mieszkańców Wrocławia i okolic. Do grupy badanej należało 181 osób (90 kobiet i 91 mężczyzn), do grupy kontrolnej 69 osób (56 kobiet i 13 mężczyzn). Średnia wieku wszystkich uczestników badania wynosiła 59,94 lat.

Dokładne kryteria włączenia i wyłączenia zaprezentowano poniżej:

- Kryteria włączenia do grupy badanej:
  - wiek > 18 roku życia,
  - BMI > 25 kg/m^2,
  - pisemna, świadoma zgoda na udział w badaniu.
- Kryteria wyłączenia:
  - wiek <18 roku życia,
  - BMI <18,5 kg/m^2,
  - uprawianie sportu wyczynowego,
  - stan po implantacji urządzenia do elektroterapii,
  - anoreksja w wywiadzie,
  - niekompletny kwestionariusz osobowy,
  - brak EKG w dokumentacji.

Charakterystykę grupy biorącej udział w badaniu przedstawiono w Tabeli 1.

Parametr	**Wszyscy badani (n = 250)**	**Otyłość (A, n = 98)**	**Nadwaga (B, n = 83)**	**Grupa kontrolna (C, n = 69)**	***p*<0,05**
Wiek (lata)	59,94 ± 13,22	61,18 ± 11,07	53,40 ± 13,70	58,83 ± 15,33	ns
Płeć (% / n)					
Męska	41,6 / 104	50,0 / 49	50,6 / 42	18,8 / 13	A vs C: 0,001
Żeńska	58,4 / 146	50,0 / 49	49,4 / 41	81,2 / 56	B vs C: 0,001
Wzrost (cm)	167,37 ± 9,76	168,14 ± 9,65	168,64 ± 10,36	164,76 ± 8,78	ns

Masa ciała (kg)	80,42 ± 17,50	95,09 ± 13,24	78,39 ± 11,10	62,02 ± 7,99	A vs B: 0,001 A vs C: 0,001 B vs C: 0,001
BMI (kg/m^2)	28,64 ± 4,99	33,62 ± 3,26	27,56 ± 1,34	22,86 ± 1,71	A vs B: 0,001 A vs C: 0,001 B vs C: 0,001
Obwód talii (cm)	95,99 ± 14,26	107,29 ± 10,16	95,29 ± 8,55	79,72 ± 7,55	A vs B: 0,001 A vs C: 0,001 B vs C: 0,001
Obwód bioder (cm)	106,60 ± 12,16	115,23 ± 7,32	104,26 ± 5,23	93,83 ± 1,14	A vs B: 0,001 A vs C: 0,001 B vs C: 0,001
WHR	0,95 ± 0,74	0,93 ± 0,08	0,91 ± 0,09	1,05 ± 1,56	ns
Nadciśnienie tętnicze (% / n)	52,8 / 132	64,3 / 63	50,6 / 42	39,1 / 27	A vs C: 0,001 B vs C: 0,048
Choroba niedokrwienna serca (% / n)	6,4 / 16	7,1 / 7	7,2 / 6	4,3 / 3	ns
Udar mózgu (% / n)	2,8 / 7	2,0 / 2	3,6 / 3	2,9 / 2	ns
Migotanie przedsionków (% / n)	8,8 / 22	8,2 / 8	12,0 / 10	5,8 / 4	ns
Zakrzepica żył głębokich (% / n)	3,6 / 9	7,1 / 7	1,2 / 1	1,4 / 1	ns
Cukrzyca typu 2 (% / n)	13,2 / 33	21,4 / 21	10,8 / 9	4,3 / 3	A vs C: 0,002
Choroba tarczycy (% / n)	16,4 / 41	16,3 / 16	13,2 / 11	20,3 / 14	ns
Nikotynizm (% / n)	13,2 / 33	9,2 / 9	15,8 / 13	15,9 / 11	ns

Tabela 1 Charakterystyka całej grupy badanej [21,22]

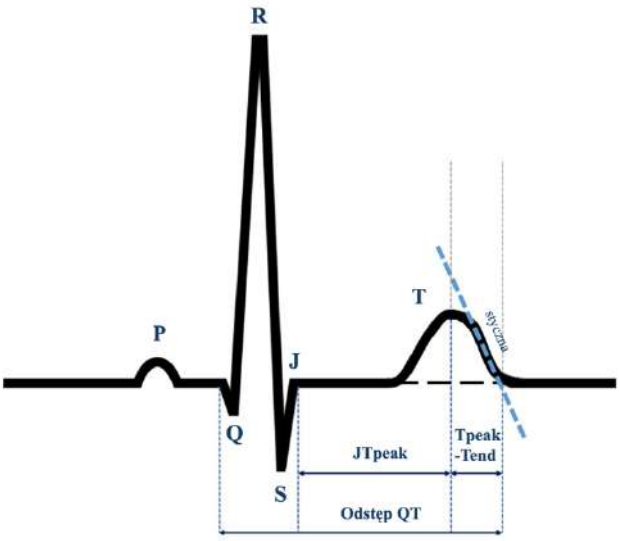
Osoby zakwalifikowane do badania otrzymały do wypełnienia kwestionariusz osobowy, obejmujący pytania dotyczące aktywności fizycznej, stosowania używek, nawyków żywieniowych, chorób oraz wywiadu rodzinnego i psychologicznego. Następnie wykonano pomiary masy ciała, wzrostu, tętna spoczynkowego i ciśnienia tętniczego. Wszyscy badani zostali poddani 12-odprowadzeniowemu badaniu EKG, jak również 24-godzinnemu badaniu EKG metodą Holtera.

Przeprowadzone badania oparte były na analizie zapisów elektrokardiograficznych oraz ocenie ankietowej, wobec czego były nieinwazyjne i jako takie nie stanowiły ryzyka zagrożenia życia lub zdrowia badanych osób. Każdy badany wyraził świadomą zgodę i w każdej chwili miał możliwość ją wycofać.

W następnym etapie badania wykonano szczegółową analizę 12-odprowadzeniowych zapisów EKG, uwzględniając, zarówno nowe, jak i standardowe wskaźniki elektrokardiograficzne

oraz analizę 24-godzinnego zapisu EKG wykonanego metodą Holtera przy użyciu oprogramowania Sentinel – Reynolds Medical. Dodatkowo przeprowadzono czasową analizę zmienności rytmu serca (HRV, *heart rate variability*).

Na rycinie 1 przedstawiono metodę pomiaru markerów okresu repolaryzacji.



Ryc. 1 – Markery okresu repolaryzacji [21]

Analiza statystyczna uzyskanych wyników została przeprowadzona za pomocą oprogramowania Statistica 13 (StatSoft Polska). Istotność statystyczną wyznaczono dla $p < 0,05$. Szczegółowa metodyka analizy statystycznej została przedstawiona w poszczególnych pracach naukowych.

Publikacje przeglądowe powstały na bazie najnowszych danych literaturowych z bazy PubMed, Embase, Cochrane Library and Google Scholar.

WYNIKI

Dokonując analizy 12-odprowadzeniowych elektrokardiogramów wykazano znamiennie większe wartości niektórych standardowych jak i nowych wskaźników elektrokardiograficznych oceniających okres repolaryzacji oraz dotyczących załamka P u osób z nadwagą i otyłością w porównaniu do grupy kontrolnej. Chorzy z otyłością w porównaniu do osób z prawidłowym wskaźnikiem masy ciała charakteryzowali się większymi wartościami czasu trwania załamka P, dyspersji załamka P, czasu trwania zespołu QRS, dyspersji odstępu QT, wskaźnika Tpeak-Tend, dyspersji wskaźnika Tpeak-Tend, wskaźnika JTpeak i wskaźnika JTpeak-JTend. Z kolei osoby z nadwagą w porównaniu do osób z prawidłowym wskaźnikiem masy ciała cechowały się większymi wartościami czasu trwania załamka P.

Przeprowadzona analiza korelacji wykazała występowanie następujących dodatnich zależności liniowych:

- dodatniej zależności pomiędzy czasem trwania załamka P i odstępu PQ a masą ciała, wskaźnikiem masy ciała, obwodem talii i bioder,
- dodatniej zależności pomiędzy dyspersją załamka P a wskaźnikiem masy ciała, obwodem talii i bioder,
- dodatniej zależności pomiędzy czasem trwania zespołu QRS a masą ciała, wskaźnikiem masy ciała i obwodem talii,
- dodatniej zależności pomiędzy wskaźnikiem Tpeak-Tend a masą ciała i obwodem talii,
- dodatniej zależności pomiędzy wskaźnikiem JTpeak a wskaźnikiem masy ciała, obwodem talii i wskaźnikiem talia-biodro,
- dodatniej zależności pomiędzy wskaźnikiem Tpeak a wskaźnikiem talia-biodro,
- dodatniej zależności pomiędzy wskaźnikiem Tpeak/JT a wskaźnikiem masy ciała i wskaźnikiem talia-biodro.

W analizie regresji wieloczynnikowej dla wskaźnika JTpeak największe znaczenie miały wskaźnik talia-biodro, wiek, cukrzyca typu 2 i palenie papierosów, a dla wskaźnika Tpeak/JT - płeć męska i wskaźnik masy ciała.

Powyższe wyniki przedstawiono w Tabelach 2-5.

Parametr	Otyłość (A, n = 98)	Nadwaga (B, n = 83)	Grupa kontrolna (C, n = 69)	$p < 0,05$
Częstość akcji serca (uderzeń/min)	66,50 ± 11,45	66,04 ± 12,10	67,90 ± 12,26	ns
Szerokość załamka P (ms)	113,12 ± 19,98	111,66 ± 17,92	102,22 ± 19,45	A, B vs. C
Dyspersja załamka P (ms)	40,08 ± 19,39	31,01 ± 21,58	30,59 ± 18,66	A vs. B, C
Odstęp PQ (ms)	177,45 ± 29,74	167,73 ± 28,92	155,58 ± 29,86	A vs. B, C B vs. C
Szerokość zespołu QRS (ms)	107,24 ± 21,34	102,47 ± 23,26	100,14 ± 13,42	A vs. C
Odstęp QT (ms)	392,66 ± 25,77	390,19 ± 40,85	385,23 ± 30,32	ns
Odstęp QTc (ms)	411,50 ± 23,43	406,95 ± 30,23	406,25 ± 21,61	ns
Dyspersja QT(ms)	39,63 ± 23,14	32,02 ± 27,95	32,06 ± 20,77	A vs. B, C
Oś QRS (°)	17,32 ± 38,36	27,05 ± 41,37	37,93 ± 42,80	ns
Wskaźnik Sokołowa LV (mm)	17,11 ± 5,15	19,77 ± 6,16	18,58 ± 6,15	ns
Wskaźnik Sokołowa RV (mm)	3,73 ± 2,23	3,32 ± 2,40	3,71 ± 2,22	ns
Tpeak-Tend (ms)	97,08 ± 23,38	95,88 ± 23,71	89,74 ± 12,88	A vs. C
Dyspersja (Tpeak-Tend) (ms)	43,29 ± 24,14	37,34 ±17,75	35,52 ± 11,03	A vs. B, C
(Tpeak-Tend)/QT	0,23 ± 0,05	0,25 ± 0,07	0,23 ± 0,03	ns
(Tpeak-Tend)/QTc	0,22 ± 0,04	0,23 ± 0,05	0,22 ± 0,03	ns
JTpeak (ms)	205,92 ± 28,04	198,77 ± 32,39	192,67 ± 34,88	A vs. C
Odstęp JT (ms)	292,82 ± 28,67	295,52 ± 36,14	292,20 ± 36,25	ns
JTpeak/JT	0,69 ± 0,07	0,67 ± 0,07	0,69 ± 0,05	ns
(Tpeak-Tend)/JTpeak	0,46 ± 0,16	0,35 ± 0,21	0,45 ± 0,11	ns
Tpeak (mV)	0,39 ± 0,26	0,40 ± 0,25	0,41 ± 0,21	ns
Tpeak/JT (mV/ms)	0,00 ± 0,00	0,00 ± 0,00	0,00 ± 0,00	ns
JTpeak-JTend (ms)	99,55 ± 34,53	95,98 ± 29,64	90,72 ± 13,54	A vs. C
Dyspersja (JTpeak-JTend) (ms)	48,22 ± 37,60	44,04 ± 26,32	41,19 ± 16,33	ns

Tabela 2 Parametry rejestrowane w 12-odprowadzenionym EKG w poszczególnych podgrupach biorących udział w badaniu [21]

Parametr	Masa Ciała (kg)	BMI (kg/m^2)	Obwód talii (cm)	Obwód bioder (cm)	WHR
Częstość akcji serca (uderzeń/min)	ns	ns	ns	ns	ns
Szerokość załamka P(ms)	0,31	0,25	0,30	0,20	ns
Dyspersja załamka P (ms)	ns	0,15	0,16	0,17	ns
Odstęp PQ (ms)	0,38	0,33	0,40	0,32	ns
Szerokość zespołu QRS (ms)	0,16	0,16	0,14	ns	ns
Odstęp QT (ms)	ns	ns	ns	ns	ns
Odstęp QTc (ms)	ns	ns	ns	ns	ns
Dyspersja QT (ms)	ns	ns	ns	ns	ns

Oś QRS (°)	ns	ns	ns	ns	ns
Wskaźnik Sokołowa LV (mm)	ns	ns	ns	ns	ns
Wskaźnik Sokołowa RV (mm)	ns	ns	ns	ns	ns
Tpeak-Tend (ms)	0,16	ns	0,16	ns	ns
Dyspersja (Tpeak-Tend) (ms)	ns	ns	ns	ns	ns
(Tpeak-Tend)/QT	ns	ns	ns	ns	ns
(Tpeak-Tend)/QTc	ns	ns	ns	ns	ns
JTpeak (ms)	ns	0,15	ns	0,19	0,18
Odstęp JT (ms)	ns	ns	ns	ns	ns
JTpeak/JT	ns	ns	ns	ns	ns
(Tpeak-Tend)/JTpeak	ns	ns	ns	ns	ns
Tpeak (mV)	ns	ns	ns	ns	0,16
Tpeak/JT (mV/ms)	ns	0,15	ns	ns	0,16
JTpeak-JTend (ms)	ns	ns	ns	ns	ns
Dyspersja (JTpeak-JTend) (ms)	ns	ns	ns	ns	ns

Tabela 3 Analiza zależności liniowej dla całej grupy badanej pomiędzy markerami między masy ciała, a parametrami 12- odprowadzeniowego EKG [21]

	Wiek	**WHR**	**Cukrzyca typu 2**	**Nikotynizm**
Współczynnik regresji	0,439	17,563	13,064	6,259
Standardowy błąd średniej dla współczynnika regresji	0,163	3,032	6,081	2,803
p	<0,01	<0,001	<0,05	<0,05
p dla modelu		$p < 0,001$		

Tabela 4 Analiza modelu wieloczynnikowej regresji całej grupy badanej dla parametru JTpeak (ms) [21]

	Płeć męska	**BMI (kg/m^2)**	**β-blokery**
Współczynnik regresji	0,001	0,001	−0,001
Standardowy błąd średniej dla współczynnika regresji	0,000	0,000	0,000
p	<0,001	<0,001	<0,05
p dla modelu		$p < 0,001$	

Tabela 5 Analiza modelu wieloczynnikowej regresji krokowej wstecznej całej grupy badanej dla parametru Tpeak/JT (mV/ms) [21]

W 24-godzinnej analizie elektrokardiogramów średnia częstość rytmu serca u wszystkich badanych osób wynosiła 72,73 ± 0,55/min, minimalna częstość rytmu serca wynosiła 53,93 ± 0,50/min, a maksymalna częstość rytmu serca wynosiła 117,33 ± 1,19/min. Pełną charakterystykę analizowanych parametrów zamieszczono w Tabeli 6.

Parametr	**Otyłość (A, n = 98)**	**Nadwaga (B, n = 83)**	**Grupa kontrolna (C, n = 69)**	***p*<0,05**
Minimalna częstość akcji serca (uderzeń/min)	54,32 ± 0,65	53,52 ± 0,73	53,87 ± 1,32	ns
Maksymalna częstość akcji serca (uderzeń/min)	113,38 ± 1,71	118,20 ± 2,18	118,89 ± 2,31	ns
Średnia częstość akcji serca (uderzeń/min)	72,47 ± 0,85	72,17 ± 0,86	73,78 ± 1,19	ns
PVB (przedwczesne pobudzenie komorowe)	573,52 ± 218,17	171,18 ± 59,07	96,87 ± 23,30	A vs C: 0,030
SPB (przedwczesne pobudzenie nadkomorowe)	620,20 ± 301,46	359,19 ± 153,89	42,49 ± 6,18	A vs C: 0,042
Bradykardia	29,96 ± 18,61	33,20 ± 15,18	18,74 ± 8,51	ns
Bradykardia (uderzeń/min)	38,00 ± 4,79	38,89 ± 4,38	38,27 ± 3,85	ns
Tachykardia	35,32 ± 31,04	19,42 ± 10,90	9,88 ± 3,10	ns
Tachykardia (uderzeń/min)	147,42 ± 19,10	151,36 ± 24,00	148,16 ± 17,42	ns
VT (częstoskurcz komorowy)	0,15 ± 0,09	0,13 ± 0,10	0,03 ± 0,02	ns
SVT (częstoskurcz nadkomorowy)	1,17 ± 0,44	3,70 ± 3,21	3,76 ± 3,17	ns
AF (średnia liczba epizodów)	0,06 ± 0,04	0,41 ± 0,36	0,00 ± 0,00	ns
Rytm komorowy (średnia liczba epizodów)	0,10 ± 0,10	0,06 ± 0,05	0,01 ± 0,01	ns

Tabela 6. Parametry rejestrowane w 24-godzinnym rejestrowaniu EKG w poszczególnych podgrupach biorących udział w badaniu [22]

U chorych z otyłością w porównaniu z badanymi kontrolnymi średnia liczba przedwczesnych pobudzeń komorowych (PVB) i przedwczesnych pobudzeń nadkomorowych (SPB) była znamiennie większa.

W grupie osób ze zwiększonym wskaźnikiem masy ciała zarejestrowano więcej epizodów migotania przedsionków niż w grupie kontrolnej (w której ich ilość wynosiła 0%), jednak ta obserwacja nie wykazała istotności statystycznej. Obserwowane epizody tachykardii zatokowej również nie były znamiennie bardziej nasilone niż w grupie kontrolnej.

W przeprowadzonej czasowej analizie HRV wskaźnik mRR podczas rejestracji całodobowej i podczas aktywności dziennej był znamiennie większy u osób z nadwagą i otyłością w porównaniu do grupy kontrolnej. Pełna analiza czasowych parametrów HRV została przedstawiona w Tabeli 7.

Parametr	**Otyłość (A, n = 98)**	**Nadwaga (B, n = 83)**	**Grupa kontrolna (C, n = 69)**	***p*<0,05**
24-godzinne monitorowanie (6:00-6:00)				
mRR (ms)	815,11 ± 77,60	867,50 ± 120,08	785,49 ± 92,20	A vs C: 0,046 B vs C: 0,014
SDNN (ms)	147,10 ± 40,67	147,35 ± 58,91	159,47 ± 46,17	ns
rMSSD (ms)	42,79 ± 63,12	29,64 ± 11,89	35,77 ± 25,09	ns
SDSD (ms)	30,72 ± 42,97	21,70 ± 9,22	28,11 ± 21,78	ns
pNN50 (%)	10,59 ± 20,16	7,72 ± 7,49	7,98 ± 9,85	ns
Aktywność dzienna (6:00-22:00)				
mRR (ms)	759,95 ± 80,95	810,30 ± 109,98	726,55 ± 105,14	A vs C: 0,045 B vs C: 0,011
SDNN (ms)	113,56 ± 34,41	107,38 ± 41,11	118,22 ± 42,24	ns
rMSSD (ms)	36,86 ± 57,20	26,88 ± 11,02	31,54 ± 24,91	ns
SDSD (ms)	26,26 ± 38,80	19,62 ± 9,00	24,82 ± 22,02	ns
pNN50 (%)	8,61 ± 19,86	5,93 ± 6,32	6,20 ± 7,97	ns
Aktywność nocna (22:00-6:00)				
mRR (ms)	938,84 ± 102,87	1003,92 ± 168,56	925,27 ± 118,54	ns
SDNN (ms)	108,81 ± 44,16	101,56 ± 32,11	115,35 ± 45,24	ns
rMSSD (ms)	54,14 ± 80,10	34,82 ± 15,26	39,38 ± 30,72	ns
SDSD (ms)	36,93 ± 52,14	24,41 ± 10,78	27,88 ± 20,27	ns
pNN50 (%)	14,86 ± 22,46	11,83 ± 11,53	11,44 ± 16,67	ns

Tabela 7 Parametry analizy czasowej HRV w poszczególnych podgrupach biorących udział w badaniu [22]

mRR—Średni odstęp RR podczas rytmu zatokowego; pNN50— Odsetek odstępów NN różniących się od sąsiadujących odstępów o > 50 ms; rMSSD— Pierwiastek kwadratowy ze średniej sumy kwadratów różnic między kolejnymi odstępami NN; SDNN— Odchylenie standardowe wszystkich odstępów NN; SDSD— odchylenie standardowe różnic między sąsiadującymi przedziałami NN.

W przeprowadzonych badaniach stwierdzono występowanie następujących dodatnich zależności liniowych (Tabela 8):

- dodatnia zależność pomiędzy minimalną częstością rytmu serca a obwodem bioder,
- dodatnia zależność pomiędzy liczbą przedwczesnych pobudzeń komorowych a masą ciała,
- dodatnia zależność pomiędzy liczbą przedwczesnych pobudzeń nadkomorowych a masą ciała, wskaźnikiem masy ciała i obwodem talii.

Parametr	Masa ciała (kg)	BMI (kg/m2)	Obwód talii (cm)	Obwód bioder (cm)	WHR
Minimalna częstość akcji serca (uderzeń/min)	ns	ns	ns	0,30 (p=0,010)	ns
Maksymalna częstość akcji serca (uderzeń/min)	ns	ns	ns	ns	ns
Średnia częstość akcji serca (uderzeń/min)	ns	ns	ns	ns	ns
PVB (przedwczesne pobudzenie komorowe)	0,14 (p=0,028)	ns	ns	ns	ns
SPB (przedwczesne pobudzenie nadkomorowe)	0,14 (p=0,028)	0,13 (p=0,043)	0,14 (p=0,031)	ns	ns
Bradykardia	ns	ns	ns	ns	ns
Bradykardia (uderzeń/min)	ns	ns	ns	ns	ns
Tachykardia	ns	ns	ns	ns	ns
Tachykardia (uderzeń/min)	ns	ns	ns	ns	ns
VT (częstoskurcz komorowy)	ns	ns	ns	ns	ns
SVT (częstoskurcz nadkomorowy)	ns	ns	ns	ns	ns
AF (średnia liczba epizodów)	ns	ns	ns	ns	ns
Rytm komorowy (średnia liczba epizodów)	ns	ns	ns	ns	ns

Tabela 8. Analiza zależności liniowej dla całej grupy badanej pomiędzy markerami między masy ciała a parametrami 24-godzinnego monitorowania EKG [22].

W analizie regresji wieloczynnikowej, w odniesieniu do liczby przedwczesnych pobudzeń nadkomorowych, jako zmiennej zależnej, zaobserwowano, że BMI (szczególnie otyłość 1 stopnia), cukrzyca typu 2 i choroba tarczycy wykazywały najwyższe współczynniki regresji, Tabela 9.

Model dla SPB			
	BMI (kg/m^2)	**Cukrzyca typu 2**	**Choroba tarczycy**
Współczynnik regresji	82,292	791,956	918,975
Standardowy błąd średniej dla współczynnika regresji	39,721	384,861	352,687
p	0,037	0,040	< 0,025
p dla modelu		0,001	

Tabela 9 Analiza modelu wieloczynnikowej regresji krokowej wstecznej całej grupy badanej dla parametru SPB [22]

OMÓWIENIE

Nadwaga i otyłość stają się coraz większym problemem współczesnego świata. Ze względu na liczne czynniki ryzyka, wpływające na zwiększenie masy ciała, dla dobra chorych niezbędna wydaje się współpraca różnych specjalistów w zakresie zwalczania epidemii otyłości. Lekarze powinni starać się uzyskać możliwie najlepszą wiedzę na temat częstości występowania zaburzeń rytmu serca u osób ze zwiększonym wskaźnikiem masy ciała, ponieważ ta grupa charakteryzuje się szczególnie wysokim ryzykiem niekorzystnych zdarzeń sercowo-naczyniowych.

Wyniki dostępnych badań wskazują, że u chorych z nadwagą i otyłością w zapisach elektrokardiograficznych obserwuje się częściej wydłużenie odstępu QT, odstępu QTc i dyspersji QT [23-25]. Zmiany te można powiązać ze wzrostem ryzyka sercowo-naczyniowego i zwiększoną śmiertelnością. W przeprowadzonych badaniach, analizując klasyczne wskaźniki elektrokardiograficzne, wykazano u osób otyłych znamiennie większą dyspersję odstępu QT w porównaniu do badanych z prawidłowym wskaźnikiem masy ciała. W badaniach Brashi i wsp. nie wykazano związku pomiędzy klasycznymi parametrami EKG a niepowikłaną, innymi chorobami współistniejącymi, nadwagą i otyłością. Stwierdzano jednak zwiększanie dyspersji odstępu QT wraz ze zwiększeniem wskaźnika masy ciała [26].

Wpływ nadwagi i otyłości na nowe wskaźniki elektrokardiograficzne jest wciąż tematem prac naukowych. Wyniki prowadzonych badań są często niejednoznaczne. W dostępnych publikacjach naukowych możemy znaleźć dowody na zwiększanie wartości parametrów Tpeak-Tend, Tpeak-Tend/QT, Tpeak-Tend/QTc wraz ze zwiększaniem wskaźnika masy ciała [27,28]. Badania prowadzone do dysertacji doktorskiej częściowo potwierdzają te obserwacje. Wykazywano w nich bowiem znamiennie większe wartości wskaźnika Tpeak-Tend, jego dyspersji oraz wskaźnika JTpeak-JTend w grupie osób z otyłością w porównaniu do grupy kontrolnej. Badania Brashi i wsp. nie wykazały, aby występowały zależności pomiędzy tymi parametrami a wskaźnikiem masy ciała. Analiza przeprowadzona przez Al-Mosawi i wsp. wykazała występowanie zależności pomiędzy wskaźnikiem Tpeak-Tend i wskaźnikiem masy ciała [29].

W przeprowadzonych do dysertacji badaniach stwierdzono również znamienne różnice w zakresie czasu trwania załamka P, dyspersji załamka P i czasu trwania zespołu QRS, których wartości były znamiennie większe u osób otyłych w porównaniu do badanych z grupy kontrolnej. Wyniki te są zgodne z wynikami badań innych badaczy. W całodobowej rejestracji EKG metodą

Holtera, u chorych z otyłością, stwierdzono znamiennie większą liczbę pobudzeń przedwczesnych nadkomorowych i przedwczesnych pobudzeń komorowych, w porównaniu do osób z grupy kontrolnej. W badaniach innych autorów, poza większą liczbą przedwczesnych pobudzeń nadkomorowych i przedwczesnych pobudzeń komorowych, w grupie chorych z otyłością, stwierdzano także większą liczbę incydentów tachykardii zatokowej i bradykardii zatokowej.

Z kolei w innych badaniach, u osób z otyłością 3 stopnia, nie stwierdzono zwiększonego ryzyka występowania zaburzeń rytmu serca, w porównaniu do osób z prawidłowym wskaźnikiem masy ciała. Wykazywano jednak w tej grupie chorych zmienioną równowagę autonomiczną w oparciu o przeprowadzoną analizę zmienności rytmu serca (HRV; *heart rate variability*) [32]. W części badań wykazywano związek pomiędzy zwiększoną częstością rytmu serca a niepowikłaną otyłością bądź otyłością współistniejącą z cukrzycą typu 2 [33]. Obserwacja ta nie potwierdziła się w badaniach prowadzonych do dysertacji doktorskiej. Jedną z możliwych przyczyn braku występowania takiej zależności może być mała liczba badanych chorych z otyłością 2 i 3 stopnia, a także stosowanie, przez część badanej populacji, leków beta-adrenolitycznych, co mogło mieć wpływ na częstość rytmu serca i występowanie zaburzeń rytmu serca. W ocenie parametrów czasowych zmienności rytmu serca u osób z nadwagą i otyłością wykazano zwiększoną wartość wskaźnika mRR w trakcie całodobowej rejestracji oraz podczas dziennej aktywności w porównaniu do grupy kontrolnej. W badaniach innych autorów stwierdzano ujemną zależność pomiędzy zmiennością rytmu serca i masą ciała, co może wskazywać na dysfunkcję układu autonomicznego u osób z otyłością [34-36].

Przeprowadzone badania posiadają pewne ograniczenia. Ze względu na jednorodność etniczną badanych osób, wyników badań nie można odnosić dla całej populacji na świecie. Zarówno standardowa rejestracja EKG, jak i całodobowe monitorowanie EKG metodą Holtera, wykonywane były dla każdej badanej osoby jednokrotnie, wobec czego nie możliwe było obserwowanie zmian elektrokardiograficznych w czasie. W perspektywie kolejnych, planowanych badań, wydaje się kluczowe włączenie szerokiej grupy badanych, w szczególności z otyłością 2 i 3 stopnia oraz wydłużenie czasu obserwacji chorych. Umożliwiłoby to przeprowadzenie bardziej szczegółowej analizy statystycznej i wyodrębnienie w sposób bardziej precyzyjny poszczególnych zmiennych wpływających na zapis EKG.

WNIOSKI

1. Na podstawie przeprowadzonych badań można stwierdzić, że nadwaga i otyłość mogą mieć wpływ na występowanie zmian w zapisie elektrokardiograficznym, zarówno spoczynkowym 12-odprowadzeniowym, jak i podczas całodobowej rejestracji EKG metodą Holtera.
2. Wykazano znamiennie większe wartości niektórych standardowych jak i nowych wskaźników elektrokardiograficznych oceniających okres repolaryzacji oraz dotyczących załamka P u osób z nadwagą i otyłością w porównaniu do osób z prawidłową masą ciała.
3. Podczas całodobowego monitorowania EKG metodą Holtera w grupie osób z otyłością wykazano znamiennie większą liczbę przedwczesnych pobudzeń nadkomorowych i przedwczesnych pobudzeń komorowych w porównaniu do osób o prawidłowej masie ciała. Poza tym stwierdzono, że większy wskaźnik masy ciała i większy obwód talii pozostawały w dodatniej zależności z występowaniem większej liczby przedwczesnych pobudzeń nadkomorowych.
4. Nadwaga i otyłość mogą mieć wpływ na parametry zmienności rytmu serca. W przeprowadzonych badaniach wskaźnik mRR był znamiennie większy u osób z nadwagą i otyłością w porównaniu do grupy kontrolnej.
5. Wykazano, że większe wartości wskaźnika JTpeak były powiązane z bardziej zaawansowanym wiekiem, większym wskaźnikiem talia-biodro, występowaniem cukrzycy typu 2 oraz paleniem papierosów.
6. Ze względu na występowanie zależności pomiędzy nadwagą i otyłością a stwierdzanymi zmianami w zapisach elektrokardiograficznych wskazane jest kontynuowanie dalszych badań w celu poszukiwania nowych wskaźników elektrokardiograficznych, pozwalających, w jeszcze bardziej precyzyjny sposób, dokonywać stratyfikacji ryzyka sercowo-naczyniowego.

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Environmental factors of obesity before and after COVID-19 pandemic: a review

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In past decades the prevalence of overweight and obesity had grown rapidly. There are numerous factors contributing to this unfavorable change in people's health. This review article investigates the environmental factors which may play a role in the prevalence of overweight and obesity and additionally the novel factors which appeared after the beginning of the COVID-19 pandemic, which caused the increase in BMI during the lockdown period. Most of the studies reveal that the COVID-19 pandemic and lockdown contributed to the growth of BMI in numerous countries and, eventually the prevalence of overweight and obesity increased. Studies suggest that the physical activity was decreased while sleep time and screen time were increased and the amount of food consumed increased, additionally more processed food with long shelf life was consumed. The diverse environmental factors may have an impact on obesity and overweight development taking into account policy and local school policy issues, socioeconomic status, lifestyle including physical activity, diet habits, and amongst others, more trivial causes such as uninteresting neighborhoods, lack of sense of security outside the place of residence or a long distance from shops. Still, this is the object of debate if air pollution is an environmental risk factor influencing the unfavorable trends towards increasing body weight.

KEYWORDS

obesity, overweight, COVID-19 pandemic, environmental factors, eating habits, pollution

Introduction

Nowadays, overweight and obesity are serious healthcare problems in most countries. The prevalence of overweight and obesity has been increasing globally continuously for several decades (1) and it seems that this trend will not change soon. Overweight is usually recognized when the BMI of an adult person is in the range of 25.0–29.9 while obesity is recognized when BMI is equal to 30 or it is higher. It is worth noting that the localization of adipose tissue is often overlooked in statistics. Central obesity, also known as visceral obesity may be in such cases neglected and, because of that, metabolically obese normal-weight people are not included in statistics, so the real prevalence of obesity might be higher. Also in some Asian countries the norms of weight BMI should be lower than it is accepted in Western countries (1, 2). Normal

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BMI in Asian populations is accepted as 18.0–22.9, the overweight range is 23–24.9 and obesity is when BMI is equal to or higher than 25 (2).

Prior to the COVID pandemic nearly 1 in 3 people worldwide was classified as overweight or obese (1). The number of people with too high body weight was rising rapidly. The prevalence of overweight and obesity doubled in the years 1980–2015. The rise in prevalence was most intense in the years 1992–2002. Obesity was more frequently affecting women and older people. In wealthy countries it affected mostly people with low socioeconomic status while in poor countries it affected mostly middle-aged people living in wealthy urban environments (3). Before the age of 45 women are less often obese than men but after that age women were more often obese than men. It might be linked to menopause. The main causes of obesity were identified as diet, lifestyle and socioeconomic status (4). The significant changes in mean adults' BMI in different regions of the world in the years from 1975 to 2016 according to WHO's Global Health Observatory (5) are presented in Figure 1.

Numerous factors may increase the risk of development of overweight and obesity including genetic, environmental, behavioral, biological, social and psychogenic ones (2). Among those, the most significant factors are physical activity, alcohol consumption and socioeconomic status. Moreover, the interplay of genes and environment further increases the risk of the development of overweight or obesity (6).

In late 2019 the SARS-CoV-2 virus responsible for the disease called COVID-19 was recognized in China. It spread rapidly to other countries and became a danger worldwide. As a result, on the day 11 March 2020, COVID-19 was declared a pandemic by WHO. To slow down the rate at which the virus spreads the governments of many countries declared a lockdown and encouraged people to stay at home and to keep a social distance. In most countries the lockdown had been expected to last a few weeks only, but then it was extended several times, which, eventually, enforced a change in people's habits. It affected various daily routines including eating behaviors and physical activity. In addition, remote education was introduced in public schools and remote work became more common. It is possible that this change of behaviors affected people's weight all over the world and, as a result, it could also contribute to the increase in the prevalence of overweight and obesity, which are conditions related to a higher risk of cardiovascular diseases, cancers and diabetes mellitus – the leading death causes worldwide (7, 8). Furthermore, both overweight and obesity also contribute to a more severe course of other diseases including COVID-19. Several studies confirmed that most of the patients admitted to Intensive Care Units in the pandemic era were overweight or obese and it had been found that both conditions increase the risk of respiratory failure in COVID-19 patients (9).

The goal of this study is to investigate the up-to-date knowledge on environmental risk factors of obesity and overweight, especially considering the influence of the COVID-19 pandemic.

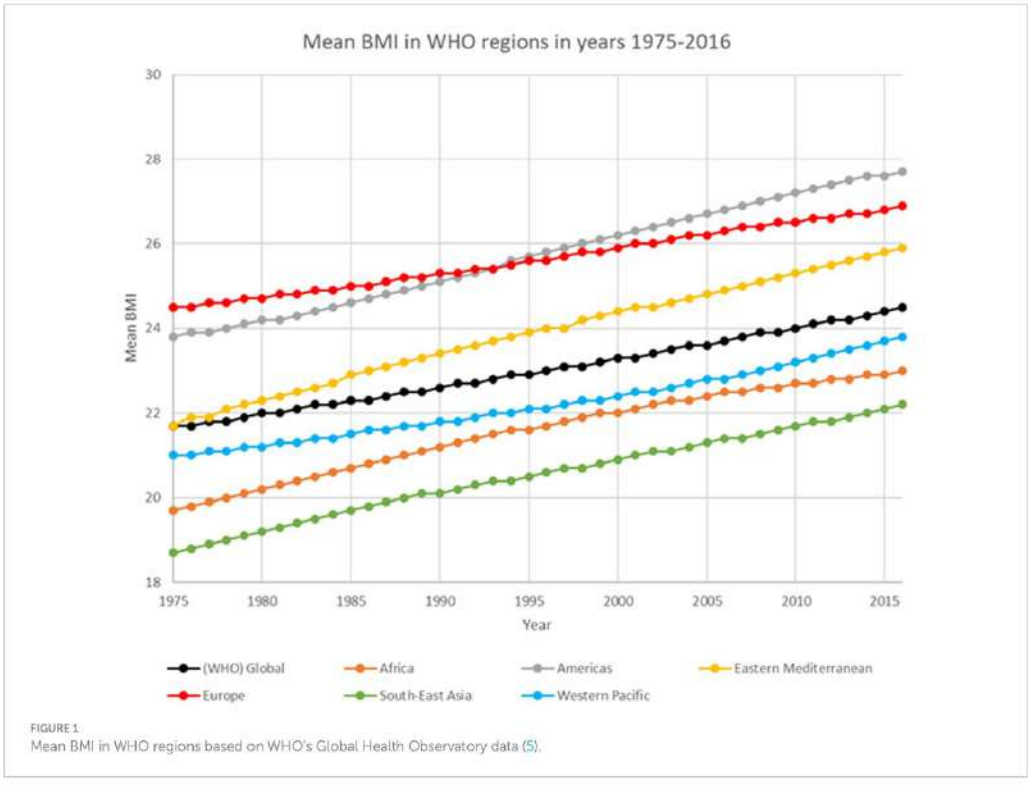

FIGURE 1
Mean BMI in WHO regions based on WHO's Global Health Observatory data (5).

Methods

The non-systematic literature review was conducted using the following databases: PubMed, Cochrane Library, Embase and Google Scholar. Articles published between 1st January 2003 and 30th June 2023 were included. Different types of articles were included: systematic reviews, meta-analyses, reviews, clinical trials, randomized controlled trials, books and documents. A special focus was placed on systematic reviews and meta-analyses published since 2018 as these articles contain up-to-date information and they have the highest level of evidence.

In the search conducted in the databases we used a combination of groups of phrases to find publications related to the subject investigated by us. The first group of phrases included: "overweight," "obesity," "body weight," "weight gain" and "food consumption." The second group of phrases included: "environmental factors," "environment," "risk factors," "epidemiology," "pandemic," "COVID-19," "SARS-CoV-2," "lockdown," "coronavirus," "air pollution," "water pollution," "pollution," "pollutants," "smoking," "e-cigarettes," "work," "shift work," "night work," "circadian rhythm," "eating habits," "transport," "rural area," "urban area," "climate," "global warming," "daylight hours," "depression," and "stress." We used the conjunction "AND" in databases search boxes to connect both groups of phrases. We connected one phrase from the first group and one or more phrases from the second group in a single search. The duplicates were removed.

In the next step articles' titles and abstracts were screened to qualify them to full-text reading. The inclusion criteria were: (a) studies related to the investigated subject, (b) English or Polish language, (c) studies published in peer-reviewed journals, (d) human studies. The exclusion criteria were: (a) animal studies, (b) abstracts without full-text article, (c) conference proceedings. We made an exception to one study (10) investigating the effect of nanocolloids in drinking water on obesity in mice due to the lack of similar studies performed on the human population.

We obtained the full text of articles that initially met our criteria and during the full text read articles that not met all inclusion criteria or met any of the exclusion criteria in the full text were removed and finally 58 articles were included in this review. Types of articles and the number of articles of a given type included in this review are presented in Table 1.

The entire process of selection of articles was presented in Figure 2.

TABLE 1 Qualitative list of articles included in the current review.

Type of the article	Number of articles of a given type
Systematic review	8
Meta-analysis	11
Original research	24
Review	13
Editorial	1
Comment	1

Environmental risk factors of obesity and overweight

General features

In the last century, various changes including the industrialization of food production (2) have been introduced, which made the world a more obesogenic place. There are some types of overweight and obesity risk factors. The prevalence of overweight and obesity is influenced by age, sex, race, and socioeconomic status (11). The environment in which people live has many components that increase the risk of developing these conditions. The environmental risk factors include geography, food availability, work environment and transport-related factors. The prevalence of obesity is higher in some regions than in others. Even regions of the same country may have different rates of obesity (12). In the United States the rate of obesity is higher in rural areas than in urban areas (12, 13), which may be an astonishing fact. However, the influencing factors include access to healthy foods and, paradoxically, fewer opportunities to be physically active (13). Moreover, it may be caused by differences in education level and income of residents of these areas and by the local infrastructure (11). Food availability is determined by how easily people can get a certain type of food. When healthy food is not easily accessible it might contribute to the growth of obesity prevalence (14). Difficult accessibility may be related to both prices and distance to the store being the source of food (11). It has been found that decreasing the distance to the shop by opening a new one in a nearer area positively affects people's diet (15). Furthermore, when unhealthy food is easily accessible, for example in a nearby fast-food restaurant, it may also increase the risk of obesity development (16).

Advertising of fast food and calorie-rich food is another factor that increases caloric intake, and it especially affects children (17). Children are a vulnerable group that can be manipulated easily into buying certain products so many advertisements are aimed at them. Advertisements may shape their needs and preferences. It results in children buying products that have unfavorable effects on their health, eating more snacks and if that repeats, what is one of the aims of advertisements, they may carry harmful dietary habits to adult life or even develop overweight or obesity (18). Moreover, they may reduce the consumption of healthy food (19).

Work environment

The development of technology caused changes in the work environment. Physical labor is less common than it was in the past and work-related screen time increased. Simultaneously, people do not need to expend that much energy during work time and eventually it is associated with increasing body weight (20).

The popularization of shift work was another change that increased the risk of developing overweight and obesity, especially abdominal obesity (2, 21, 22). The most adverse effect was observed in people working permanently on night shifts. Mechanisms proposed to explain body weight gain are circadian rhythm disorders associated with the inability to adapt to working at night and sleeping during the day and sleep deprivation (21, 22). Other mechanisms included more opportunities to eat during night shifts, hormonal disturbances and fatigue, which promotes eating more and reduces physical activity (22). Bonham et al.'s study found that the energy intake in the groups of shift workers and day workers was similar so the weight gain may

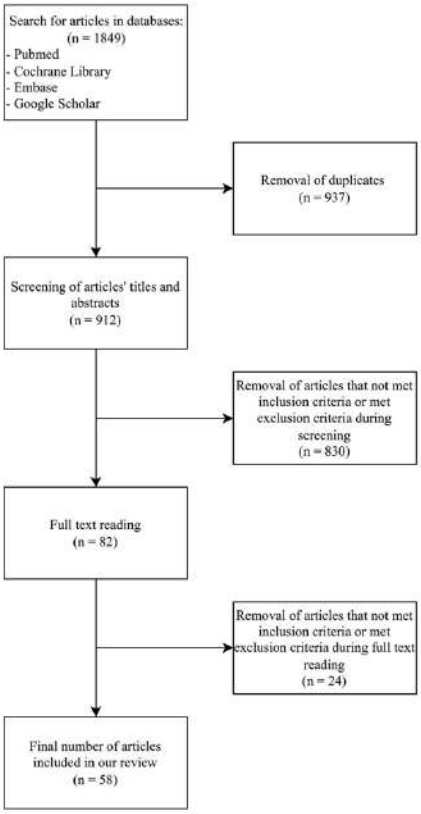

FIGURE 2
Summary of the article selection process.

be caused by meal timing, the type of consumed food and circadian rhythm disturbance (23).

Natural vs. built environment and transport

The means of transport also affect the prevalence of obesity (11). In areas in which people are more willing to walk the overweight and obesity rates are lower (24). People prefer to walk in areas with a good landscape, which have good pedestrian infrastructure including sidewalks and paths and which have parks and recreational facilities (25). However, people are more reluctant to be physically active in places that are dangerous because of high crime rates (26) and traffic-related risks (27). Because of that people living in well-kept locations with extensive pedestrian infrastructure are less likely to be overweight and obese while people living in areas that are neglected or have high crime rates or huge traffic are more likely to develop obesity. It is also known that environmental factors interact with the individual factors of a person (11). A study conducted in Nigeria found that people living in developing countries in Africa are affected by similar overweight and obesity risk factors to those in developed countries. The neighborhood which was inviting to go out was linked to lower overweight and obesity rates while poor and dangerous areas were associated with higher overweight prevalence. The presence of garbage, unpleasant smell, crime and long distance to shops were factors linked to being overweight. There were also other factors that were significant but only to males or only to females. Lack of good pedestrian infrastructure and low residential density increased the overweight rate in males. Meanwhile, heavy traffic and the lack of interesting surroundings in the neighborhood were associated with higher overweight prevalence in females. Other factors that might contribute to the occurrence of overweight in developing countries are bad transport infrastructure, lower income and the status of being married. It was estimated that environmental factors increased the risk of being overweight by 40 to 60% (27).

Leisure time

In other studies authors suggest that numerous other factors might be associated with the prevalence of obesity (28). The lack of recreational facilities may increase the chance of obesity in younger children by 68% (29). People who spend 3 h daily watching TV have two times greater prevalence of overweight than people who do not watch TV (28). These people are also more likely to be obese. Spending much time using smartphones and playing video games is even more likely to contribute to developing obesity because during these activities people often eat junk food which contains many obesogenic ingredients (28).

Smoking and eating habits

It has been found that smoking before and during pregnancy increases two times the risk of developing obesity during childhood (28). Moreover, gaining weight after smoking cessation is a very common phenomenon (30, 31). The cause of gaining weight after quitting smoking is excessive calorie intake, decreased resting metabolism rate, decreased physical activity and increased lipoprotein lipase activity (32, 33). However, smoking is harmful to the extent that the health damage from weight gain is less than the damage from continued smoking (32). Fortunately, there are interventions to prevent or reduce body weight gain, e.g., using bupropion (33), modifying diet or exercising (34). The role of e-cigarettes in terms of body weight is still unclear and requires more research on the human population. The conclusions of the current research are contradictory (35, 36). Some studies found that people using e-cigarettes had a higher prevalence of obesity than the normal-weight population. However, no significant causal link was found between e-cigarettes and obesity (36, 37).

Eating faster (38) and huge portions (39) of food are also factors that might contribute to higher calorie intake occurrence of obesity. Consumption of sweet beverages both with sugar and artificial sweeteners also increases the risk of body weight gain (28, 40). Poverty which is linked to low income and low education level also contributes to increasing obesity prevalence (41, 42). Social norms, prices of different types of food and fashion may both increase or decrease the rate of obesity occurrence (28). Families in which parents are overweight or obese have greater chances of having overweight children (43). This relationship is independent of genetic factors (28).

Climate, sun exposure, depression and stress

Changing climate and global warming also might be factors that increase the risk of obesity (44). There are reports that more energy is expended to digest colder food, and simultaneously it means, more calories are acquired by eating food at higher temperature than eating the same food at cold temperature. However, the potential effect of global warming on body weight is not large and is even less marked than the effect of owning a microwave (45).

The low number of daylight hours may also contribute to body weight gain by developing depression which increases the amount of food consumed by affected people (46). According to Luppino et al.'s meta-analysis depression increases the risk of developing obesity in both men and women due to hormonal changes (chronic activation of the hypothalamic–pituitary–adrenal axis), usage of antidepressants and lifestyle changes including the decreased amount of physical activity, switching to an unhealthy diet and eating an excessive amount of food when they feel bad (47). It is worth noting that obesity also may contribute to the development of depression. This reciprocal association has been found in many studies (47–49). However, according to Mannan et al.'s study, the risk of developing obesity due to depression is higher than the risk of developing depression due to obesity (48). Furthermore, Kanellopoulou et al.'s study found an association between depression and obesity in children (50).

Similarly, chronic stress also may contribute to excessive body weight gain. Nowadays, due to the constant rush and ambition, people are almost constantly exposed to chronic stress. Stress affects weight in many ways including overeating, eating calorie-rich food, decreasing the level of physical activity, decreasing the amount of sleep, disrupting intentional weight control, disrupting HPA axis, disrupting the reward center, changes in the gut microbiome and modifying the amount of synthesized regulatory peptides and hormones (neuropeptide Y, leptin, ghrelin). Furthermore, stigmatizing obese people increases the amount of stress they experience (51, 52). Moreover, some people may be more susceptible to stress due to individual factors such as the level of glucocorticosteroids and their sensitivity to glucocorticosteroids (53).

The impact of pollution on the prevalence of overweight and obesity

Because of the industrial development of the world the natural environment is becoming more and more degraded. The exploitation of the environment leads to climate change and the emission of pollutants, which decrease the quality of the air, water and soil. All these factors may cause adverse effects on human health.

Air pollution is one of the most important environmental problems related to human health. Air pollutants are responsible for health problems including cardiovascular system diseases, neoplastic diseases and respiratory system diseases. These three types of diseases are the leading cause of death worldwide. The most important air pollutants are carbon monoxide (CO), lead, nitrogen oxides (NOx), ground-level ozone (O3), particulate matter (PM), and sulfur oxides (SOx). The impact of air pollution depends on sex, age and which pollutant is present in the air. There are some hypothetical mechanisms in which air pollution contributes to weight gain. The pollutants may cause oxidative stress and inflammations which leads to metabolic disorders. These metabolic disorders may further contribute to the development of obesity. Pollutants also contribute to other diseases like asthma which make people less capable of physical activities and as a result abstain from exercise. People are also less likely to go outside and exercise when they know that the air is polluted and when they see that there is smog. It also decreases the amount of physical activity. It is to some extent controversial if air pollution contributes to obesity, as a similar number of studies support or deny this idea. However, it should be highlighted that fewer studies have shown that air pollution contributes to decreased risk of obesity (54). Studies investigating the impact of air pollution on body mass changes according to An et al. are presented in Figure 3.

It appears that children are more susceptible to the obesogenic impact of air pollution than adults (54). An association between PM2.5 exposure and increased adult BMI was found while no association was observed when it comes to PM10 and NO2 exposure (55). It is likely that skipping activity due to pollution is the main mechanism by which air pollution affects the obesity rate in adults (54). It is also found that air pollution may slow down the metabolism of young adults and increase the risk of obesity (56). It has been found that even prenatal exposure to pollutants in the air may affect obesity (55). Children who were affected prenatally by polycyclic aromatic hydrocarbons (PAHs), NO2, PM2.5 or benzopyrene were more likely to be obese in their childhood. Smoking is a source of PAHs so children of women who smoke during pregnancies are more likely to be overweight or obese. Traffic air pollution may affect the metabolism of newborns and lead to obesity. Children living close to places with large traffic like major streets had higher BMI than those who live further to these places (55, 56). Another possible mechanism is affecting the endocrine system by pollutants (55). It is hypothesized that high levels of NOx from traffic may cause inflammatory changes. There are studies that found no associations between low-level NOx exposure and overweight or obesity rates in children. Most of the research point that air pollution increases obesity in children (54–56). The pollutants that are most significant in childhood obesity are PM2.5, PM10, and NO2 (56). PM may also cause sleep disorders that contribute to weight gain.

Water pollution also may affect the prevalence of overweight and obesity. Both organic and inorganic water pollutants may create the nanocolloids which are contributing to obesity. It was found that exposure to nanocolloids increased the weight of mice. After the exposure there was a change in gut microbes, namely toward the status that is commonly present in obese individuals. These microbes generate then long-chain fatty acids. Also, the level of leptin increased, and the expression of adiponectin decreased. Nanocolloids are also responsible for disorders in blood lipid metabolism (10).

Overweight and obesity prevalence during the COVID-19 pandemic

Children and youths

In 2020 the hypothesis was made that lockdown might affect children's weight similarly to summer vacations because of the school closures (57). The hypothesis was based on the study which had been carried out prior to the pandemic. This study included a group of

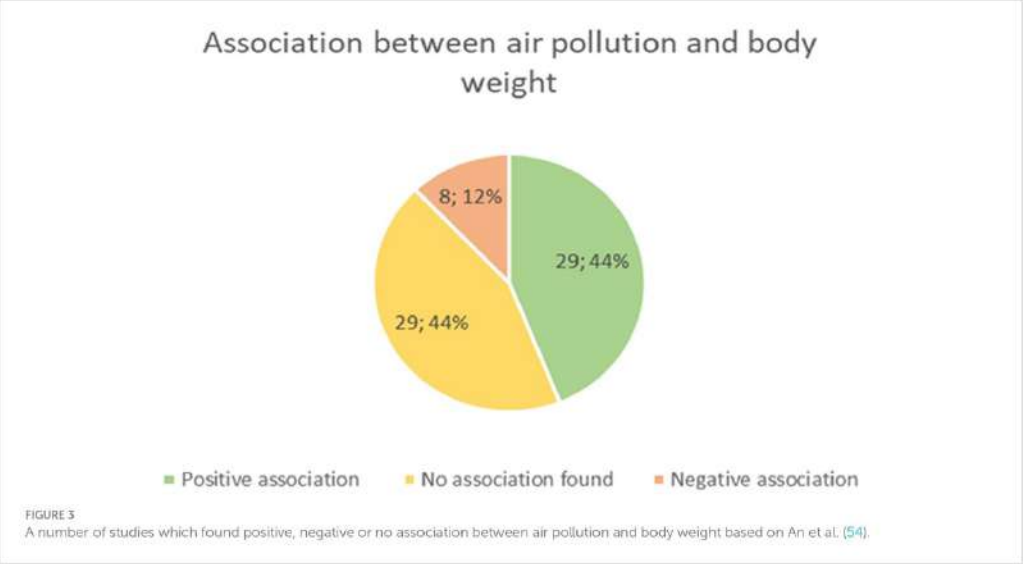

FIGURE 3
A number of studies which found positive, negative or no association between air pollution and body weight based on An et al. (54).

children whose BMI was monitored from kindergarten to second grade and it revealed that children's BMI increased faster during summer vacation compared to the school year and that prevalence of overweight and obesity increased only during summer vacations (58), Table 2.

That suggested that school attendance might reduce the impact of risk factors causing the growth of BMI. The hypothesis assumed that the pandemic would increase the screen time and consumption of snacks and shelf-stable food, which is usually highly processed and less healthy, and that social distancing will reduce physical activity in children, especially those who live in an urban environment (57).

Low physical activity and high screen time are likely to be risk factors for overweight and obesity in children (59). The low sample (41 participants) longitudinal study which was carried out in Italy based on telephone interviews with parents of obese children supports this hypothesis. The food consumption during the lockdown increased in this group: the consumption of unhealthy food (red meat, potato chips, and sweet beverages) increased significantly. The consumption of fruits also increased but its significance is not marked as clearly as the increased consumption of unhealthy food. Also, the number of meals consumed every day increased, especially in the group of males. There was also observed a change in the amount of time spent on different activities: sleeping time and screen time increased while the amount of time spent on doing sports decreased (60).

Another large sample (10,082 participants) retrospective study carried out in China based on a social media survey supports the statement that lockdown contributed to weight gain in youths. The study included youths between the age of 16 and 28 years. The average age of participants was 19.8 years. The data about BMI, the prevalence of overweight (defined in that study as BMI ≥23) and obesity (defined as BMI ≥27) and the lifestyle of youths before and during the lockdown were collected. The mean BMI increased from 21.8 before the lockdown to about 22.6 during the lockdown. The prevalence of both overweight and obesity increased. The screen time and sleeping

TABLE 2 A change of investigated parameters during school years and summer vacations based on von Hippel et al.'s study (58).

	Mean BMI	Prevalence of overweight	Prevalence of obesity
School years	↑	↓	↓
Summer vacations	↑↑↑	↑	↑

time increased. Most of the participants kept a moderate level of physical activity. However, the rest of them rather decreased their physical activity due to the lockdown. Also, the amount of time spent on transport-related actions like walking and cycling decreased during the lockdown (61).

Furthermore, the meta-analysis encompassing 12 studies (including the two mentioned before) revealed that children's body weight and BMI have increased during the lockdown. Also, the prevalence of overweight and obesity increased in studied groups during the pandemic, especially in younger children aged from 5 to 9 years. The weight increase in the group of children affected by diabetes mellitus was not statistically significant. It was stated that the COVID-19 pandemic has worsened the epidemic of childhood obesity (62).

Adults

The lockdown and COVID-19 caused unfavorable changes in adults as well. Both the COVID-19 pandemic and all the rules introduced by different countries to prevent infection like lockdown or social distancing caused the change in people's diet and activity forms. In many cases the amount of physical activity decreased while sleep time and screen time increased. Additionally, the amount of food consumed increased. People were eating more processed food with long shelf life. Because of that it was more difficult for people to

control their body weight. These changes likely contributed to body weight gain (62–66).

The study conducted in the UK revealed that due to the lockdown adults encountered many barriers which were hindering them from maintaining the proper body weight. There were 2002 participants who completed the questionnaire about their behaviors during the lockdown. Adults have eaten more snacks, especially the ones who had high BMI prior to the lockdown. People who had high BMI also were overeating more frequently and had worse diet quality than people with normal BMI. The diet quality of most participants worsened. Because of panic people bought a lot of highly processed food with long shelf lives and ate it instead of fresh, nutritious and healthy food which was less accessible during the lockdown. Levels of physical activity were also lowered, again especially in the group of people with higher BMI as many people were afraid to exercise outside. Because of that people lost control of keeping their weight within the correct values (63).

In the meta-analysis including adults, weight gain was observed in 12.8–29.9% of cases during the lockdown (64). In one of the Iraqi studies the weight increased in over 30% of people (65). On the contrary, according to Italian authors weight loss was observed in 35.7% of people while weight gain was observed only in 11.1% of people, although, the study group included only people aged 60 and more (66). In another study including only obese people 36.3% of them gained weight during lockdown (67). The lockdown had the greatest impact on those who were already overweight and obese (63). Moreover, it was also found that younger participants gained weight faster than older ones (64).

Most likely lockdown contributed to the acceleration of weight gain, growth of BMI and increased prevalence of both overweight and obesity. This fact is particularly unfavorable because excess body weight is one of the factors associated with the severe course of COVID-19 (9).

Conclusion

Most of the studies reveal that the COVID-19 pandemic and lockdown contributed to the growth of BMI in many countries and in different populations of people and it increased the prevalence of overweight and obesity. Restrictions introduced to prevent infection including lockdown and social distancing caused changes in people's diet and activity forms. The physical activity was decreased while sleep time and screen time were increased and the amount of food consumed increased. More processed food with long shelf life was consumed. However, still it should be remembered that the background of the development of obesity and overweight is complex, and it employs a variety of components such as socioeconomic problems, diet habits, lifestyle, type of work, and even the neighborhood view quality. Additionally, air pollution may be associated with obesity prevalence, especially in children, while the impact of water pollution on obesity is less studied.

Author contributions

IW and MP: conceptualization. IW and KK: resources and writing—original draft preparation. PG, RP, and MP: writing—review and editing. IW and KK: visualization. RP and MP: supervision. PG: funding acquisition. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The effect of obesity on repolarization and other ECG parameters

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Article

The Effect of Obesity on Repolarization and Other ECG Parameters

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Abstract: Background: Overweight and obesity are important risk factors in the development of cardiovascular diseases. New repolarization markers, such as the Tpeak-Tend interval and JTpeak intervals, have not yet been profoundly studied in obese patients. The study aims to analyze whether, in patients with obesity and overweight, repolarization markers, including the Tpeak-Tend interval, are prolonged and simultaneously check the frequency of other ECG pathologies in a 12-lead ECG in this group of patients. **Methods**: A study group consisted of 181 adults (90 females and 91 males) with overweight and first-class obesity. The participants completed a questionnaire, and the ECG was performed and analyzed. **Results**: When analyzing the classic markers, only QT dispersion was significantly higher in obese people. The Tpeak-Tend parameter (97.08 ms ± 23.38 vs. 89.74 ms ± 12.88, respectively), its dispersion, and JTpeak-JTend parameters were statistically significantly longer in the obese group than in the controls. There were also substantial differences in P-wave, QRS duration, and P-wave dispersion, which were the highest in obese people. Tpeak-Tend was positively correlated with body mass and waist circumference, while JTpeak was with BMI, hip circumference, and WHR. Tpeak/JT was positively correlated with WHR and BMI. In backward stepwise multiple regression analysis for JTpeak-WHR, type 2 diabetes and smoking had the highest statistical significance. **Conclusions**: Only selected repolarization markers are significantly prolonged in patients with class 1 obesity and, additionally, in this group, we identified more pathologies of P wave as well as prolonged QRS duration,

Keywords: electrocardiography; repolarization markers; obesity; overweight

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1. Introduction

Overweight and obesity are characterized by abnormal and excessive adipose tissue deposition in the body [1]. These states are important risk factors in the development of several diseases, including cardiovascular diseases, diabetes, and neoplastic diseases, which are leading causes of death worldwide [2]. They may also increase the risk of death by exacerbating symptoms of respiratory disorders [3] and infectious diseases, including COVID-19 [4,5]. Moreover, overweight and obesity often lead to lowering the quality of life as risk factors for diabetes mellitus, respiratory disorders, and musculoskeletal disease development. In connection with these risks, the governments of numerous countries allocate considerable resources to prevent and treat obesity; for example, the USA's healthcare system spends about USD 173 billion annually for that purpose only [6].

Nowadays, obesity is considered a separate disease entity, and its prevalence is common; sometimes, the term "a pandemic of obesity" is used [7]. In 2016, globally, about 13% of all adults were classified as obese, and 39% were classified as overweight [1]. The

epidemiological situation regarding these states looks very pessimistic. The number of obese people has almost tripled in the last 50 years [7]. In Poland, there is also a continuing trend of increasing incidence of obesity. In 1975, the prevalence of obesity in Polish adults was estimated to be 10.6%, which grew by about 0.3% per year until 2006. After 2006, this trend accelerated to about 0.5% per year. In 2016, the prevalence of obesity in Poland was estimated to be 25.6%. The prevalence of obesity in Polish children and adolescents also become higher over the years, and in 2016, it was estimated to be 9.1%. Similarly, the prevalence of overweight and obesity among children and adolescents increased globally—in 1975, 4.3% were classified as overweight and 0.8% as obese, while in 2016, 18.4% were classified as overweight and 6.8% as obese [8].

A standard 12-lead ECG has numerous clinical applications, including screening for cardiac abnormalities in asymptomatic individuals, diagnosing and monitoring cardiac conditions, assessing response to treatment, guiding medical decisions, and evaluating perioperative risk in surgical patients. In the context of obesity, this condition may be associated with various ECG abnormalities [9–11]. ECG findings can provide valuable information for risk stratification, identifying potential complications, and guiding management strategies in obese individuals at risk for cardiovascular disease.

The evidence of the relationship between obesity and ECG findings is inconsistent across studies, showing conflicting results [12–15]. Until now, most commonly reported ECG findings in obese patients include increased heart rate, prolonged QT interval, increased QRS duration and R wave amplitude, and altered T wave morphology [9–11].

In recent years, new repolarization markers have been proposed. The new repolarization markers can be divided into early and late repolarization indices. Early repolarization indices include the JTpeak interval, while late repolarization indices include the Tpeak-Tend interval (Tp-e) and, additionally, the JTpeak/JT, Tp-e/Jtpeak, and Tpeak/JT ratios have been introduced as playing a role in the potential use in patients after myocardial infarction [16]. There are still not many studies establishing the role and clinical significance of the novel repolarization parameters regarding a group of people with obesity and overweight. The Tpeak to Tend interval is one of the most promising novel ventricular repolarization parameters. Tp-e is potentially helpful as a predictor of mortality in patients with heart failure [17,18], as a predictor of cardiac events in long QT syndrome [19–21], and its prolongation may be used as a risk factor of ventricular arrhythmia in STEMI patients after percutaneous coronary interventions [22,23]. Current studies are inconsistent regarding whether Tp-e is HR (heart rate)-dependent [24,25]. For this reason, the Tp-e/QT ratio was proposed as an indicator independent of HR.

This study aims to analyze whether, in patients with obesity and overweight, the classic repolarization markers, as well as the novel ones, including the Tpeak-Tend interval, are prolonged. Additionally, we have attempted to determine if other ECG pathologies are present in this group of patients.

2. Materials and Methods

2.1. Study Population and Trial Design

The study was conducted at the Department of Pathophysiology of Wroclaw Medical University in 2020–2023. The Wroclaw Medical University Ethics Committee approved the study, which was conducted following Good Clinical Practice and the Declaration of Helsinki. The population of the examined patients included adult residents of Wroclaw and its vicinity. We created the initial study group of 303 people out of the adult volunteers who agreed to participate in the study and gave their written consent.

The inclusion criteria for the study group were age over 18 and BMI above 25. Adult patients with a BMI below or equal to 25 were recruited to the control group. We excluded seven patients due to the following causes: one was underage at the moment of recruitment, one person was an athlete, which could affect the ECG results, and for similar reasons, four patients with implantable devices and one person with a history of anorexia in the questionnaire. After collecting the data, we excluded 46 patients due to incomplete infor-

mation in the questionnaire or the lack of ECG. Figure 1 presents the process of selection of participants, and the characteristics of the comorbidities are presented in Tables 1 and 2.

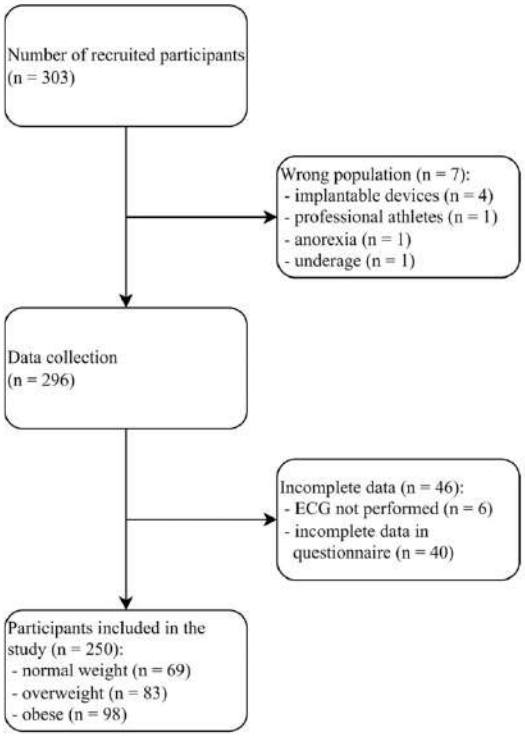

Figure 1. Flowchart presenting the selection of participants.

Table 1. Clinical characteristics of the entire study group.

Parameter	%/n or Mean ± SD
age (years)	59.94 ± 13.22
sex (%/n)	
Male	41.6/104
Female	58.4/146
height (cm)	167.37 ± 9.76
weight (kg)	80.42 ± 17.50
BMI (kg/m^2)	28.64 ± 4.99
waist circumference (cm)	95.99 ± 14.26
hip circumference (cm)	106.60 ± 12.16
WHR	0.95 ± 0.74
hypertension (%/n)	52.8/132
myocardial infarction (%/n)	6.4/16
stroke (%/n)	2.8/7
atrial fibrillation (%/n)	8.8/22
deep vein thrombosis (%/n)	3.6/9
type 2 diabetes (%/n)	13.2/33
thyroid disease (%/n)	16.4/41
smoking (%/n)	13.2/33

BMI—body mass index, WHR—waist-hip ratio.

Table 2. Clinical characteristics of the studied subgroups.

Parameter	Obesity (A, n = 98)	Overweight (B, n = 83)	Control Group (C, n = 69)	$p < 0.05$
age (years)	61.18 ± 11.07	53.40 ± 13.70	58.83 ± 15.33	ns
sex (%/n)				
Male	50.0/49	50.6/42	18.8/13	A, B vs. C
Female	50.0/49	49.4/41	81.2/56	A, B vs. C
height (cm)	168.14 ± 9.65	168.64 ± 10.36	164.76 ± 8.78	ns
weight (kg)	95.09 ± 13.24	78.39 ± 11.10	62.02 ± 7.99	A vs. B, C B vs. C
BMI (kg/m^2)	33.62 ± 3.26	27.56 ± 1.34	22.86 ± 1.71	A vs. B, C B vs. C
waist circumference (cm)	107.29 ± 10.16	95.29 ± 8.55	79.72 ± 7.55	A vs. B, C B vs. C
hip circumference (cm)	115.23 ± 7.32	104.26 ± 5.23	93.83 ± 14.14	A vs. B, C B vs. C
WHR	0.93 ± 0.08	0.91 ± 0.09	1.05 ± 1.56	ns
hypertension (%/n)	64.3/63	50.6/42	39.1/27	A, B vs. C
myocardial infarction (%/n)	7.1/7	7.2/6	4.3/3	ns
stroke (%/n)	2.0/2	3.6/3	2.9/2	ns
atrial fibrillation (%/n)	8.2/8	12.0/10	5.8/4	ns
deep vein thrombosis (%/n)	7.1/7	1.2/1	1.4/1	ns
type 2 diabetes (%/n)	21.4/21	10.8/9	4.3/3	A vs. C
thyroid disease (%/n)	16.3/16	13.2/11	20.3/14	ns
smoking (%/n)	9.2/9	15.8/13	15.9/11	ns

BMI—body mass index, WHR—waist-hip ratio, ns—not significant.

A research group of 181 adults (female/male 90/91) whose BMI exceeds 25 qualified for the study. Among this group, 83 participants were classified as overweight (BMI in the range of 25.0–29.9 kg/m^2; female/male 41/42), and 98 were classified as obese (BMI equal or higher than 30 kg/m^2; female/male 49/49). The control group consisted of 69 volunteers (females/males 56/13) with a normal BMI. The mean BMI of the obese patients was 33.6 kg/m^2, and all participants belonged to the class 1 obesity category; the mean in the group with overweight was 27.5 kg/m^2, and in the controls, 22.8 kg/m^2.

The first stage of the research was to fill out a proprietary questionnaire, including questions about physical activity, the use of stimulants, eating habits, comorbidities, and family and psychological history. In the next step, the basic anthropometric measurements were carried out: weight, height, heart rate, and blood pressure. Then, the appropriate calculations were made (including BMI and WHR). Then, a 12-lead ECG was performed. The analysis of electrocardiogram recordings included standard ECG measurements and the novel electrocardiographic markers currently used in literature.

2.2. Electrocardiographic Analysis

The standard electrocardiographic parameters such as heart rate, P-wave width, P dispersion, PQ interval, QRS complex width, QT interval, QTc interval, and QT dispersion were measured. Novel repolarization parameters measured were: Tpeak-Tend, (Tpeak-Tend) disp, (Tpeak-Tend)/QT, (Tpeak-Tend)/QTc, JTpeak, JT interval, JTpeak/JT, (Tpeak-Tend)/JTpeak, Tpeak, Tpeak/JT, JTpeak-Jtend, and (JTpeak-JTend) dispersion. The Tpeak-Tend was measured using the tangent method based on Rosenthal's method [26], as shown in Figure 2. All measured parameters are presented in Table 3.

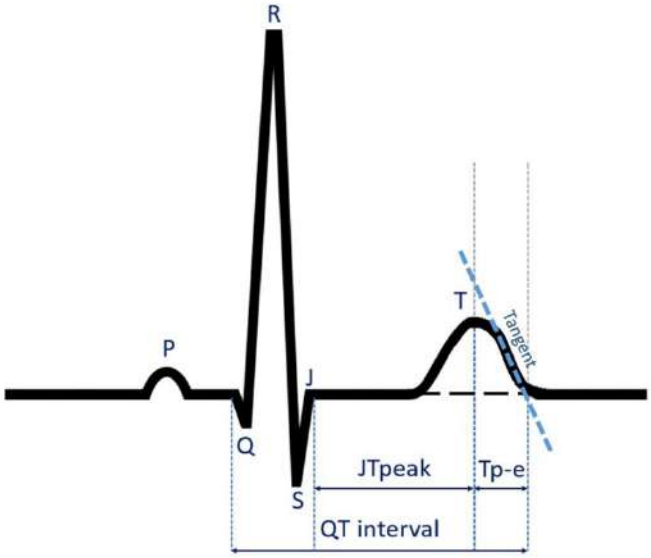

Figure 2. ECG repolarization intervals—QT, JTpeak, Tp-e.

Table 3. 12-lead ECG parameters in the entire study group.

Parameter	Mean	Confidence Interval −95.000%	Confidence Interval +95.000%	SD	Coefficients of Variability
HR (bpm)	66.73	66.25	68.21	11.87	17.79
P-wave width (ms)	109.63	107.18	112.08	19.65	17.92
P disp (ms)	34.45	31.91	36.99	20.38	59.16
PQ interval (ms)	168.19	164.37	172.01	30.68	18.24
QRS complex width (ms)	103.70	101.17	106.23	20.34	19.62
QT interval (ms)	389.79	385.72	393.86	32.69	8.39
QTc interval (ms)	408.54	405.37	411.71	25.46	6.23
QTd (ms)	35.02	31.97	38.06	24.45	69.82
QRS axis (°)	26.24	21.09	31.38	41.31	157.46
Sokolow–Lyon index LV (mm)	18.40	17.67	19.13	5.87	31.93
Sokolow–Lyon index RV (mm)	3.63	3.27	3.99	2.26	62.20
Tpeak-Tend (ms)	94.66	92.01	97.31	21.28	22.48
(Tpeak-Tend) disp (ms)	39.17	36.76	41.59	19.38	49.46
(Tpeak-Tend)/QT	0.24	0.23	0.24	0.05	23.28
(Tpeak-Tend)/QTc	0.22	0.22	0.23	0.04	19.35
JTpeak (ms)	199.89	195.92	203.85	31.83	15.92
JT interval (ms)	293.54	289.39	297.70	33.34	11.36
JTpeak/JT	0.69	0.68	0.69	0.07	10.03
(Tpeak-Tend)/JTpeak	0.42	0.40	0.44	0.17	40.93
Tpeak (mV)	0.40	0.37	0.43	0.24	61.05
Tpeak/JT (mV/ms)	0.00	0.00	0.00	0.00	62.92
JTpeak-JTend (ms)	95.93	92.37	99.49	28.57	29.79
(JTpeak-JTend) disp (ms)	44.90	41.23	48.56	29.34	65.36

HR—heart rate, P disp—P wave dispersion, QTc interval—corrected QT interval, QTd—QTd interval dispersion, Sokolow–Lyon index LV—Sokolow–Lyon criteria for left ventricular hypertrophy, Sokolow–Lyon index RV—Sokolow–Lyon criteria for right ventricular hypertrophy, (Tpeak-Tend) disp—Tpeak-Tend dispersion, (JTpeak-JTend) disp—Jtpeak-JTend dispersion.

The electrocardiography was performed using the CardioExpress SL 12 (Spacelabs Health Care Ltd., Hertford, UK) employing the Sentinel cardiology information manage-

ment system (Spacelabs Health Care 2017 (Sentinel v10.5.0.8939). The 12-lead ECG was performed with a standard chart speed of 25 mm/s and a 10 mm/mV voltage. The acquisition mode of the ECG was 10 s of 12-lead simultaneous recording. The calibration signal input was 1 mV ± 2%, and the sample frequency—1000 Hz. The filters used included an enabled network filter, 0.15 Hz isoline filter, 25 Hz muscle filter, and 100 Hz low-pass filter.

The ECG recordings included between 7 and 21 full ECG cycles, depending on the patient's heart rate. Two independent researchers, medical students and a physician blinded to the clinical status, performed the ECG measurements. Two qualified cardiologists were in the group of researchers; in any case of problematic ECG recording, the cardiologist finally accepted the results.

2.3. Statistical Analysis

The statistical package "Dell Statistica 13.1" (Dell Inc., Round Rock, TX, USA) was used for statistical analysis. The arithmetic means and standard deviations of the estimated parameters were calculated for the quantitative variables. For the 12-lead ECG parameters in the whole study group, the values of the −95.000% confidence interval, +95.000% confidence interval, and coefficients of variability were also calculated. The distribution of variables was examined using the Lilliefors test and the W-Shapiro–Wilk test. The results for qualitative (nominal) variables were expressed as percentages. In comparative analyses, three subgroups of patients were compared: obese, overweight, and normal body mass. Therefore, multiple comparison was used. ANOVA was used for further statistical analysis in the case of quantitative independent variables with a normal distribution. The homogeneity of variances was checked using Levene and Brown–Forsyth tests. In the absence of homogeneity of variances, the Kruskal–Wallis ANOVA test was used to compare the significance of mean differences in 3 subgroups. In the case of variables with a distribution other than normal, the Kruskal–Wallis ANOVA test, a non-parametric equivalent of the analysis of variance, was used for quantitative independent variables. Statistically significant differences between individual arithmetic means were then determined with the Newman–Keuls post hoc test. For independent qualitative variables, multi-way tables and the maximum likelihood chi-square test were used for further statistical analysis. Correlation and regression analyses were performed to determine the relationship between the analyzed variables. In the case of quantitative variables with a normal distribution, Pearson's r correlation coefficients were determined, and in the case of quantitative variables with a non-normal distribution, Spearman's r coefficients were determined. The parameters of the models obtained in the backward stepwise multivariable regression analysis were estimated using the least squares method. The results were statistically significant at $p < 0.05$.

3. Results

3.1. Baseline Characteristic

The mean age in the entire study group was 59.94 ± 13.22, with a BMI of 28.64 ± 4.99. In the study group, 104 patients (41.6%) were men, and 146 were female (58.4%). The mean BMI was 28.64 ± 4.99. The comorbidities in the study group are shown in Table 1. When divided into subgroups, obesity A vs. overweight B and control group C, the mean BMI for the subgroups were 33.62, 27.56, and 22.86, respectively. There were no statistically significant differences in WHR. However, significant differences were noted in waist values: 107.29, 95.29, and 79.72, respectively, and in hip circumference: 115.23, 104.26, and 93.83, respectively. In the subgroups with obesity and overweight, hypertension was significantly more commonly present even in 64.3% of patients with obesity as well as type 2 diabetes, and the highest incidence was in patients with obesity, ranging to 21.4%.

Tables 1 and 2 summarize the study group and subgroups' baseline characteristics. On analyzing the regular medication use in the whole study group, it was found that 16.4% (41 persons) of participants were on thyroid hormones, 27% (68 persons) were on beta-blockers, 14.5 (36 persons) were on dihydropyridine calcium channel blockers, and 36.4% (91 persons) declared the use of other drugs. Among them, there were patients

after stroke and myocardial infarction who declared acetylsalicylic acid, patients with paroxysmal atrial fibrillation 8% (22 patients) were on NOAC treatment, 13.2% (33 patients) were on oral medication for diabetes treatment, mainly biguanides; few patients declared other drugs such ACE inhibitors and proton-pump inhibitors.

3.2. Analysis of 12-Lead ECG Parameters in Studied Subgroups

Statistically significant differences were found in subsequent subgroups in P-wave width, with the highest values for obesity and overweight groups (A 113.12 ± 19.98 ms, B 111.66 ± 17.92 ms) as well as in the case of P-wave dispersion, which was the highest for obese people (A 40.08 ± 19.39 ms, B 31.01 ± 21.58 ms, 30.59 ± 18.66 ms). There were also differences in the PQ interval, which was the longest for the obese people but still within the norm (A 177.45 ± 29.74 ms, B 167.73 ± 28.92 ms, C 155.58 ± 29.86 ms). QRS complex width was the highest for obese people and statistically longer than in controls (A 107.24 ± 21.34 ms, B 102.47 ± 23.26 ms, C 100.14 ± 13.42 ms, p A vs. C).

When analyzing the classic depolarization and repolarization markers, slight differences in QT and QTc intervals were observed. However, they were not significant, and only QT dispersion was significantly higher in obese people when compared to patients with overweight and normal body mass (A 39.63 ± 23.14 ms, 32.02 ± 27.95 ms, C 32.06 ± 20.77 ms). All data are presented in Table 4.

Table 4. Parameters of the 12-lead ECG recording in the studied subgroups.

Parameter	Obesity (A, n = 98)	Overweight (B, n = 83)	Control Group (C, n = 69)	$p < 0.05$
HR (bpm)	66.50 ± 11.45	66.04 ± 12.10	67.90 ± 12.26	ns
P-wave width (ms)	113.12 ± 19.98	111.66 ± 17.92	102.22 ± 19.45	A, B vs. C
P disp (ms)	40.08 ± 19.39	31.01 ± 21.58	30.59 ± 18.66	A vs. B, C
PQ interval (ms)	177.45 ± 29.74	167.73 ± 28.92	155.58 ± 29.86	A vs. B, C B vs. C
QRS complex width (ms)	107.24 ± 21.34	102.47 ± 23.26	100.14 ± 13.42	A vs. C
QT interval (ms)	392.66 ± 25.77	390.19 ± 40.85	385.23 ± 30.32	ns
QTc interval (ms)	411.50 ± 23.43	406.95 ± 30.23	406.25 ± 21.61	ns
QTd (ms)	39.63 ± 23.14	32.02 ± 27.95	32.06 ± 20.77	A vs. B, C
QRS axis (°)	17.32 ± 38.36	27.05 ± 41.37	37.93 ± 42.80	ns
Sokolow-index LV (mm)	17.11 ± 5.15	19.77 ± 6.16	18.58 ± 6.15	ns
Sokolow-index RV (mm)	3.73 ± 2.23	3.32 ± 2.40	3.71 ± 2.22	ns
Tpeak-Tend (ms)	97.08 ± 23.38	95.88 ± 23.71	89.74 ± 12.88	A vs. C
(Tpeak-Tend) disp (ms)	43.29 ± 24.14	37.34 ±17.75	35.52 ± 11.03	A vs. B, C
(Tpeak-Tend)/QT	0.23 ± 0.05	0.25 ± 0.07	0.23 ± 0.03	ns
(Tpeak-Tend)/QTc	0.22 ± 0.04	0.23 ± 0.05	0.22 ± 0.03	ns
JTpeak (ms)	205.92 ± 28.04	198.77 ± 32.39	192.67 ± 34.88	A vs. C
JT interval (ms)	292.82 ± 28.67	295.52 ± 36.14	292.20 ± 36.25	ns
JTpeak/JT	0.69 ± 0.07	0.67 ± 0.07	0.69 ± 0.05	ns
(Tpeak-Tend)/JTpeak	0.46 ± 0.16	0.35 ± 0.21	0.45 ± 0.11	ns
Tpeak (mV)	0.39 ± 0.26	0.40 ± 0.25	0.41 ± 0.21	ns
Tpeak/JT (mV/ms)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	ns
JTpeak-JTend (ms)	99.55 ± 34.53	95.98 ± 29.64	90.72 ± 13.54	A vs. C
(JTpeak-JTend) disp (ms)	48.22 ± 37.60	44.04 ± 26.32	41.19 ± 16.33	ns

HR—heart rate, P disp—P wave dispersion, QTc interval—corrected QT interval, QTd—QTd interval dispersion, Sokolow–Lyon index LV—Sokolow–Lyon criteria for left ventricular hypertrophy, Sokolow–Lyon index RV—Sokolow–Lyon criteria for right ventricular hypertrophy, (Tpeak-Tend) disp—Tpeak-Tend dispersion, (JTpeak-JTend) disp—Jtpeak-JTend dispersion; ns—not significant.

Taking into account the novel electrocardiographic parameters, we found that in the whole study group, the mean Tpeak to Tend interval was 94.66 ± 21.28 ms, (Tpeak-Tend) dispersion was 39.17 ± 19.38 ms, (Tpeak-Tend)/QT was 0.24 ± 0.05 ms and (Tpeak-Tend)/QTc was 0.22 ± 0.04 ms. All the novel parameters of repolarization are presented in Table 3, together with classical parameters. Confidence intervals and coefficients of

variability of ECG parameters in the entire study group were also presented in Table 3. Tpeak-Tend and its dispersion were statistically significantly longer in the obese group than in the control group. Additionally, the JTpeak-JTend parameter was significantly longer in obese patients than in people with normal body mass.

The differences in repolarization markers are shown in Table 4.

3.3. Linear Relationship between Body Mass Parameters and 12-Lead ECG Parameters in the Entire Study Group

There were positive linear correlations between both atrial parameters, P-wave and PQ interval, and some body mass parameters, that is, body mass, BMI, waist and hip circumference, and between P dispersion and BMI, waist and hip circumferences. Moreover, a relationship existed between QRS complex width and body weight, BMI, and waist circumference.

Amongst novel electrocardiographic parameters, Tpeak-Tend was positively correlated with body mass and waist circumference, while JTpeak was associated with BMI, hip circumference, and WHR. Additionally, Tpeak was correlated with WHR. Also, Tpeak/JT was positively correlated with WHR and BMI. The correlations are summarized in Table 5.

Table 5. Linear relationships between body weight parameters and 12-lead ECG parameters in the entire study group.

Parameter	Body Weight (kg)	BMI (kg/m^2)	Waist Circumference (cm)	Hip Circumference (cm)	WHR
HR (bpm)	ns	ns	ns	ns	ns
P-wave width (ms)	0.31	0.25	0.30	0.20	ns
P disp (ms)	ns	0.15	0.16	0.17	ns
PQ interval (ms)	0.38	0.33	0.40	0.32	ns
QRS complex width (ms)	0.16	0.16	0.14	ns	ns
QT interval (ms)	ns	ns	ns	ns	ns
QTc interval (ms)	ns	ns	ns	ns	ns
QTd (ms)	ns	ns	ns	ns	ns
QRS axis (°)	ns	ns	ns	ns	ns
Sokolow-index LV (mm)	ns	ns	ns	ns	ns
Sokolow-index RV (mm)	ns	ns	ns	ns	ns
Tpeak-Tend (ms)	0.16	ns	0.16	ns	ns
(Tpeak-Tend) disp (ms)	ns	ns	ns	ns	ns
(Tpeak-Tend)/QT	ns	ns	ns	ns	ns
(Tpeak-Tend)/QTc	ns	ns	ns	ns	ns
JTpeak (ms)	ns	0.15	ns	0.19	0.18
JT interval (ms)	ns	ns	ns	ns	ns
JTpeak/JT	ns	ns	ns	ns	ns
(Tpeak-Tend)/JTpeak	ns	ns	ns	ns	ns
Tpeak (mV)	ns	ns	ns	ns	0.16
Tpeak/JT (mV/ms)	ns	0.15	ns	ns	0.16
JTpeak-JTend (ms)	ns	ns	ns	ns	ns
(JTpeak-JTend) disp (ms)	ns	ns	ns	ns	ns

HR—heart rate, P disp—P wave dispersion, QTc interval—corrected QT interval, QTd—QTd interval dispersion, Sokolow–Lyon index LV—Sokolow–Lyon criteria for left ventricular hypertrophy, Sokolow–Lyon index RV—Sokolow–Lyon criteria for right ventricular hypertrophy, (Tpeak-Tend) disp—Tpeak-Tend dispersion, (JTpeak-JTend) disp—Jtpeak-JTend dispersion, ns—not significant.

3.4. Backward Stepwise Multiple Regression Model

After implementing a backward stepwise multivariable regression model for JTpeak and Tpeak/JT as dependent variables, we assessed the specific models presented in Tables 6 and 7.

Table 6. Backward stepwise multivariable regression model in the entire study group for JTpeak (ms) as the dependent variable.

	Age	WHR	Type 2 Diabetes	Smoking
Regression coefficient (RC)	0.439	17.563	13.064	6.259
SEM of Rc	0.163	3.032	6.081	2.803
p	<0.01	<0.001	<0.05	<0.05
p for the model		$p < 0.001$		

Table 7. Backward stepwise multivariable regression model in the entire study group for Tpeak/JT (mV/ms) as the dependent variable.

	Male	BMI (kg/m^2)	β-Blockers
Regression coefficient (RC)	0.001	0.001	−0.001
SEM of Rc	0.000	0.000	0.000
p	<0.001	<0.001	<0.05
p for the model		$p < 0.001$	

For the 12-lead ECG JTpeak, age, WHR, type 2 diabetes, and smoking had the highest statistical significance (p for the model $p < 0.001$), as for the Tpeak/JT as the dependent variable, male sex and BMI had a positive effect on the model. B-blockers had a negative impact on the model (p for the model $p < 0.001$).

The backward stepwise multivariable regression model is summarized in Tables 6 and 7.

The summary of the results of our research and the effects of obesity and overweight on repolarization and other ECG parameters are presented in Figure 3.

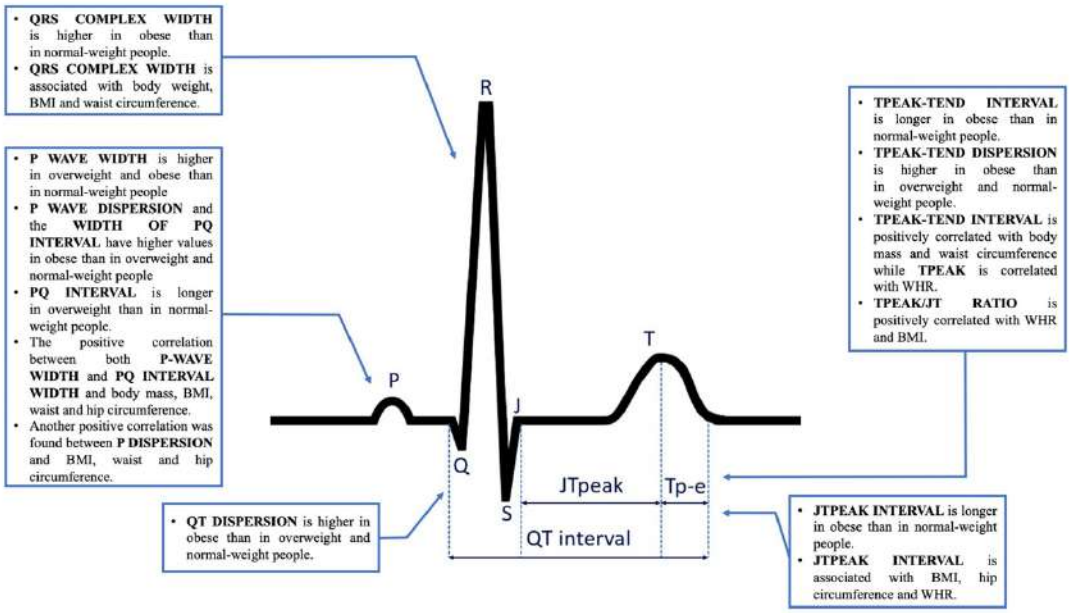

Figure 3. Effects of obesity and overweight on repolarization and other ECG parameters in our study.

4. Discussion

The current study investigated the alterations of ECG parameters in people with overweight and obesity, especially the ones concerning repolarization parameters. We

found an increase in P-wave dispersion and QRS complex width in obese individuals and an increase in P-wave width and PQ interval in both overweight and obese individuals. Moreover, taking into consideration classic repolarization parameters, we found that obese individuals have significantly higher values of QT dispersion, and analyzing novel repolarization parameters, we found that Tp-e interval, Tp-e dispersion, and JTpeak-JTend have substantially higher values in obese individuals. Our study found that alterations in repolarization parameters in obese individuals are marked mostly in novel rather than classic repolarization parameters. This may indicate the potential clinical use of parameters such as Tp-e interval, Tp-e dispersion, and JTpeak-JTend after standardizing the normal values of these parameters. We also found positive linear correlations between ECG parameters (P-wave width, PQ interval, QRS complex width, Tp-e interval, JTpeak, Tpeak amplitude) and body mass parameters (body mass, BMI, waist circumference, hip circumference, WHR), which may be related to electrophysiological changes present in obese people secondary to remodeling of the myocardium in both atria and ventricles.

Other studies investigating ECG changes in obese people also reported an increased prevalence of left ventricular hypertrophy, left atrial enlargement, and left axis deviation in obese patients, which may indicate structural changes in the heart [9,10]. These findings suggest potential alterations in cardiac electrophysiology, myocardial function, and ventricular repolarization in obese individuals. We did not observe the criteria for left ventricular hypertrophy, which is more common in obese people, even though hypertension was the most common in this group. However, the study group should be highlighted as being comprised mainly of class 1 obesity patients. The most significant electrocardiographic changes could be expected in patients from classes 2 and 3, where chamber overload and enlargements are higher, more comorbidities are identified, and cardiovascular risk is higher.

Regarding classic repolarization parameters, Omran et al.'s meta analysis found that obesity or overweight is related to an increase in the length of QT and QTc intervals and QTc dispersion. Moreover, weight loss was able to revert these alterations [11]. Seyfeli et al. also associated increased QTc dispersion with obesity in women [27]. In Kumar et al.'s study, obese adults aged 18–40 had significantly higher width of QT intervals than adults without obesity. Moreover, Kumar et al. associated prolongation of QT interval with a higher risk of left ventricular hypertrophy and ventricular fibrillation [10].

Furthermore, Waheed et al. found that obese people have wider QTc interval than normal-weight people and associated this prolongation with increased cardiovascular and all-cause mortality [28]. Our study showed slight differences in QT and QTc intervals between BMI groups. However, the trend of these changes was consistent with the conclusions of the previously mentioned studies. On the contrary, Braschi et al. found no significant differences in classical repolarization parameters between normal-weight people and people with uncomplicated overweight or obesity. Moreover, they found a trend in QT dispersion that increased with BMI without reaching the significance condition [14]. Our study also found this trend, and it was statistically significant. Furthermore, Guo et al. associated the prolongation of QTc with metabolic syndrome, which often co-exists with obesity [29]. Analyzing the abovementioned studies to estimate the potential risk, we should consider the class of obesity and co-existing comorbidities, which increase with the increase in body mass.

There are still not many research studies investigating the changes in novel repolarization parameters in overweight and obese individuals. The results of previous studies on these parameters are not consistent. Inanir et al.'s study found that the novel repolarization parameters Tp-e interval, Tp-e/QT, Tp-e/QTc, Tp-e/JT, and Tp-e/JTc are significantly higher in individuals with BMI $\geq$ 40 than in individuals with normal body weight [12]. Moreover, Bağcı et al. found that the alterations concerning the Tp-e interval and Tp-e/QT and Tp-e/QTc ratios progress gradually with the growth of BMI [13]. Our study partly supports these results regarding Tp-e interval width. However, we found no significant differences between BMI groups regarding Tp-e/QT, Tp-e/QTc, and Tp-e/JT ratios. Con-

trary to these studies and ours, a study conducted by Al-Mosawi et al. found that Tp-e interval width decreased with the growth of BMI, although this change did not reach significance [15]. Al-Mosawi et al.'s study is the only study we have found with this negative relationship between Tp-e width and BMI. Furthermore, Braschi et al.'s study found no significant changes in Tp-e interval, Tp-e dispersion, and Tp-e/QT ratio between groups of normal-weight people, people with uncomplicated overweight, and people with uncomplicated obesity [14].

Kosar et al. found that P-wave dispersion was increased in obese individuals and that P-wave dispersion was correlated positively with BMI. They also found that obese people had higher values of maximal P-wave duration than normal-weight people. They hypothesized that obesity might be a factor leading to the development of atrial fibrillation [30]. Moreover, Cosgun et al.'s study associated obesity with no other comorbidities to the increase in maximal values of P-wave width and the prolongation of P-wave dispersion [31]. Bocchi et al.'s study also associated BMI and abdominal obesity with an increase in P-wave dispersion [32], and Seyfeli et al.'s study associated obesity with an increase in P-wave dispersion [27]. Our research also found that P-wave duration and dispersion have higher values in overweight and obese people. Therefore, our study supports previously mentioned studies.

Furthermore, Russo et al. found that P-wave dispersion can be significantly reduced by bariatric surgery in morbidly obese patients without comorbidities [33]. Similarly, weight loss due to diet and medical therapy or diet only resulted in decreased P-wave duration and dispersion [34,35]. Prolonging P-wave width or dispersion is associated with a higher risk of developing supraventricular arrhythmias, including atrial fibrillation [36–44].

Another alteration reported in obese people's ECG is a prolongation of QRS complex in comparison to normal-weight people [45,46]. Furthermore, a recent study by Sobhani et al. also found that higher BMI was associated with prolonged QRS complex [47]. Our study supports these findings. We also observed that obese people have a statistically significant increase in QRS complex duration compared with people with normal weight.

Additionally, children and adolescents with abdominal obesity were revealed to have longer PQ intervals, wider QRS complex, and leftward shifts in frontal P-wave, QRS, and T-wave axes in comparison to normal-weight children adolescents. In this group, a positive correlation between PQ interval and QRS duration and BMI, waist circumference, and WHR was also found [48]. We found similar changes in the adult population: an increase in PQ interval and QRS complex width in obese and similar positive correlations between ECG and body weight parameters.

Apart from the ECG parameters examined in this study, there are others that are potentially useful in practice, which we did not take under study. Among them is a microvolt T-wave alternans, potentially useful for patients with coronary artery disease [49]. However, this method has several limitations. Applying this method requires special equipment and the proper heart rate.

There are multiple theories explaining the changes in ECG repolarization parameters due to obesity. Firstly, the changes in P-wave and T-wave morphology may be associated with myocardial fibrosis of ventricles or within the atria [50]. Secondly, obesity may affect ion channels, which may change the potential of myocytes [51]. Obesity may influence I_{Na}, $I_{Ca,L}$, and I_{to} ion channels, increasing the risk of long QT syndrome and atrial fibrillation in obese patients. According to Aromolaran et al., the candidates for modulation by obesity are cardiac, such as the abovementioned ion channels and Ca handling proteins. However, the underlying mechanisms of such interactions remain incompletely understood [51]. In research studies on the relationships between obesity and atrial fibrillation in mice, it has been found that the process was partly mediated by a combined effect of sodium, potassium, and calcium channel remodeling and atrial fibrosis [52].

Moreover, mitochondrial antioxidant therapy reduced atrial fibrillation burden, restoring I_{Na}, $I_{Ca,L}$, and I_{Kur}, resulting in shorter action potential duration and reversed atrial fibrosis. Obesity may be connected with fibrosis and the increased secretion of pro-

inflammatory cytokines, hyperglycemia, and insulin resistance, leading to electrical remodeling and thus predisposing to arrhythmias [51]. Additionally, the adipose tissue is associated with subcutaneous and visceral fat accumulation, causing distinct signaling mechanisms. Eventually, some differences may be present in the regional distribution of fat deposits, affecting ion channel/Ca handling protein expression. Other authors found that cardiomyocytes of obese and diabetic patients have increased lipid accumulation, which contributes to the pathophysiology of heart failure and arrhythmia [53,54]. It is known that diabetes quite commonly co-exists with obesity; even in our study subgroup with class 1 obesity, it was identified in 21% of patients. Morrow et al. demonstrated on transgenic models that cardiac lipid overload causes spontaneous arrhythmias, and Purohit et al. revealed that oxidative stress may partly mediate the arrhythmogenic effect [55,56]. Furthermore, in other studies, authors have found that cardiomyocyte lipid overload may increase oxidative stress by activating the protein NOX2, causing mitochondrial dysfunction and abnormalities of internal calcium handling, promoting arrhythmia [57]. More experimental studies in this area are needed.

Obesity may affect survival, and it has been proven in numerous studies that it is associated with the increased risk of several diseases and death, particularly from cardiovascular diseases and cancer; however, only grade 2 and 3 obesity was associated with significantly higher all-cause mortality [58–60]. Interestingly, in a comprehensive meta-analysis, it was shown that patients with low weight and overweight had a higher mortality risk during acute coronary syndrome than normal-weight patients [61]. The results showed the U-shaped nonlinear association detected between body mass index and mortality risk with higher mortality risk for BMI < 21.5 kg/m^2 and >40 kg/m^2. In contrast, the lowest mortality risk was detected at approximately 30 kg/m^2, called the "obesity paradox" effect. Additionally, it has been clearly shown that the most severe clinical complications and increase in risk are dedicated to class 3 obesity, which is also called high-risk obesity. In such patients, we may expect the most frequent remodeling of the heart muscle and, secondarily, ECG changes and arrhythmias. From this point of view, class 1 obesity and overweight are theoretically connected with not-severe initial stages changes within the cardiovascular system and heart muscle, resulting in less frequent and minor ECG pathologies.

The association between obesity and cardiovascular diseases has been widely studied. However, this issue is still not fully understood and is complex. Discussing briefly several methods determining cardiovascular risk in obese people, several data present the risk of obese patients in the context of coronary artery disease. Even metabolically healthy obese subjects have a higher incidence of subclinical coronary artery atherosclerosis when compared to normal-weight individuals, which was diagnosed by the calcium scores in cardiac computer tomography (CCT). Furthermore, every 1 kg/m^2 increase in BMI led to a 5–7% increase in the incidence of CAD across all BMI categories [62,63]. CCT has relatively good sensitivity and specificity; however, even using modern and up-to-date equipment could not always guarantee high image quality for overweight or obese patients [64]. Echocardiography also needs a good visualization, which may be impaired in this group of patients. In uncomplicated obesity cases, the enlarged left ventricular mass in echocardiography might often be an early adaptation of cardiac function, compensating for the greater hemodynamic and metabolic demand. It should be underlined that increased body mass leads to increased metabolic requirements, which may be a step towards the development of CAD [65]. Single-photon emission CT (SPECT) is used in lower-weight patients and avoided in patients whose BMI is more than 35 kg/m^2 [66]. However, in some studies in which obese people were participating, it was found that, although the obese had a higher risk profile than their non-obese counterparts, obesity was not an independent predictor of abnormal MPS (myocardial perfusion SPECT), raising the possibility that other risk factors associated with obesity (e.g., diabetes) have a much higher impact on the occurrence of coronary artery disease than obesity per se [67]. Nevertheless, there are some limitations of this technique in the obese. Electrocardiography is extensively

available and cheap, so it is the first-line test. The common ECG changes in obese people have been commented on within this article, mainly including the increased heart rate, which has not been proven in our study, as we only noted insignificant differences. Other typical pathologies include increased QRS and QT interval. In light of CAD, there are no specific parameters in obese people that could be proposed as specific prognostic markers, especially for obese people. It is noteworthy that the baseline ECG may be influenced by obesity, especially in more advanced obesity stages. ST-T changes are found due to ventricular hypertrophy and overload, which may perplex the diagnostic process [68]. For this reason, non-invasive testing for CAD often has a suboptimal performance.

It is also worth mentioning that being overweight or obese is not the only factor that impacts changes in repolarization parameters. Other factors include the effects of the autonomic nervous system, hormonal metabolism, especially steroid hormones and sex hormones, hyper- and hypokalemia, other electrolyte disorders, using medications, medical procedures performed, and metabolic diseases [69,70]. Moreover, the influence of genetic factors is also possible, e.g., by modifying the operation of ion channels, as in congenital long QT syndrome (LQTS). There are also reports of the potential impact of hyperventilation on disturbances in ventricular repolarization [71]. The influence of air pollution, especially $PM_{2.5}$, cytokines, stress and emotions, and the menstrual cycle's influence on ventricular repolarization cannot be definitively denied [69,72–74].

A growing number of drugs are influencing ventricular repolarization and prolonging the QT interval, potentially also new electrocardiographic repolarization markers. In this group, there are numerous medications, including noncardiac ones. In our study group, patients did not declare any anti-arrhythmic drugs having a significant impact on repolarization; however, some minor relations could have happened, which may have been a confounding factor to some extent. As presented in Table 2, 64%, 50%, and 39% of patients had hypertension, consecutively in obesity, overweight, and normal-weight subgroups. However, only a few participants were treated with ACE inhibitors, which may have a beneficial and protective effect on repolarization and affect the results. Sixty-eight patients (27.2%) were treated with beta-blockers, which also have beneficial activity.

Moreover, we found a negative relation in regression analysis between beta-blockers and one of the repolarization markers (Tpeak/JT) [75,76]. It may explain slight differences in some repolarization parameters between the studied subgroups. It is also possible that some other agents used by patients could affect the repolarization. The majority of agents may have a potential influence on repolarization; one example may be varenicline, approved to help in smoking cessation, which led to prolongation of ventricular repolarization parameters QTc, Tp-e, and Tp-e/QTc ratio [77]. However, in our study group, no one declared the use of this drug. Additionally, 16% of our study group also proclaimed the use of thyroid hormones and 14% of calcium channel blockers, mainly nifedipine and lercanidipine, which may have some effect. More and more evidence is gathered on the relationship between various medications and repolarization markers; however, when patients use various drugs and agents in real-life clinical conditions, the ultimate effect may be complex and unpredictable.

The significance of our study assumes that it may increase our knowledge of pathophysiological changes in the cardiovascular system, especially within the heart and its electrical system function in people with obesity and overweight, as there are still some controversies. Mainly, we have found more pathologies connected to repolarization in patients with class 2 obesity, and probably further studies should employ more patients with class 3 obesity, in whom we expect more cardiovascular and non-cardiovascular complications. The study may contribute to improving the understanding of the role of repolarization indices with the increase in body weight even in the setting of the usual physician's practice, as the analysis of the electrocardiogram is frequently rather superficial. Numerous studies, including this one, are focused on the detailed ECG examination. It is possible that in the future, Tp-e and its derivates will also be included in computed

electrocardiogram analysis, and all the markers, including the classic and the novel ones, will be presented in the report.

4.1. Limitations

Our study also has some limitations. We analyzed the 12-lead ECG only once for every participant. Therefore, we could not observe changes in ECG in the long term. Furthermore, the Polish population is mostly ethnically monogenic and does not include minorities. Therefore, we cannot guarantee that the results of our study are universal for all populations. The other limitation mentioned in the last paragraph of the Discussion addresses the medications used by some of the study participants, mainly antihypertensive ones. Potentially, it may constitute a confounding factor.

4.2. Future Perspectives

Despite emerging trends and relationships, current research still has many inconsistencies regarding novel repolarization parameters. There is a need for studies with large-scale research and control groups. Thanks to large-scale studies, it would be possible to distinguish subgroups based on age and smaller ranges of BMI (e.g., distinction of alterations in every obesity class). Especially within the study group, there should be more patients with class 2 and 3 obesity in the future perspective.

Furthermore, examining these relationships in more homogenous subgroups, such as diabetes mellitus and hypertension, would also allow for a better understanding of studied ECG alterations. Eventually, ECG, as a simple and easily feasible, as well as widely available, technique, may serve as a first-line tool to estimate the initial pathologies and indicate the increasing cardiovascular risk in obese patients. Paying attention to even minor changes could help to select patients at higher risk.

5. Conclusions

We can hypothesize that considering all the limitations and confounding factors, the results we have analyzed may be addressed to class 1 obesity and overweight people.

In patients with class 1 obesity, only QT dispersion was significantly higher in obese people when compared to patients with overweight and normal body mass, and QTc was only insignificantly higher.

The novel repolarization indices, Tpeak-Tend, and its dispersion were statistically significantly longer in the obese group than in the control group, and the JTpeak-JTend parameter was considerably longer in obese patients. Additionally, Tpeak-Tend was positively correlated with body mass and waist circumference.

We revealed significant differences in P-wave and QRS duration and P-wave dispersion in obese people with class 1 obesity, with positive correlations between these parameters and anthropometric parameters such as BMI and waist and hip circumferences.

This study is the introduction for further research on novel electrocardiographic parameters in the future, that is, the Tpeak-Tend and its derivates, and especially interesting would be employing more patients with class 3 obesity, where the number of cardiovascular and non-cardiovascular complications increases.

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Review Article

Tpeak-Tend ECG Marker in Obesity and Cardiovascular Diseases: A Comprehensive Review

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Globally, cardiovascular diseases are still the leading cause of death. Numerous methods are used to diagnose cardiovascular pathologies; there is still a place for straightforward and noninvasive techniques, such as electrocardiogram (ECG). Depolarization and repolarization parameters, including QT interval and its derivatives, are well studied. However, the Tpeak-Tend interval is a novel and promising ECG marker with growing evidence for its potential role in predicting malignant arrhythmias. In this review, we discuss the association between the Tpeak-Tend interval and several cardiovascular diseases, including long QT syndrome, cardiomyopathies, heart failure, myocardial infarction, and obesity, which constitutes one of the risk factors for cardiovascular diseases.

1. Introduction

Cardiovascular diseases (CVDs) are among the most important and growing healthcare problems. They are the leading cause of death worldwide. In 2019, according to WHO data [1], nearly 17.9 million people died due to CVDs, and they accounted for almost 1/3 of all deaths worldwide. Due to this, research has been conducted to evaluate tools for finding pathology early or helping prevent sudden cardiac death (SCD) and other serious events. For this reason, there is still a search for novel and noninvasive or less invasive tools to detect and eventually monitor cardiovascular pathologies effectively.

Electrocardiography is a technique that is used to visualize and assess the heart's electrical activity. Information obtained with this test is helpful in the diagnostics of heart diseases, including arrhythmias, ventricular hypertrophy, ischemia, and myocardial infarction (MI). An electrocardiogram (ECG) may also be useful in detecting asymptomatic disorders, e.g., long QT syndrome (LQTS). Moreover, ECG has an application in risk stratification, monitoring of cardiac conditions, and response to treatment. ECG stands out from other tests mainly due to its safety, noninvasive character, easy and quick testing, and low cost. ECG can be widely used in almost every healthcare facility.

Numerous markers have been extracted from the ECG record, which reflects the various stages of the heart's function. Among them, there is a need to search for markers reflecting the myocardial depolarization and repolarization associated with malignant ventricular arrhythmias or predicting sudden cardiac death [2]. Some of these parameters,

e.g., QT interval and calculated consistent with Bazett's formula-corrected QT interval (QTc), are commonly used to determine the risk of malignant arrhythmias. Other novel ECG markers, like Tpeak to Tend interval (Tp-e) and its derivatives, are still not used routinely.

The novel repolarization markers include Tpeak-Tend dispersion, JTpeak/JT, Tp-e/JTpeak, and Tpeak/JT ratios [3]. The JTpeak interval reflects early repolarization, while the Tp-e reflects late repolarization. Despite numerous studies, there is still uncertainty regarding the clinical application of the new parameters. Furthermore, no normal reference values of Tp-e and parameters and ratios are associated with that interval [4].

Describing the physiological role of the new marker Tp-e is an index of the transmural dispersion of ventricular repolarization, and it reflects the different durations of the action potential in the epicardium, endocardium, and M cells from the heart. As explained by Castro-Torres, the cellular mechanisms are translated to the T wave on the surface 12-lead electrocardiogram and allow the determination of an increase in the transmural dispersion of the ventricular repolarization through a measure from the peak or nadir to the end of the T wave. The Tp-e/QTc ratio includes values of ventricular repolarization's transmural and spatial dispersion [5].

As new knowledge about QT interval, Tp-e, and other repolarization markers is still increasing, comprehensive reviews are needed to summarize the current knowledge about their role and the circumstances influencing their variations. This study aims to discuss the current state of knowledge and the most recent studies regarding the meaning and application of the Tp-e interval in selected disease entities and its predictive value. It also aims to identify gaps and inaccuracies in the current knowledge regarding this parameter (Figure 1).

2. Methods

2.1. Search Strategy. The review was conducted by searching PubMed, Embase, and Cochrane Library databases using keywords: Tpeak-Tend, Tp-e, TpTe, obesity, long QT syndrome, cardiomyopathy, heart failure, and myocardial infarction.

2.2. Inclusion and Exclusion Criteria. The inclusion criteria were (I) Tp-e-related studies; (II) disease associations with Tp-e among studies; (III) English language; (IV) publication in peer-reviewed journals; (V) adult population; and (VI) human population. We excluded animal studies, conference proceedings, case reports, and abstracts without complete text publication.

2.3. Literature Selection. We assessed the most relevant randomized controlled trials, case-control, cohort studies, and meta-analyses published between 2017 and 2023. Two reviewers independently evaluated three hundred seventy-eight articles according to the title, abstract, text, and scientific validity. As reported in the PRISMA flowchart, after removing duplicates ($n = 163$), 190 studies were initially screened, and 84 were found appropriate for a full assessment. In the end, 66 articles fulfilled the inclusion criteria (Figure 2).

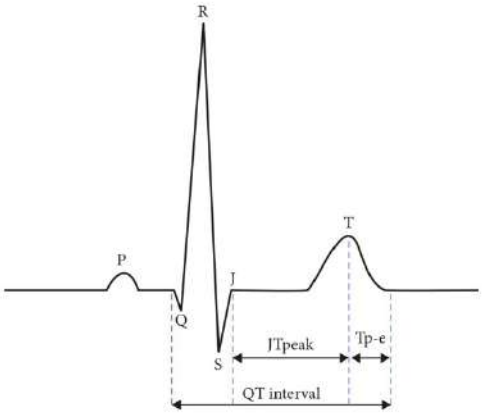

FIGURE 1: ECG repolarization intervals: QT, JTpeak, and Tp-e.

3. Results and Discussion

3.1. ECG Parameters in the Prediction of Malignant Arrhythmias. The parameter considered, especially in the past, useful in predicting ventricular arrhythmias, including ventricular fibrillation (VF), is QT dispersion (QTd). QTd is defined as a difference between the longest and the shortest QT in the specific lead. Although QT interval has been confirmed to correlate with ventricular arrhythmias (VA), QT dispersion ranges vary widely between 10 and 71 ms, which may cause difficulties in its proper assessment [6]. QTd appears unreliable, even when appropriately measured, and is being questioned in extensive prospective studies [7]. Moreover, the correct measurement of QT dispersion is difficult and time-consuming. Other parameters have not yet been sufficiently researched for general use. Furthermore, it is believed that QT dispersion has been shown to reflect not the extent of heterogeneity of ventricular repolarization itself but the spatial position of the vectorcardiographic T loop [8].

Other markers can be used to assess heart function. Heart rate turbulence (HRT) is used to detect the impairment of the autonomic system and baroreflex, and it also has a prognostic role in assessing the risk of all-cause or sudden death [9]. HRT includes two parameters: turbulence onset and turbulence slope. Turbulence onset is a percentage of the length change between the mean of 2 RR intervals before and 2 RR intervals after ventricular premature beat. The turbulence slope is the steepest slope of the regression line of 5 consecutive RR intervals in the range of 15 RR intervals after ventricular premature beat.

Heart rate variability (HRV) is another marker used in cardiovascular risk stratification. It is measured as a change in the length of consecutive RR intervals. HRV is used to detect autonomic system dysfunction [10]. This method uses

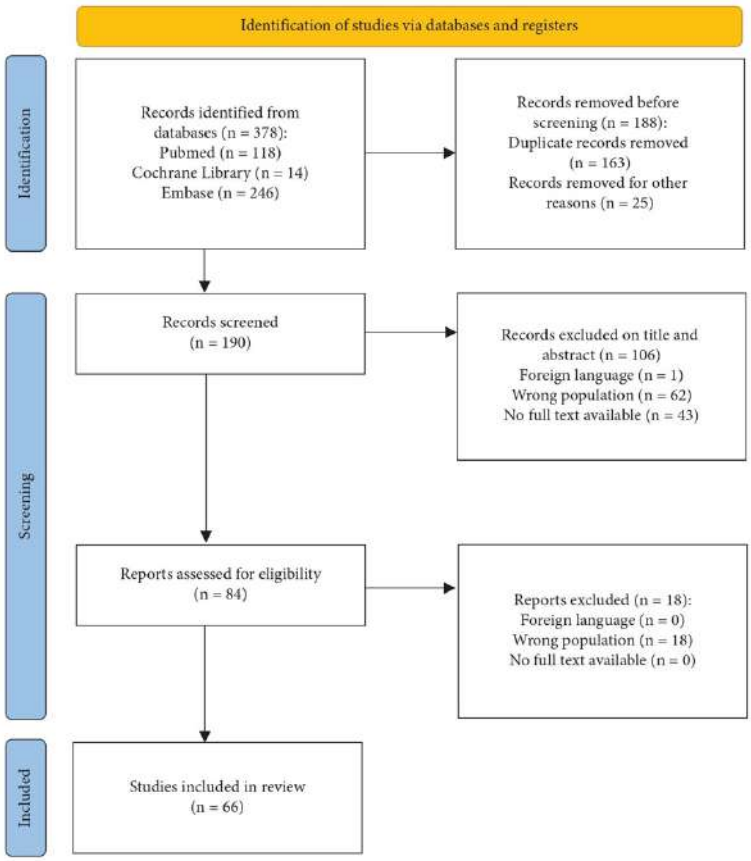

FIGURE 2: PRISMA flowchart for study selection.

two HRV types: time-domain analysis and frequency domain (spectral). Both have been widely evaluated in the last decades. However, they are not routinely used in clinical settings as different studies are rather diverse. Secondly, markers of HRV are very dependent on sympathetic and parasympathetic balance. However, this analysis is applied in numerous 24-hour Holter systems. It was observed that HRV in frequency domain analysis was changed toward the sympathetic predominance in people with higher values of premature ventricular contractions in Holter monitoring, simultaneously in patients with higher blood pressure [11]. In the study by Cosgun and Oren authors compared repolarization markers: T-wave peak-end interval (Tp-e), QT, corrected QT (QTc), Tp-e/QT, Tp-e/corrected QT, and heart rate variability values in healthy men and women and to investigate their daily variations [12]. There were statistically significant differences in Tp-e and cTp-e intervals at various hours of the same day in both groups (women and men). In addition, there were statistically substantial moderate negative correlations between Tp-e intervals and SDNN at various hours of the same day. Some experts propose in this view that T peak-end markers should probably be adjusted to heart rate or use ratios such as Tp-e/QT and Tp-e/QTc, which is a better tool, independent from any changes in RR cycles and heart rate. This question should be studied in the coming years. Additionally, it should be commented on that the Tp-e/QTc ratio remains relatively constant between a heart rate of 60 and 100 beats/min. However, some researchers have recently published good outcomes after the correction of this parameter by the heart rate [13, 14].

Akdi et al. compared two groups of patients with higher and lower numbers of premature ventricular contractions in 24-hour Holter monitoring, and no significant differences were found in HRV time-domain indices. However, the study revealed that the Tp-e interval and Tp-e/QT are associated with the frequency of PVCs. HRV reflects the other type of physiological balance, that is, in the case of T peak indices and their derivatives [15]. In the different studies by Cosgun and Oren, including 500 healthy males categorized by five age subgroups, it occurred that there were significant

differences between these groups in repolarization parameters in terms of Tp-e interval but not Tp-e/QT and Tp-e/QTc ratios. Considering the HRV parameters, there were statistically significant differences between the five male healthy groups in terms of HRV temporal parameters and no significant differences in HRV frequency parameters. The authors concluded that as the age increases, basal Tp-e interval increases and HRV temporal parameters decrease significantly in the male subjects aged between 30 and 79 years, but HRV frequency parameters do not change. The relations between the markers from the repolarization group and heart rate variability seem complex and need further evaluation [16].

T-wave alternans (TWA) is another marker with potential clinical use. TWA is the difference between consecutive T-wave amplitude and morphology. It may be helpful in the assessment of the risk of lethal ventricular arrhythmias and death due to cardiovascular events. Eventually, more studies are needed to confirm its usefulness, and this method requires more sophisticated equipment [17]. In 2008, in the AHA/ACCF/HRS Scientific Statement, TWA was listed as one of the potentially valuable markers of SCD risk due to a moderate amount of data. However, the measurement of TWA requires proper heart rate and regular RR interval duration. It was often inaccurate for many reasons, including failure to achieve the appropriate heart rate during gradual exercise and arrhythmias [18]. In most recent ventricular arrhythmias guidelines of AHA and ESC, it has no significant role [19, 20]. In ESC Guidelines, TWA is only used in modified LQTS diagnostic scores. Positive TWA adds 1 point to the score, requiring >3 points to diagnose LQTS [20].

Until now, QT interval has been well studied. There are commonly known factors influencing its duration, such as heart rate, age, hormone concentration, time of the day of the examination, potential imbalances in water volume and electrolyte concentrations, the influence of medications, and autonomic system nervous tension. In addition, essential QT interval changes may be observed in patients with heart failure and other heart diseases [21]. In contrast to QT or JTpeak intervals, studies claim that Tp-e duration is independent of HR [22]. However, it has been previously proposed that it be corrected with Bazett's formula, so it remains equivocal. Some studies reveal the Tp-e dependence of HR and suggest the Tp-e/QT ratio to be more appropriate in repolarization characteristics due to minimizing HR-influenced alterations [14]. In addition, Tp-e time may vary in different ECG leads [22].

The Tpeak-Tend interval (Tp-e) can be measured in many ways. Tp-e can be measured in a single lead or from the earliest Tpeak among all leads to the latest Tend throughout all leads. The second method is often used in research studies [23–25]. Moreover, the measurement of Tp-e in multiple leads is preferred to measurement in single lead because it allows the calculation of Tp-e dispersion, which is a difference between the highest and the lowest value of Tp-e in all leads [26]. Such an approach yields better results, especially when local changes are expected in myocardial ischemia. In one of the studies, the authors compared single-lead and multilead measurements of Tp-e and presented findings in favor of multilead measurements. Automated measurement is the most accurate Tp-e measurement method; among the manual methods, the tangent method is the most useful. The lead optimal for this measurement is the lead V2 [27].

Tp-e interval is the ECG parameter representing the dispersion of repolarization across the ventricles [28]. Notably, the predictive role of Tp-e prolongation and occurrence of SCD have been found, for example, in Oregon Sudden Unexpected Death Study [29]. The authors proved that prolonging the Tp-e interval was independently associated with SCD, with particular utility when the QTc was normal or not measurable because of prolonged QRS duration. In another study, the Tp-e interval is associated with SCD in adults with congenital heart diseases [30]. The potential mechanisms underlying the alterations visible in ECG as a Tp-e prolongation leading to the SCD may be driven by abnormal ion channel function, pathophysiological dispersions of repolarization providing a substrate for reentrant arrhythmias or autonomic dysfunction [31]. As suggested by Vehmeijer et al., various studies have demonstrated that there may be the transmural dispersion of repolarization due to prolonged repolarization of the subendocardial M cells or overall dispersion of repolarization [23, 30, 32].

Several authors discuss the importance of several parameters in repolarization characteristics, including Tp-e prolongation, compared to classical CVD risk factors, such as diabetes mellitus, hypertension, and smoking [33–35]. Moreover, obesity and structural and ischemic heart diseases also impact myocardial repolarization heterogeneity [36–38].

3.2. Tp-e Interval in Overweight and Obese People. Obesity is a disease characterized by excessive adipose tissue deposition in the body [39]. Obese individuals are more susceptible to developing cardiac diseases and dying of cardiovascular disorders, including SCD. Many changes indicate heart disease found more often in ECG records of obese people than in ECG records of people with normal weight, including prolongation of QT and QTc interval, prolongation of QT or QTc dispersion, tachycardia and higher heart rate, atrial and ventricular enlargement, conduction defects, left axis deviation, features of ischemia, old infarction, and repolarization abnormalities [40–42]. Moreover, obesity was associated with changes in the QRS complex in premenopausal women [43]. In children, obesity is associated with prolonged QT interval, longer QRS complex, and leftward shifts in frontal P-wave, QRS, and T-wave axes [44].

Several studies examining the connection between obesity and repolarization markers such as Tp-e, Tp-e/QT, and Tp-e/QTc support this association. Inanir et al.'s study [45] found that previously mentioned repolarization parameters, Tp-e/JT and Tp-e/JTc, were significantly increased in patients with class 3 obesity (body mass index (BMI) ≥40) in comparison with patients with normal body weight. Furthermore, according to Bağcı et al.'s research [46], Tp-e, Tp-e/QT, and Tp-e/QTc increase gradually with the growth

of BMI. The association was found by examining these parameters in four groups of patients: normal weight (BMI: 18.0–24.9), overweight (BMI: 25–29.9), obese (BMI: 30.0–39.9), and class 3 obese (BMI ≥ 40). The same study found that Tp-e length was significantly positively correlated with age and systolic and diastolic blood pressure. This study suggests that repolarization impairment occurs before reaching class 3 of obesity.

On the contrary, Al-Mosawi et al. [47] associated the prolongation in repolarization markers (Tp-e, Tp-e/QT) with pericardial fat volume measured by multidetector computer tomography. They found no significant association between them and the growth of BMI. They found a significant association only in the group of patients with coronary atherosclerosis. In contrast to other studies, the Tp-e value decreased sequentially in groups of normal weight, overweight, and obese patients. The Tp-e interval was the shortest in the group of obese people, whereas, in most other studies, the obese have the most prolonged Tp-e interval. The result of this study may seem controversial because of this negative correlation. Some recent studies evaluated how weight loss due to bariatric surgery and sleeve gastrectomy surgery affected the change in markers of repolarization.

In trying to explain the conflicting results, it should be taken into account that both cardiac and extracardiac factors matter in the case of surface ECG. There may be a potential effect of extracardiac factors such as subcutaneous fat, heart position, fluid overload, and body habitus on the temporal parameters, not only on voltage parameters, which cannot be excluded entirely [48]. Generally, Tp-e is thought to reflect dispersion of repolarization, and this is an intracardiac factor. However, it should be considered that both obesity and weight loss may involve a change in extracardiac factors. This consideration might account for conflicting results.

It is also worth noting that values of Tp-e and its derivatives change after surgical procedures, leading to weight loss. Gul et al.'s study [49] included class 3 obesity patients and found a significant reduction in Tp-e, Tp-e/QT, Tp-e/QTc, Tp-e/JT, and Tp-e/JTc after bariatric surgery (measured 1 and 6 months after operation). The change in these parameters was also significantly correlated with weight loss. Ibisoglu et al. [50] also found a significant reduction in Tp-e, Tp-e/QT, Tp-e/QTc, Tp-e/JT, and Tp-e/JTc 6 months after bariatric surgery and stated that this change may reduce the risk of developing ventricular arrhythmia. Moreover, Inanir et al. [51] found that Tp-e interval, Tp-e/QT, Tp-e/QTc, Tp-e/JT, and Tp-e/JTc ratios decreased significantly after sleeve gastrectomy surgery in class 3 obesity patients, which suggests that weight loss by this surgery also reduces the risk of arrhythmias and SCD.

In conclusion, most studies support the statement that Tp-e duration and other repolarization parameters positively correlate with BMI. This indicates a higher risk of developing arrhythmias, including VAs, which may result in SCD, especially in obese patients. Opposing these findings, a study also shows the opposite trend: normal-weighted patients have the longest Tp-e, and obese patients have the shortest Tp-e. Moreover, studies agree that these parameters should be improved after weight loss due to bariatric surgery. However, only some studies examine the association between body weight and novel repolarization parameters, even though some are contradictory.

3.3. Tp-e Interval in Long QT Syndrome. LQTS is an electrical disorder that is characterized by the prolongation of QT interval [52] (QTc >440 ms in men and QTc >460 ms in women) [53]. LQTS increases the risk of polymorphic ventricular tachycardia (torsade de pointes), which might result in SCD. LQTS can be congenital or acquired. It may have an asymptomatic course in some people, and cardiac arrest may be the first sign of this disorder.

The length of the QT interval provides data about the time between depolarization and repolarization of cardiomyocytes. In addition to these data, the Tp-e interval includes information about the dispersion of repolarization. The Tp-e interval may be helpful in diagnostics and risk stratification in this condition.

Firstly, the Tp-e interval, along with other markers, may be used to determine whether the case of LQTS is congenital or acquired, which is essential because depending on the cause of the disease, the prognosis and treatment vary. Sugrue et al. [54] investigated T-wave morphology to differentiate whether LQTS is congenital or acquired. They found that patients with acquired LQTS had longer Tp-e in V5 lead than those with congenital LQTS. Patients with acquired LQTS also had a shallower right slope and a smaller T-wave centre of gravity. They suggested that T-wave morphology may also be useful in assessing IKr ion channel (a potassium channel that takes part in cardiac repolarization) activity in drug testing, especially in association with arrhythmogenesis. The Tp-e interval is a marker that appears to be effective in evaluating the risk of arrhythmogenesis, so the Tp-e interval could be one of the markers in this process.

Furthermore, Tardo et al.'s systematic review [55], apart from Sugrue et al.'s research, included Johannesen et al.'s [56] study, which found J-Tp and Tp-e intervals useful in the differentiation of IKr ion channel block and multichannel block in acquired LQTS. The block of IKr was associated with longer J-Tp and Tp-e intervals. The multichannel block (block of both IKr and calcium or sodium channel) was associated with shorter J-Tp and longer Tp-e and QT intervals.

Apart from differentiating congenital and acquired LQTS, Tp-e can potentially be used as a marker for assessing cardiac event risk in LQTS patients. Tse et al.'s meta-analysis [57] found that Tp-e is significantly longer in people with LQTS suffering from cardiac events than those without cardiac events and suggested that Tp-e may be useful in risk stratification. It was also found that the Tp-e/QTc ratio is also higher in high-risk patients, making it a useful risk marker. Furthermore, according to Markiewicz-Łoskot et al.'s study [58], Tp-e, combined with QTc, may have potential use in detecting affected relatives of people with congenital LQTS. They found that Tp-e is significantly longer in relatives affected by LQTS than in those unaffected and associated this marker with the possibility of cardiac events. They also

found significant differences in Tp-e in LQTS type 1, LQTS type 2, and unaffected people when divided into groups based on sex. The Tp-e interval was also longer in LQTS type 2 than in LQTS type 1 without reaching statistical significance.

Moreover, according to Krych et al., longer Tp-e was associated with a higher risk of arrhythmia and cardiac events in people with LQTS type 7 (Andersen-Tawil syndrome). According to the same study, the higher value of Tp-e, QT, and U-wave presence in V2–V4 leads may also be related to the presence of KCNJ2 mutation [59]. Additionally, the meta-analysis by Tse et al. showed that the values of Tp-e and Tp-e/QT ratio among people with acquired QT interval prolongation were higher in patients with torsade de pointes incidents than in those without them, and due to that, these markers can be used in the stratification of risk in acquired LQTS [60]. Tp-e was longer in people with atrioventricular block-related LQTS and cardiac events than those without cardiac events, whereas Tp-e/QT was higher in people with drug-related LQTS and cardiac events than those without cardiac events.

In conclusion, the Tp-e interval may be a useful marker in differentiating congenital and acquired LQTS and assessing risk in LQTS independently from its cause.

3.4. Tp-e in Cardiomyopathies. According to ESC Guidelines, cardiomyopathy is a morphological and functional abnormality of the ventricular myocardium not caused by coronary artery flow limitation or abnormal loading conditions [61].

Furthermore, it is possible to distinguish five different subtypes of cardiomyopathy, each with genetic or nongenetic etiology. Those subtypes are hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and the fifth, which consists of those unclassified [61].

According to HCM, the dominant cause of cardiomyopathy is sarcomeric protein gene mutation ranging about 40–60%, then 25–30% have unknown reasons, and 5–10% are other genetic or nongenetic causes, such as inborn errors of metabolism (e.g., glycogen storage diseases), neuromuscular diseases (e.g., Friedreich's ataxia), mitochondrial diseases (MELAS, MERFF), malformation syndromes (Noonan, LEOPARD, Costello, and CFC), amyloidosis, newborn of the diabetic mother, and drug-induced HCM [62].

Referring to SCD among HCM patients, there is a suggestion that Tp-e does not have a significant prognostic value in that group. However, QTc may be an appropriate tool for risk stratification in patients with HCM [63]. Another study revealed the utility of T-wave amplitude and traditional risk factors as an SCD marker in this group of patients. In contrast, this research did not show the statistical significance of Tp-e [64]. Importantly, in a large cohort of patients with HCM, it has been proven that a significant difference between genotype-positive and genotype-negative HCM patients in spatial mean and spatial peak QRS-T angles exists, which could be a better tool in identifying patients with HCM than traditional Seattle criteria. Moreover, Tp-e was significantly higher among genotype-positive patients than those without genetic backgrounds [65]. In addition, spatial QRS-T angle was shown to be significantly associated with VF and SCD in Brugada syndrome (BS) patients, who usually have structurally normal heart muscle; however, recently, the association between ARVC and BS molecular insight of pathogenesis was taken under scientific discussion [38, 66, 67]. The same study revealed that Tp-e does not have a predictive value in the BS group of patients according to malignant arrhythmias and SCD.

Dinshaw et al. showed that Tp-e prolongation in HCM patients is associated with VA, such as ventricular tachycardia (VT) and ventricular fibrillation (VF). It assessed its predictive role in SCD risk stratification. Besides, it is underlined that Tp-e < 78 ms among HCM patients with implanted ICDs is associated with a low risk of VA [67]. There were no significant differences among patients with transthyretin cardiac amyloidosis (TTR-CA) compared to the control group referring to Tp-e and Tp-e/QTc [68].

On the other hand, in the HCM population without a sarcoidosis background, Tp-e and Tp-e/QTc were significantly higher. They trended toward increased QT dispersion compared to the group without cardiac disease. The result present in the TTR-CA group is consistent with observed low-range SCD in that group of patients due to homogenous amyloid distribution [69]. Furthermore, the long-term prognostic value of ventricular repolarization dispersion in cardiac sarcoidosis patients was investigated. Endpoint was defined as the occurrence of the atrioventricular block (AVB), VT/VF, heart failure (HF) hospitalization, and all-cause death. That study assessed Tp-e/QT as an independent positive predictor of previously mentioned adverse events. VT/VF and SCD were observed more often in patients with greater Tp-e/QT ratios of ≥0.242 ms [70]. It was also confirmed that in patients without apparent heart involvement at early-stage sarcoidosis, QTcd, Tp-e, and Tp-e/QT ratios were significantly higher than in the control group [71].

Cardiomyopathy in Fabry disease is the most frequently present as left ventricular hypertrophic cardiomyopathy—in that group, ECG abnormalities included shorter P-wave and T-wave peak time, what was observed as a more symmetric T wave with lower T-wave time ratio described by Tonset-Tpeak/Tp-e compared to the control group [71]. There are contrasting results regarding the predictive value of Tp-e among HCM patients, especially its role in SCD prediction. The issue needs more studies and meta-analyses to assess its role in that population. In addition, a study confirmed that higher Tp-e among patients with nonischemic dilated cardiomyopathy was associated with malignant ventricular arrhythmias [72]. Lopez et al. investigated how ECG parameters predict SCD change after cardiac resynchronization therapy (CRT) with His bundle pacing. There was an improvement in QT interval, QT dispersion, and Tp-e dispersion, and Tp-e was shortened [73].

The study of Ponnusam et al. also noticed a significant improvement in repolarization parameters after His bundle pacing using QTc, Tp-e, and Tp-e/QTc ratio parameters. Those results prove a reasonable option for CRT among patients with left bundle branch block (LBBB)-induced cardiomyopathy with an improvement visible as normalization of electrical and mechanical pathologies [74]. However, in a group of HF patients with implantable cardioverter-defibrillator (ICD), in which 85.5% of patients ($n = 272$) were diagnosed with dilated cardiomyopathy, postimplantation Tp-e was revealed as an independent predictive factor of VT, VF, and all-cause mortality [75]. According to ARVC, one study corresponds to this review criterion, which revealed the association in longitudinal follow-up poorer prognosis and fragmented QRS, longer Tp-e in lead V2, and definite ARVC [76].

ESC Guidelines currently describe unclassified cardiomyopathies in Takotsubo cardiomyopathy and left ventricular noncompaction. Those pathologies found their association with ECG parameters. Patients with Takotsubo syndrome who suffered from major adverse cardiovascular events (MACE) (defined as acute heart failure, cardiogenic shock, sustained ventricular tachycardia, ventricular fibrillation, and death) had more often ST-segment elevation and their Tp-e/QT ratio was significantly higher. Tp-e/QT range >0.27, accompanied by low ejection fraction (EF), was defined as the subpopulation at higher risk of MACE [77].

When considering left ventricular noncompaction cardiomyopathies, patients compared to groups with normal cardiac ultrasound, Tp-e, and Tp-e/QT ratio were revealed as potential risk markers of that pathology presentation. These may be helpful markers before invasive procedures such as cardiac biopsy [78].

In conclusion, the role of Tp-e and its derivatives in assessing patients with cardiomyopathy may vary between its subtypes according to malignant ventricular arrhythmias. However, it can be an attractive parameter for monitoring a patient's prognosis after electrotherapy devices or LVAD implantation procedures. Furthermore, Tp-e can be a potential ECG marker, allowing preliminary diagnosis according to HCM genetic background and noncompaction cardiomyopathy suspicion before performing the cardiac biopsy.

3.5. Tp-e Interval in Heart Failure. Heart failure (HF) is when the cardiac output is reduced, and the heart cannot pump enough blood to meet the body's needs. The prevalence of HF grows rapidly in many countries because of the aging society. UpToDate shows about 64 million people worldwide suffered from this condition in 2022 [79]. A report from the American Heart Association estimated that the lifetime risk of heart failure development is 20–45% of people over 45, depending on the racial and ethnic group. Many circulatory diseases, including hypertension or coronary heart disease, may cause this condition. Heart failure increases the risk of death and reduces the quality of life [80].

In recent years, Piccirillo et al. conducted several studies [81–85] on patients suffering from heart failure and assessed the role of repolarization markers, including Tp-e, in chronic heart failure. There were attempts to find the use of repolarization markers in predicting hospital length of stay and the mortality of patients with acute decompensated heart failure [81]. It has been found that mean Tp-e was helpful as the predictor of mortality in the next 30 days, while Tp-e variance normalized and Tp-e standard deviation (Tp-eSD) was useful as the predictor of length of hospital stay and thus a predictor of severity. It was also suggested that these markers may be used to monitor both morphological and structural alterations of the heart.

It was also found that in patients with heart failure with a reduced ejection fraction (HFrEF), mean Tp-e and its standard deviation were higher than in those with heart failure with preserved ejection fraction (HFpEF) [82]. However, Son et al. found no difference in Tp-e and Tp-e/QT ratio based on ejection fraction in three groups of heart failure patients (preserved, midrange, and reduced ejection fraction) [86].

Mean Tp-e was also significantly correlated with mortality [81]. Patients who responded to the heart failure therapy had reduced Tp-eSD compared to nonresponders. Moreover, people with higher Tp-eSD died more often. In another study, mean Tp-e was related to chronic heart failure mortality, and Tp-eSD was a risk factor for aggravation and complications of this disease [83]. Another Piccirillo et al. study found an association between Tp-e and mortality in acutely decompensated chronic heart failure [84]. In a study including patients with decompensated heart failure and atrial fibrillation (AF), mean Tp-e was again associated with mortality, while higher Tp-eSD was associated with permanent AF [85]. The important conclusion from the last study is that Tp-e is not affected by atrial fibrillation.

Several recent studies have investigated repolarization markers in heart failure therapies. Usalp et al. investigated the length of Tp-e and T wave in cardiac resynchronization therapy. They found that a reduction in the duration of these markers was a significant predictor of a favorable response to the treatment [87]. Moreover, Banavalikar et al. found that Tp-e predicts ventricular tachyarrhythmias in heart failure patients after cardiac resynchronization therapy [88]. Furthermore, Li et al. investigated the association between left bundle branch area pacing (LBBAP) and echocardiographic response in heart failure patients. They found that Tp-e is useful as the predictor of response to the therapy, especially in patients without left bundle branch block [89]. Patients with Tp-e shorter than 81.2 ms after therapy were significantly more likely to be responders than those with longer Tp-e. They also found that Tp-e interval duration and Tp-e/QTc ratio were reduced considerably after therapy in patients with QRS >130 ms. Also, Xue et al. investigated Tp-e in patients with heart failure and ICD and its use in predicting VA and mortality [75]. It was found that a longer duration of Tp-e was positively associated with VT, VF, and mortality.

In conclusion, the Tp-e interval and its derivatives may be practical in predicting mortality and severity during heart failure. Moreover, it may be used to monitor the

effectiveness of therapy. It should be kept in mind that most of the studies conducted in recent years have been carried out by one research team, and there is a need to replicate these studies in other populations.

3.6. Tpeak-Tend in Myocardial Infarction. Tpeak-Tend interval and Tpeak-Tend/QT ratio were essential predictors among patients with myocardial infarction (MI), mainly in those with ST-segment elevation myocardial infarction (STEMI). However, groups with myocardial infarction with nonobstructive coronary artery disease (MINOCA) were investigated according to repolarization parameters, including Tp-e.

Prolonged Tp-e was confirmed to be an independent risk factor of VA in STEMI patients after percutaneous coronary intervention (PCI) [90, 91]. In addition, the Tp-e interval measured before the procedure was found to be an independent predictor of reperfusion VF [92]. One study did not confirm the Tp-e association with VF, as it was statistically insignificant among other investigated parameters [93]. Patients described with MINOCA had a significantly higher risk of VA, and Tp-e Tp-e/QT was longer in that group [94]. According to myocardial reperfusion, Tp-e >72.5 ms and Tp-e/QT ratio >0.18 independently predicted procedure impairment, in-hospital MACEs, and poorer 6-month survival rate [93]. Moreover, the 3-year survival rate among patients with prolonged Tp-e/QT in infarct-related leads corresponded with patients' higher mortality [95].

Namazi et al. retrospectively confirmed the statistical significance of QT dispersion, Tp-e value, and in-hospital mortality in STEMI patients with those parameters measured before PCI [96]. In addition, Tp-e was revealed to be an independent predictive factor of incomplete ST-segment resolution in STEMI patients treated with PCI [97]. However, there was a trial analyzing only patients with acute anterior MI. Its results contradicted those previously mentioned, revealing no statistical significance of Tp-e or Tp-e/QT in patients undergoing PCI [96]. Moreover, Wang et al. assessed Tp-e as an independent predictive factor of 1-year MACE defined as cardiac death and malignant arrhythmia event [90].

An analysis according to preinfarction angina (PIA) was conducted and revealed that STEMI patients with PIA had a lower chance of suffering from VA than those without PIA–who had longer Tp-e, Tp-e/QT ratio, which independently predicted in-hospital VA [98]. Interestingly, Tp-e was found to predict Intensive Care Unit (ICU) stay among patients with acute coronary syndrome (ACS) with COVID-19 [99].

Tp-e prolongation was also associated with the marker of coronary artery disease (CAD) severity [100]. One of those markers is the SYNTAX score; its higher scores were associated with prolonged Tp-e and Tp-e/QT in patients with CAD [101–103]. These results may be an interesting potential noninvasive predictive marker of CAD severity.

In conclusion, those findings may help invasive cardiologists stratify the procedural and periprocedural risk, including VA, MACE, mortality, and long-term prognosis.

3.7. Tpeak-Tend in Valvular Heart Disease. Changes in Tp-e length and derived parameters have been reported in valvular heart diseases. Most studies focus on the relationship between Tp-e and its derivatives and aortic stenosis (AS). Patients with aortic stenosis have significantly higher values of Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios than healthy people [104]. The more severe the AS, the more significant the parameter increase. Moreover, a positive correlation was found between the Tp-e/QTc ratio and the mean aortic gradient.

Furthermore, the Tp-e/QTc ratio was a significant and independent predictor of severe AS. Another study observed increases in Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios [105]. In this study, again Tp-e/QT and Tp-e/QTc ratios were significantly associated with AS, and mean aortic gradient was positively correlated with Tp-e, Tp-e/Qt, Tp-e/QTc, and Tp-ed. Also, a negative correlation between aortic valve areas and Tp-e, Tp-e/Qt, Tp-e/QTc, and Tp-ed was found.

In several studies, after transcatheter aortic valve implantation (TAVI), there was a significant reduction in values of Tp-e, Tp-e/Qt, Tp-e/QTc, and Tp-ed, indicating that TAVI might reduce the risk of ventricular arrhythmias and mortality [105, 106]. Moreover, before TAVI, there was a positive correlation among Tp-e, Tp-e/QT, Tp-e/QTc, and left ventricular mass index (LVMI) [106]. Tp-e was also independently associated with LVMI.

Another study found Tp-e and its derivatives useful in predicting complete atrioventricular blocks after TAVI [107]. Tp-e, Tp-e/QT, Tp-e/QTc, Tp-e/JT, and Tp-e/JTc were significantly higher in patients requiring permanent pacemaker after TAVI and, additionally, Tp-e/QTc and Tp-e/JTc were significantly associated with the presence of complete atrioventricular block. Moreover, Tp-e/JTc was a potential independent predictor of complete atrioventricular block after TAVI.

Tp-e, Tp-e/QT, Tp-e/QTc, and Tp-ed also had higher values in the group of patients who died after successful treatment of AS with surgical aortic valve replacement (SAVR) in comparison with patients who survived within a mean follow-up period of 66.3 ± 42.4 months [108]. Tp-e, Tp-e/QT, Tp-e/QTc, and Tp-ed were independent mortality predictors after SAVR. Higher values of Tp-e/QT and Tp-e/QTc were associated with a lower chance of long-term survival. In another study, lower values of preprocedural Tp-e were associated with better survivability after TAVI [109]. The follow-up period in this study was one year.

Contrary to most previously mentioned studies, Chino et al.'s study showed no significant changes in Tp-e, Tp-e/QT, and Tp-e/QTc after neither TAVI nor surgical aortic valve replacement [110].

Similarly to patients with aortic stenosis, the patients with severe mitral stenosis have significantly higher values of Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios than the healthy population [111]. Moreover, after percutaneous mitral balloon valvuloplasty, the value of these parameters significantly decreased, revealing the beneficial effect of this procedure on the mentioned repolarization parameters. Furthermore, the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios also had higher values in children with mitral valve

prolapse when compared to healthy children [112]. Moreover, the value of Tp-e/QTc correlated positively with the degree of mitral regurgitation. It is suspected that these changes might be associated with the increased risk of ventricular arrhythmias and SCD in patients with mitral valve prolapse.

In conclusion, most studies suggest that Tp-e and its derivatives have increased values in valvular heart disease, and the proper treatment of this disease might reduce the values of these parameters. The high values of these parameters are also associated with a worse prognosis after treatment of valvular disease.

3.8. Tpeak-Tend in Brugada Syndrome. Patients with Brugada syndrome (BS) are more susceptible to ventricular arrhythmia and sudden cardiac death if the Tp-e interval is prolonged [113]. In BS, the ajmaline challenge is performed to provoke BS, and there was research investigating whether prolonged Tp-e or the corrected interval can predict the positive result of the ajmaline challenge. However, its role declined [114]. Other studies revealed a significant correlation between Tp-e prolongation and the occurrence of life-threatening arrhythmic events among patients with BS [115, 116].

Importantly, Tp-e was found to be the most promising ECG marker together with QTc interval in predicting malignant arrhythmias among BS patients. However, there is a need to assess the cut-off for the Tp-e value, which significantly increases the risk of life-threatening arrhythmias [117]. Interestingly, when the BS typical ECG pattern was observed in precordial leads V1–V3, it was simultaneously revealed that the Tp-e interval in V1 lead was significantly higher among patients with malignant arrhythmias. In contrast, in the other leads, no significant differences were noted [113]. However, in the bigger cohort, it was observed that among BS patients in the mean follow-up of 88 months, Tp-e was not significantly prolonged in those with syncope or malignant arrhythmias [118].

A consistent statement on the role of the Tp-e interval in risk stratification in BS should be evaluated in further research. The pathophysiological mechanism is still under debate with the considered potential mechanisms including the "depolarization hypothesis" and "early repolarization hypothesis" [119].

Similarly, as in BS, in patients with J wave syndrome who were aborted from sudden cardiac death, the Tpeak-Tend interval and Tp-Te/QT ratio are significantly increased [120].

3.9. Other Cardiovascular Diseases and Sleep Apnea. The role of Tp-e has been noted concerning various clinical conditions. Importantly, acute myocarditis (AM) is one of these conditions, and prolonged Tp-e, Tp-e/QT, and Tp-e/QTc ratios have been observed in patients with AM [121]. What makes an interesting insight into the AM patient's characteristics in terms of ECG changes as usually observed abnormalities are sinus tachycardia or nonspecific ST-T wave changes [122]. However, elucidating the patients' prognosis revealed in the Ucar et al. study parameters among AM patients would make a practical application of these results [121].

Tp-e characteristics in hypertension have been confirmed to be prolonged in nondipper hypertension and positively correlated with the cardio-ankle vascular index in this population [123, 124]. Tp-e and Tp-e/QTc parameters in patients with arterial hypertension increased in patients with subclinical myocardial dysfunction diagnosed by the echocardiography parameter, left ventricular global longitudinal strain (LV-GLS) [125].

Tp-e and its derivatives were essential parameters in patients with hypothyroidism, where they were prolonged in both overt and subclinical presentations [126, 127]. As the cardiovascular system is significantly affected in liver cirrhosis, it has been revealed that heart rate, Tp-e, Tp-e/QT, and Tp-e/QTc were considerably higher in the diseased group than in the control group [128]. Moreover, the same study showed the predictive value of heart rate, Tp-e, and Tp-e/QT for end-stage liver cirrhosis, although no correlation with Child stages was observed. Another study confirmed that Tp-e, QTc interval, Tp-e/QTc ratio, and fQRS are increased in liver cirrhosis, noting a parallel association of these parameter prolongations with disease severity [129]. However, this contradicted the findings of the previously mentioned study, as it showed a significant correlation with the Pugh-Child classification.

Obstructive sleep apnea (OSA) is a risk factor for ventricular arrhythmias. Assessing which patients are at a higher risk of this complication is important, as demonstrated in Yan et al.'s study [130]. According to their retrospective analysis, patients who presented nocturnal premature ventricular contractions had a significantly higher Tp-e/QT ratio than those with OSA. Another study conducted among patients with OSA revealed a significant correlation between moderate and severe OSA and increased Tp-e, Tp-e/QT, and Tp-e/QTc ratios [131]. However, findings describe Tp-e, Tp-e/QT, and Tp-e/QTc prolongation only during the apnea period, with a decrease in the postapnea hyperventilation period [132].

Another disease confirmed to be correlated with altered repolarization is chronic obstructive pulmonary disease (COPD), where significant prolongation of Tp-e, Tp-e/QT, and Tp-e/QTc ratio compared to the control group was observed [133]. According to blood test results, it was revealed that low ferritin levels among female patients without anemia or history of cardiac disease, as well as vitamin B12 deficiency in the healthy adult population, influence their arrhythmogenic susceptibility, which was observed by increased Tp-e, Tp-e/QT, and Tp-e/QTc parameters [134, 135]. Moreover, the significantly higher values of Tp-e, Tp-e/QT, and Tp-e/QTc were also observed in patients with benign paroxysmal positional vertigo who were admitted to the emergency department when compared to the healthy population, suggesting that these patients might be prone to cardiac arrhythmias [136].

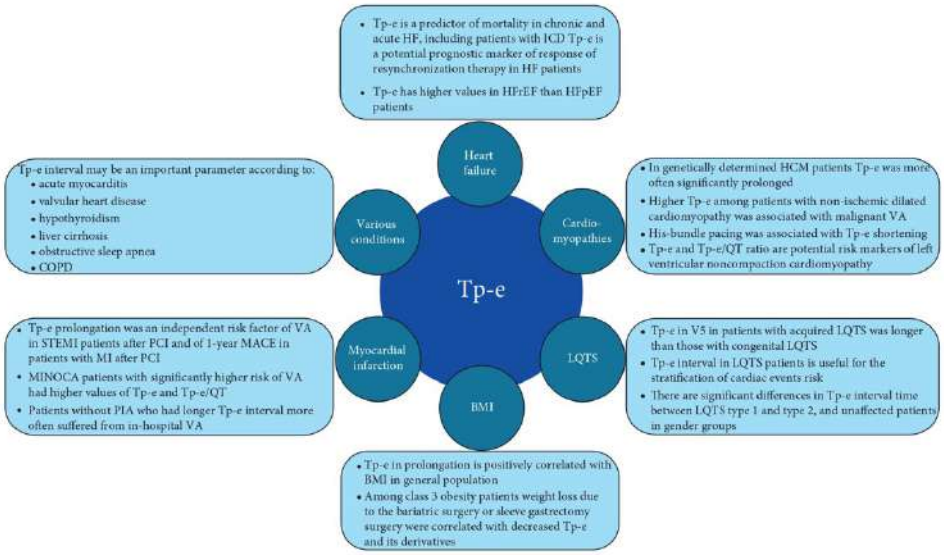

FIGURE 3: Tp-e interval: current state of knowledge summary.

4. Conclusions

In conclusion, Tp-e and its derivatives are very promising ECG markers. Tp-e may be a potential marker in several groups of patients; in each, it may provide different vital clinical prognoses. It can be associated with the genetic background of certain diseases, e.g., LQTS or HCM. Moreover, its prolongation may help stratify patients' prognosis among patients with HF cardiomyopathy after several invasive management procedures and those with MI treated by PCI.

In the case of obesity, studies considering conditions from normal weight through overweight and subsequent classes of obesity would be particularly valuable. The role of Tp-e in VA and SCD is visible, although situations should be evaluated in meta-analysis to reach a consensus on that issue. More randomized trials are needed to define the parameters influencing Tp-e duration and the value of its derivatives, and more studies are required to precisely evaluate the association between Tp-e and derived parameters of diseases examined in this study (Figure 3).

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this study.

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PUBLIKACJA 4

The Prevalence of Arrhythmias, Including Premature Supraventricular and Ventricular Beats and Other Electrocardiographic Patterns, in 24-Hour Holter Monitoring in Patients with Overweight and Obesity

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The Prevalence of Arrhythmias, Including Premature Supraventricular and Ventricular Beats and Other Electrocardiographic Patterns, in 24-Hour Holter Monitoring in Patients with Overweight and Obesity

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Abstract: Objectives: this study aims to evaluate the prevalence of various arrhythmias and other electrocardiographic patterns within the group of individuals with overweight and obesity. Methods: One hundred eighty-one adults (90 females and 91 males) were qualified for inclusion in the experimental group. All participants had a body mass index (BMI) exceeding 25 kg/m^2 (98 patients with obesity and 83 with overweight). The mean BMI in the obesity group was 33.6 kg/m^2, and all participants had class 1 obesity. The control group comprised 69 individuals (56 females and 13 males) with normal BMI. The basic measurements were performed, and the participants filled out questionnaires describing their health conditions and lifestyles. Each participant underwent an electrocardiographic (ECG) examination and a 24 h Holter ECG examination. Results: In patients with class 1 obesity compared to the control patients, the average numbers of premature ventricular beats (PVBs) and premature supraventricular beats (SPBs) were statistically significantly higher ($p = 0.030$ and $p = 0.042$). There was a positive correlation between body weight and PVB ($p = 0.028$) and between body weight and SPB ($p = 0.028$). Moreover, BMI and waist circumference were correlated with SPB ($p = 0.043$ and $p = 0.031$). In the backward stepwise multivariate regression model considering 24 h Holter ECG monitoring, concerning SPB as the dependent variable, it was observed that BMI (especially obesity class 1), type 2 diabetes, and thyroid disease exhibited the highest regression coefficients. Conclusions: obesity, even in class 1, might be a factor in a more frequent occurrence of abnormalities in electrocardiographic tests.

Keywords: electrocardiography; body mass index; premature ventricular beats; premature supraventricular beats; waist–hip ratio

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1. Introduction

In recent decades, the global prevalence of obesity and overweightness has reached pandemic proportions, giving rise to a myriad of health concerns. According to the World Health Organization (WHO), in 2022 [1], the global population of individuals with overweight and obesity reached 2.5 billion. Approximately 43% of all adults worldwide were classified as overweight and 16% as obese. An even more alarming fact is that the number of individuals with obesity nearly doubled between 1990 and 2022. Eurostat reported that 53% of the

combined adult population of the EU, Norway, Serbia, and Turkey had BMI > 25 kg/m^2. Moreover, according to data from a European health interview survey, more men than women were overweight in each country. There was also a noticeable relationship between an increase in the percentage of the overweight population and age [2]. According to data published in 2021 by GUS (Polish Central Office of Statistics), in Poland, in 2019, 57% of adults had excessive body weight (overweight or obesity), whereas in 2014, it was slightly over 53%. Over the past few years, the percentage of adults with obesity in Poland has been steadily increasing [3]. It has been estimated that by 2025, in Poland, 26% of women and 30% of men will be classified as obese.

One particularly concerning aspect is the intricate relationship between excessive body weight and the development of cardiac arrhythmias. Heart rhythm is usually characterized by abnormal heart rate and has attracted considerable attention due to its potential relationship with cardiovascular events. As a consequence of the obesity epidemic, understanding the underlying mechanisms that link obesity and arrhythmias has become imperative in the realm of both clinical and research endeavors. To date, there have been studies addressing the issue of arrhythmia in individuals with overweight and obesity. Mainly, the currently available literature on this topic suggests an increased prevalence of arrhythmia among these patients, especially in the form of atrial fibrillation (AF) [4]. Other available studies have revealed similar results. They also describe the relationship between the incidence of AF and weight loss [5–7].

Noting that excessive weight has emerged as a significant global health issue and some reports have indicated that being overweight and obese could predispose individuals to arrhythmia, this study aims to evaluate the prevalence of various arrhythmias and other electrocardiographic patterns within the group of individuals with overweight and obesity.

2. Materials and Methods

2.1. Study Population

This study was conducted at the Department of Pathophysiology of Wroclaw Medical University from 2020 to 2023. Ethical consent for this study was obtained from the Wroclaw Medical University Ethics Committee, ensuring adherence to the principles of Good Clinical Practice and the Declaration of Helsinki.

A total of 181 adults (90 females and 91 males) of the Caucasian race were qualified for the experimental group. The patients were selected from the population of Wroclaw and the nearby regions of Lower Silesia, Poland. Studies were carried out in the Department of Pathophysiology, and all participants were volunteers who had previously participated in other studies in the department. They were recruited when they met the inclusion criteria and signed the informed consent form after accepting the study rules. No payment or incentive was offered for participation. The exclusion criteria were age below 18 years, BMI below 18.5 kg/m^2, presence of implantable devices, and being a professional athlete. Moreover, the participants whose ECG was missing or whose questionnaires were filled out incompletely were excluded from this study. All these participants had a BMI exceeding 25 kg/m^2 (98 patients had obesity, and 83 were overweight). The control group comprised 69 individuals (56 females and 13 males) with normal BMI—the characteristics of the study and control groups are presented in Table 1. Appendix A includes a flowchart illustrating the selection of participants (Figure A1).

Table 1. Clinical characteristics of the studied subgroups.

Parameter	Entire Study Group (n = 250)	Obesity (A, n = 98)	Overweight (B, n = 83)	Control Group (C, n = 69)	$p < 0.05$
Age (years)	59.94 ± 13.22	61.18 ± 11.07	53.40 ± 13.70	58.83 ± 15.33	ns
Gender (%/n)					
Male	41.6/104	50.0/49	50.6/42	18.8/13	A vs. C: 0.001
Female	58.4/146	50.0/49	49.4/41	81.2/56	B vs. C: 0.001

Table 1. *Cont.*

Parameter	Entire Study Group (n = 250)	Obesity (A, n = 98)	Overweight (B, n = 83)	Control Group (C, n = 69)	$p < 0.05$
Height (cm)	167.37 ± 9.76	168.14 ± 9.65	168.64 ± 10.36	164.76 ± 8.78	ns
Weight (kg)	80.42 ± 17.50	95.09 ± 13.24	78.39 ± 11.10	62.02 ± 7.99	A vs. B: 0.001 A vs. C: 0.001 B vs. C: 0.001
BMI (kg/m^2)	28.64 ± 4.99	33.62 ± 3.26	27.56 ± 1.34	22.86 ± 1.71	A vs. B: 0.001 A vs. C: 0.001 B vs. C: 0.001
Waist (cm)	95.99 ± 14.26	107.29 ± 10.16	95.29 ± 8.55	79.72 ± 7.55	A vs. B: 0.001 A vs. C: 0.001 B vs. C: 0.001
Hip circumference (cm)	106.60 ± 12.16	115.23 ± 7.32	104.26 ± 5.23	93.83 ± 14.14	A vs. B: 0.001 A vs. C: 0.001 B vs. C: 0.001
WHR	0.95 ± 0.74	0.93 ± 0.08	0.91 ± 0.09	1.05 ± 1.56	ns
Hypertension (%/n)	52.8/132	64.3/63	50.6/42	39.1/27	A vs. C: 0.001 B vs. C: 0.048
Myocardial infarction (%/n)	6.4/16	7.1/7	7.2/6	4.3/3	ns
Stroke (%/n)	2.8/7	2.0/2	3.6/3	2.9/2	ns
Atrial fibrillation (%/n)	8.8/22	8.2/8	12.0/10	5.8/4	ns
Deep vein thrombosis (%/n)	3.6/9	7.1/7	1.2/1	1.4/1	ns
Type 2 diabetes (%/n)	13.2/33	21.4/21	10.8/9	4.3/3	A vs. C: 0.002
Thyroid disease (%/n)	16.4/41	16.3/16	13.2/11	20.3/14	ns
Smoking (%/n)	13.2/33	9.2/9	15.8/13	15.9/11	ns

BMI—body mass index; WHR—waist–hip ratio; ns—not statistically significant ($p > 0.05$).

2.2. Trial Design

The participants filled out the informed consent form to participate in this study and were subsequently provided with a detailed description of the procedures. In the initial phase of the research, the participants were asked to fill out a specialized questionnaire, including inquiries about various domains of their lifestyle, such as physical activity, the consumption of alcohol and other stimulants, smoking, dietary patterns, medical conditions, family medical history and psychological background. None of the participants declared in the questionnaire a personal and/or family history of genetic rhythm disorders. Additionally, none of them stated an incidence of illicit drug use, as well as any other stimulants except for coffee, which was used in small quantities, 1–3 cups per day. BMI was calculated by dividing body weight in kilograms by the square of height in meters. WHR (waist-to-hip ratio) was calculated by dividing waist circumference by hip circumference in centimeters. Both measurements adhered to the guidelines specified in the WHO protocol [8,9]. The 12-lead ECG and 24 h Holter ECG examination were performed in the next part of the study. Twenty-four-hour Holter ECG was performed on a typical day for participants to ensure that the collected data were reliable and that they were not affected by unusual behavior from the participants.

The ECG was recorded and analyzed at a speed of 25 mm/s. At first, ECGs were analyzed by two medicine students trained in electrocardiography and verified by two cardiologist members of the study team. Twenty-four-hour Holter ECG analysis was examined by the cardiologist-in-training and then verified by the skilled cardiologist. The values of each parameter were presented as the maximum, minimum, and mean values with SD. Additionally, this study was extended to include the RR interval variability, that is, time-domain heart rate variability analysis according to the classic standards by the Task

Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology [10].

2.3. Statistical Analysis

A statistical analysis was conducted using the licensed CSP "STATISTICA 13" (StatSoft Poland, Kraków, Poland). For quantitative variables, arithmetic means (x) and standard deviations (SD) were calculated for the parameters recorded in the studied groups. The distribution of variables was tested with the W Shapiro–Wilk test. In the case of the quantitative variables of normal distribution, a further statistical analysis used the univariate ANOVA variance analysis. The ANOVA Kruskal–Wallis analysis was also used for non-normally distributed and quantitative variables. Statistically significant differences between the arithmetic means were determined by the post hoc Newman–Keuls test. Results for qualitative variables were expressed in the form of percentage lists. The chi-squared test of maximum likelihood was used in further statistical analysis for qualitative variables. Correlation and regression analyses were performed to determine the relationship between the studied variables. In the case of variables with normal distribution, the Pearson r correlation coefficients were determined; in the case of variables not normally distributed, the Spearman r coefficients were established. Regression analysis was performed using the multivariate backward stepwise method. The parameters of models obtained in the regression analysis were estimated using the technique of least squares. Results at $p < 0.05$ were assumed to be statistically significant.

3. Results

There were statistically more arterial hypertension patients in the group of individuals with obesity and overweight in comparison to the control group, as well as more type 2 diabetes cases in patients with obesity than in the control group. All characteristics of the entire study group and its subgroups are presented in Table 1.

During the 24 h Holter ECG monitoring, the mean heart rate (HR) was 72.73 ± 0.55 bpm, with a minimum of 53.93 ± 0.50 bpm and a maximum of 117.33 ± 1.19 bpm. Instances of bradycardia (27.94 ± 9.15 with a mean of 38.39 ± 4.37 bpm) and tachycardia (23.02 ± 12.70 with 149.16 ± 20.39 bpm) were observed. The occurrence of premature ventricular and supraventricular beats was as follows: PVBs (premature ventricular beats) 308.39 ± 88.75 and SPBs (premature supraventricular beats) 374.10 ± 129.18. Then, the variability of the RR interval and time-domain heart rate was analyzed. The full results are summarized in Tables 2 and 3.

Table 2. Parameters of 24 h Holter ECG monitoring in the entire study group.

Parameters	Mean ± SD
HR min (bpm)	53.93 ± 0.50
HR max (bpm)	117.33 ± 1.19
HR mean (bpm)	72.73 ± 0.55
SPB	308.39 ± 88.75
PVB	374.10 ± 129.18
Bradycardia	27.94 ± 9.15
Bradycardia (bpm)	38.39 ± 4.37
Tachycardia	23.02 ± 12.70
Tachycardia (bpm)	149.16 ± 20.39
VT	0.11 ± 0.05
SVT	2.72 ± 1.38
AF (average number of episodes)	0.16 ± 0.12
Ventricular rhythm	0.06 ± 0.04

HR max—maximum heart rate; HR mean—average heart rate; HR min—minimum heart rate; SPB—premature supraventricular beat; PVB—premature ventricular beat; bradycardia min—minimum beats per minute; tachycardia max—maximum beats per minute; VT—ventricular tachycardia; SVT—supraventricular tachycardia; AF—atrial fibrillation.

Table 3. Parameters of time-domain heart rate variability (HRV) analysis in the entire study group.

Parameters	Mean ± SD
24 h monitoring (6:00–6:00)	
mRR (ms)	828.42 ± 103.06
SDNN (ms)	150.05 ± 49.14
rMSSD (ms)	36.11 ± 41.46
SDSD (ms)	26.65 ± 29.06
pNN50 (%)	8.88 ± 13.98
Daily activity (6:00–22:00)	
mRR (ms)	771.61 ± 102.59
SDNN (ms)	112.26 ± 38.55
rMSSD (ms)	31.79 ± 37.79
SDSD (ms)	23.37 ± 26.65
pNN50 (%)	7.02 ± 13.36
Night rest (22:00–6:00)	
mRR (ms)	960.74 ± 137.51
SDNN (ms)	107.57 ± 39.93
rMSSD (ms)	43.30 ± 52.70
SDSD (ms)	30.03 ± 34.42
pNN50 (%)	12.90 ± 17.38

mRR—mean RR interval during sinus rhythm; pNN50—NN50 count divided by the total number of all NN intervals; rMSSD—the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDNN—standard deviation of all NN intervals; SDSD—standard deviation of differences between adjacent NN intervals.

In the 24 h Holter ECG monitoring within the study subgroups (A, B, C), statistical significance was observed in the incidence of PVB and SPB, with these findings being significantly more common in the obese group when compared with the control group. No other significant differences in 24 h Holter ECG parameters, indicating irregular rhythm, were observed between the groups. The prevalence of atrial fibrillation in both the overweight and obesity groups was slightly higher than in the control group (where it was 0%). However, atrial differences are not significant. Tachycardia incidence in the obese and overweight groups was higher than in the control individuals; however, the difference did not reach significance. Figure 1 contains representative ECG recordings of SPB and PVB.

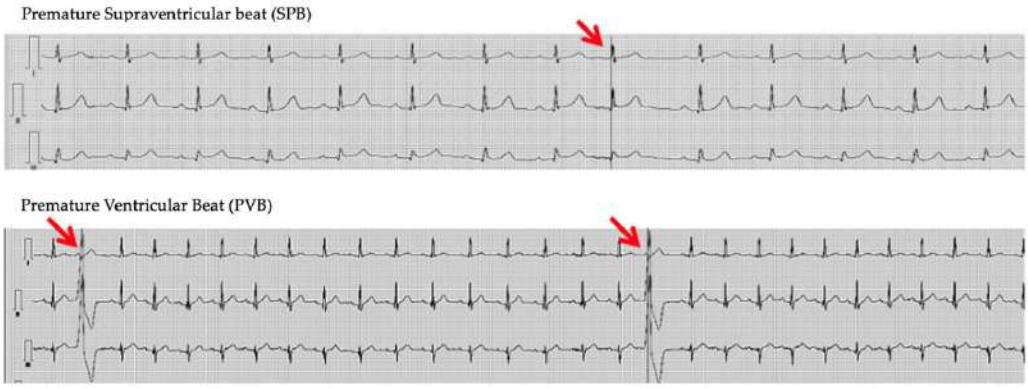

Figure 1. Typical ECG recordings of SPB and PVB found in our study group (indicated by the arrow).

Tables 2 and 4 summarize the 24 h Holter ECG monitoring parameters for the entire study group and its subgroups.

Table 4. Parameters of 24 h Holter ECG monitoring in the study subgroups.

Parameter	Obesity (A, *n* = 98)	Overweight (B, *n* = 83)	Control Group (C, *n* = 69)	$p < 0.05$
HR min (bpm)	54.32 ± 0.65	53.52 ± 0.73	53.87 ± 1.32	ns
HR max (bpm)	113.38 ± 1.71	118.20 ± 2.18	118.89 ± 2.31	ns
HR mean (bpm)	72.47 ± 0.85	72.17 ± 0.86	73.78 ± 1.19	ns
PVB	573.52 ± 218.17	171.18 ± 59.07	96.87 ± 23.30	A vs. C: 0.030
SPB	620.20 ± 301.46	359.19 ± 153.89	42.49 ± 6.18	A vs. C: 0.042
Bradycardia	29.96 ± 18.61	33.20 ± 15.18	18.74 ± 8.51	ns
Bradycardia (bpm)	38.00 ± 4.79	38.89 ± 4.38	38.27 ± 3.85	ns
Tachycardia	35.32 ± 31.04	19.42 ± 10.90	9.88 ± 3.10	ns
Tachycardia (bpm)	147.42 ± 19.10	151.36 ± 24.00	148.16 ± 17.42	ns
VT	0.15 ± 0.09	0.13 ± 0.10	0.03 ± 0.02	ns
SVT	1.17 ± 0.44	3.70 ± 3.21	3.76 ± 3.17	ns
AF (average number of episodes)	0.06 ± 0.04	0.41 ± 0.36	0.00 ± 0.00	ns
Ventricular rhythm	0.10 ± 0.10	0.06 ± 0.05	0.01 ± 0.01	ns

HR max—maximum heart rate; HR mean—average heart rate; HR min—minimum heart rate; ns—not statistically significant ($p > 0.05$); SPB—premature supraventricular beat; PVB—premature ventricular beat; bradycardia min—minimum beats per minute; tachycardia max—maximum beats per minute; VT—ventricular tachycardia; SVT—supraventricular tachycardia; AF—atrial fibrillation.

In HRV analysis, only mRR in 24 h monitoring and mRR during daily activity were significantly higher in the obese and overweight subgroups than in the control subgroup. As for SDNN, the known time-domain parameter, there was only a trend toward lower values in the overweight subgroup compared to the controls; however, it did not reach statistical significance.

No statistically significant correlations were found between the study group's body mass parameters and time-domain heart rate variability parameters. The results of this analysis are presented in Table 5.

Table 5. Parameters of time-domain heart rate variability (HRV) analysis in the study subgroups.

Parameters	Obesity (A, *n* = 98)	Overweight (B, *n* = 83)	Control group (C, *n* = 69)	$p < 0.05$
24 h monitoring (6:00–6:00)				
mRR (ms)	815.11 ± 77.60	867.50 ± 120.08	785.49 ± 92.20	A vs. C: 0.046 B vs. C: 0.014
SDNN (ms)	147.10 ± 40.67	147.35 ± 58.91	159.47 ± 46.17	ns
rMSSD (ms)	42.79 ± 63.12	29.64 ± 11.89	35.77 ± 25.09	ns
SDSD (ms)	30.72 ± 42.97	21.70 ± 9.22	28.11 ± 21.78	ns
pNN50 (%)	10.59 ± 20.16	7.72 ± 7.49	7.98 ± 9.85	ns
Daily activity (6:00–22:00)				
mRR (ms)	759.95 ± 80.95	810.30 ± 109.98	726.55 ± 105.14	A vs. C: 0.045 B vs. C: 0.011
SDNN (ms)	113.56 ± 34.41	107.38 ± 41.11	118.22 ± 42.24	ns
rMSSD (ms)	36.86 ± 57.20	26.88 ± 11.02	31.54 ± 24.91	ns
SDSD (ms)	26.26 ± 38.80	19.62 ± 9.00	24.82 ± 22.02	ns
pNN50 (%)	8.61 ± 19.86	5.93 ± 6.32	6.20 ± 7.97	ns
Night rest (22:00–6:00)				
mRR (ms)	938.84 ± 102.87	1003.92 ± 168.56	925.27 ± 118.54	ns
SDNN (ms)	108.81 ± 44.16	101.56 ± 32.11	115.35 ± 45.24	ns
rMSSD (ms)	54.14 ± 80.10	34.82 ± 15.26	39.38 ± 30.72	ns
SDSD (ms)	36.93 ± 52.14	24.41 ± 10.78	27.88 ± 20.27	ns
pNN50 (%)	14.86 ± 22.46	11.83 ± 11.53	11.44 ± 16.67	ns

mRR—mean RR interval during sinus rhythm; ns—not statistically significant ($p > 0.05$); pNN50—NN50 count divided by the total number of all NN intervals; rMSSD—the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDNN—standard deviation of all NN intervals; SDSD—standard deviation of differences between adjacent NN intervals.

The were correlations between body weight and the occurrence of PVB (r = 0.14, $p = 0.028$) and SPB (r = 0.14, $p = 0.028$). Furthermore, both BMI and waist circumference were found to be positively correlated with SPB. The linear relationship found in the current study is presented in Table 6.

Table 6. Correlations between body mass parameters and 24-hour Holter ECG monitoring parameters in the entire study group.

Parameter	Body Weight (kg)	BMI (kg/m^2)	Waist Circumference (cm)	Hip Circumference (cm)	WHR
HR min (bpm)	ns	ns	ns	0.30 ($p = 0.010$)	ns
HR max (bpm)	ns	ns	ns	ns	ns
HR mean (bpm)	ns	ns	ns	ns	ns
PVB	0.14 ($p = 0.028$)	ns	ns	ns	ns
SPB	0.14 ($p = 0.028$)	0.13 ($p = 0.043$)	0.14 ($p = 0.031$)	ns	ns
Bradycardia	ns	ns	ns	ns	ns
Bradycardia (bpm)	ns	ns	ns	ns	ns
Tachycardia	ns	ns	ns	ns	ns
Tachycardia (bpm)	ns	ns	ns	ns	ns
VT	ns	ns	ns	ns	ns
SVT	ns	ns	ns	ns	ns
AF	ns	ns	ns	ns	ns
Ventricular rhythm	ns	ns	ns	ns	ns

BMI—body mass index; WHR—waist–hip ratio; HR max—maximum heart rate; HR mean—average heart rate; HR min—minimum heart rate; ns—not statistically significant ($p > 0.05$); SPB—premature supraventricular beat; PVB—premature ventricular beat; bradycardia min—minimum beats per minute; tachycardia max—maximum beats per minute; VT—ventricular tachycardia; SVT—supraventricular tachycardia; AF—atrial fibrillation.

Regression analysis assessed the importance of other variables and co-occurring conditions for the linear relationships shown in the correlation analysis. Models were estimated for PVB and SPB as dependent variables using anthropometric parameters, comorbidities, and smoking as potential independent variables. The estimation was made using backward stepwise multivariate analysis. A statistically significant model was obtained for SPB: SPB = 82.292 BMI + 791.956 type 2 diabetes + 918.975 thyroid disease. It was observed that higher BMI, type 2 diabetes, and thyroid disease are independently associated with higher SPBs. The full results are summarized in Table 7. Appendix A includes a chart presenting this study's key findings (Figure A2).

Table 7. Backward stepwise multiple regression models in the entire study group for SPB as the dependent variable.

Model for: SPB			
	BMI (kg/m^2)	**Type 2 Diabetes**	**Thyroid Disease**
Regression coefficient (RC)	82.292	791.956	918.975
SEM of Rc	39.721	384.861	352.687
p	0.037	0.040	<0.025
p for the model	0.001		

4. Discussion

Obesity is the excessive accumulation of body fat, which can result in health problems [1]. Visceral abdominal fat poses a greater health risk compared to total body fat. There are many indicators proposed for patient evaluation, such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), fat mass index (FMI), fat-free mass index (FFMI), and fat mass body percentage (FM%). Body mass index has been the standard measure used to classify obesity for years and is still widely utilized for its feasibility and non-invasive character. Nevertheless, none of the above indices individually was an effective cardiovascular predictor [11].

A holistic approach allows for the more efficient treatment of complex diseases such as obesity. Patients with obesity are in the risk group for many cardiovascular and noncardiovascular diseases. Due to obesity's impact on the cardiovascular system, cardiologists need to be involved in the diagnostic team. Countless studies unequivocally demonstrate that excess body weight is a significant risk factor for mortality and morbidity, including sudden cardiac death (SCD) [12]. Various underlying pathophysiological mechanisms contribute to this association. These include a higher prevalence of risk factors for cardiovascular diseases, as well as the presence of both electrical and structural ventricular remodeling, chronic inflammation, and an imbalance in the autonomic nervous system [11].

In our study, the prevalence of arrhythmias and other pathologies in 24-hour Holter monitoring in people with class 1 obesity and overweight was investigated. The analysis of the collected data indicates a significant increase in premature supraventricular beat (SPB) and premature ventricular beat (PVB), respectively, among participants with obesity (subgroup A) and participants who were overweight (subgroup B) when compared to the control group (subgroup C). PVB exhibited a strong correlation with body weight and both weight indexes. Moreover, our study revealed a positive linear correlation between body mass, SPB, and PVB. It is important to emphasize that while a linear correlation was observed between SPB and body weight, WHR, and BMI, in the case of PVB, this linear relationship was only observed according to body weight. The other types of arrhythmias occurred infrequently and were consistent with the prevalence in the normal weight control group.

Similar studies have been recently conducted by Skovgaard et al., and they included adults with overweight or obesity without cardiovascular diseases [13]. During a 24-hour Holter examination, they observed sinus tachycardia, which was present in 97% of participants, being the most common arrhythmia in this group. SPBs were present in 68% of patients, PVBs in 64% of patients, and sinus bradycardia in 34% of patients. There was a low prevalence of cases when PVBs were more than 200/24 h, only in 3% of the study group, and supraventricular premature beats were only generally presented without a detailed analysis. Ultimately, the authors claimed that these arrhythmias occur with the same frequency in people with normal weight, and additionally, no association between BMI and the occurrence of arrhythmias was found. However, the study has some flaws. First, it aims to analyze a healthy population with the strict inclusion criteria used during screening: the phase 1 clinical trial participants. It may be suggested that the authors' policy was to select the proper group of participants with obesity or who were overweight for the forthcoming experiments. Moreover, it was commented that higher numbers of arrhythmias could be expected if less strict screening is applied. In this aspect, the data may not represent the frequency of abnormalities in an unselected population. In the abovementioned study, there was no division of the study group according to class of obesity, and it was mixed with overweight in statistical analysis. Eventually, the mean age was 36, compared to around 59.94 years in our study.

In the study from 2016 by Hingorani et al. conducted on 1363 healthy subjects, 1000 males and 273 females, aged 18–65 years, the authors found the general occurrence of SPBs at 60.8% and PVBs at 43.4%, when >200 PVBs per 24 h was detected in 3.3% patients. Supraventricular tachycardia was present in 2.2% of cases. Then, nonsustained ventricular tachycardia was present in 0.7% and second-degree AV block in 2.4% [14]. The group under study consisted of healthy volunteers in a clinical trial. The goal was like the abovementioned study of Sovgaard et al. from 2023; however, it was simultaneously not devoted to those with obesity and overweight [13]. Comparing the mentioned research studies with ours, it should be underlined that the unique feature of our study is the selection of random volunteers who were obese and overweight who suffered from some complications that are common in this group, including hypertension and diabetes mellitus. From this point of view, we present a more realistic survey of the arrhythmia prevalence in class 1 obesity and overweight. Moreover, we carried out a comparison of both subgroups, finding more pathologies in the class one obesity group than in overweight. Another

study worth mentioning was conducted by Bienias et al., which included healthy young adults with class 3 obesity (BMI >40 kg/m2). The authors found no increased risk of arrhythmias in them compared to adults with normal weight. However, cardiac autonomic dysfunction was observed in morbidly obese participants through the assessment of heart rate variability and turbulence, which was impaired [15].

Some authors found a relationship between higher heart rate and obesity alone or co-existing with diabetes mellitus; however, in our study, we observed a higher prevalence of tachycardia in individuals with obesity, which did not reach statistical significance [16]. The explanation for the findings may be that the group was not numerous enough in our study, and first of all, our study group consisted of patients with obesity class 1 only. Moreover, some of our patients were taking beta blockers, which could have affected the occurrence of tachycardia in the studied population. In a recent study conducted by Binu et al., it was found that tachycardia is quite a common phenomenon in obese individuals (14.7%) and even more common in patients with morbid obesity (23.3%) [16].

The relationship between obesity and the sympathetic nervous system is still being discussed in the literature. Some studies have stated that increased sympathetic activity is an effect of obesity [17–19]. The review by Valensi describes sympathetic nervous system dysfunction leading to obesity, especially with visceral adiposity [20]. McCully et al.'s study showed, in mice, that autonomic dysfunction can affect excessive epicardial fat and lead to chronic inflammation and oxidative stress [21]. Moreover, people with obesity had higher heart rates than individuals with normal weight. The authors have explained it via the imbalance in the autonomic nervous system caused by a reduction in parasympathetic function in people with obesity [18,22]. Other studies have found that autonomic imbalance is connected to a higher risk of ventricular arrhythmia and sudden cardiac death in people who are obese [17,18]. It is also worth mentioning that in the study by Espinoza-Salinas et al., autonomic dysregulation was found both in adults who were overweight r had obesity [23].)

HRV is one method that can be used to evaluate sympathetic activity. In our study on analysis of the HRV time domain, only mRR in 24-hour monitoring and mRR during daily activity were significantly higher in patients who were obese and overweight than in the control group, and there was only a trend toward lower SDNN values in people with obesity. However, it did not reach the statistically significant level. In our study group, there were people only with class one obesity, and it is possible that if more individuals from class 2 and 3 were included, these differences would be significant. We also found no significant correlations between the study group's body mass parameters and time domain heart rate variability parameters.

A study on a healthy Korean population found that body mass parameters were negatively associated with HRV parameters. However, the association of WHR and percentage of body fat mass were stronger indicators of HRV changes than BMI [24]. Another study including Taiwanese nurses found that nurses with higher waist circumferences had significantly lower power of low-frequency spectrum (LF), power of high-frequency spectrum (HF), and SDNN from time domain HRV analysis. BMI had a significant negative association with the power of very low-frequency spectrum (VLF) and SDNN [25]. Yadav et al.'s study found that increased WHR was strongly associated with reduced cardiac parasympathetic activity (measured as SDNN, RMSSD, NN50 count, pNN50, HF indices in milliseconds squared, and SD1) and increased sympathetic activity (LF/HF) in patients with obesity [22].

There are many other ways by which obesity might influence the pathophysiology of arrhythmia. They include metabolic disturbances, structural and electrical remodeling, neurohormonal adaptation, and associated diseases. Obesity is often associated with coexisting conditions like hypertension and obstructive sleep apnea. Hypertension leads to left ventricular hypertrophy (LVH) and can result in heart failure, which itself increases the prevalence of ventricular arrhythmia and SCD [26]. Valencia-Flores et al. found that patients who were morbidly obese with severe sleep apnea and oxygen saturation $\leq$65%

had a higher risk of cardiac arrhythmias [27]. However, obesity may also lead to the development of atrial cardiomyopathy by affecting the hemodynamics of the heart [28].

Hemodynamic stress that comes from hypervolemia in patients with obesity increases cardiac output and leads to LVH [17,26]. Obesity causes an increase in pressure in the pulmonary circulation, resulting in right ventricular hypertrophy, which further leads to left ventricular hypertrophy. Subsequently, LVH contributes to left atrial dysfunction and hypertrophy, which may predispose to the development of AF. Fibrotic atrial cardiomyopathy (FACM) may contribute to AF and reduce the odds of spontaneous conversion to sinus rhythm [29]. Obesity also leads to chronic systemic inflammation, an important factor for FACM development and progression, because of the high metabolic activity of pro- and anti-inflammatory adipokines [17,29].

The high metabolic activity of adipocyte tissue leads to many metabolic disturbances. Some of the most important adipokines that should be mentioned are leptin, adiponectin, and ghrelin [11,26]. Leptin, primarily produced by white adipose tissue, significantly impacts various body functions [11,26]. High leptin levels were associated with LVH, increased myocardial fat volume, and cardiomyocyte hypertrophy [17]. It is also believed to stimulate the sympathetic component of the autonomous nervous system and be a factor in LVH inpatients with obesity [17,30,31]. The activity of the parasympathetic component is reduced, and the activity of the sympathetic component is increased, and as a result, both heart rate and blood pressure increase. Furthermore, leptin plays a crucial role in regulating the phenotype of fibroblasts, thus initiating a fibrogenic process [17].

A low adiponectin level, another important adipokine found in individuals with obesity, might result in LVH [26]. Adiponectin, a remarkable insulin-sensitizing adipokine, is produced solely by adipocytes. It is pivotal in enhancing insulin sensitivity, warding off arteriosclerosis, and reducing inflammation [17].

Neurohormonal adaptation associated with modification of the autonomic tone leads to a decrease in HRV. It also impacts the activation of the renin-angiotensin–aldosterone system, leading to high levels of Aldactone and, as a result, systolic and diastolic dysfunction, LVH, and myocardial fibrosis—another important factor of ventricular arrhythmia susceptibility [26]. Due to obesity, changes in cardiac cellular electrophysiology can lead to alterations in ion channels I_{Na}, $I_{Ca,L}$, and K_{ATP}. In animal models of obesity, the expression of the inward potassium current clearly decreases and results in action potential prolongation, QTc prolongation, and a higher incidence of PVBs. Using a K_{ATP} channel opener reduced that effect, showing K_{ATP} channel inhibition in obese cardiomyocytes. Some studies also describe other proarrhythmic changes to calcium and sodium channels resulting in severe disturbance in calcium metabolism, which could lead to a higher incidence of ventricular arrhythmias [17].

Patel et al. suggested that obesity's pro-arrhythmogenic role results from atrial remodeling and increased epicardial adipose tissue volume. Both were proven to cause changes in the heart's conduction parameters, especially the P-wave parameters. Moreover, the role of comorbidities often coexisting with obesity was also highlighted as a possible factor leading to AF [4,32].

The literature documents the association between excessive body weight and AF. Several studies correlated a higher risk of AF with obesity, as the growing occurrence of transition from paroxysmal to persistent atrial fibrillation [11,32–35]. In our study, we observed an increase in the occurrence of AF among individuals with obesity or who were overweight compared to patients with normal weight. However, this observation did not reach statistical significance. Additionally, in patients with class 1 obesity, cases of atrial fibrillation and other serious arrhythmias were not frequent. There are also studies in the literature that commented on a relationship between weight loss and reduction in the incidence of AF [5–7].

PVBs and especially frequent PVBs ($\geq$ one time during a standard electrocardiographic recording or $\geq$30 times over a 1-hour recording) were found to be linked with increased probability for SCD in patients with structural heart disease [26,36].

In the retrospective cohort study of cardiac MRI conducted by Wang et al., epicardial adipose tissue was linked to a higher incidence of PVBs and all-cause of mortality from SCD [26,37]. However, Wang's study also revealed higher occurrences of tachyarrhythmia and atrial fibrillation, which was less observed in our cohort. The study mentioned above was conducted on 402 patients with PVBs, among whom 249 were at least overweight (defined as BMI $\geq$24 kg/m^2). The control group consisted of 249 participants; in this group, 207 individuals were classified as having excessive weight.

PVBs are predictors of numerous cardiovascular diseases. However, von Rotz et al.'s study investigated the occurrence of PVBs in healthy young adults, and it was found that PVBs are common even in populations without any cardiovascular comorbidities. PVBs occurred at least once in 68,7% of participants in their study. However, the number of PVBs depended on several risk factors, including increased WHR [38].

Sabbag et al.'s study found that individuals who were overweight and obese have a higher risk of occurrence of ectopic ventricular arrhythmia during exercise than individuals with normal weight [39]. The risk increased gradually with an increase in BMI. Moreover, the authors suggested that the increased risk of ventricular arrhythmias may predict a higher risk of sudden cardiac death in featured susceptible populations.

Our findings met statistical significance, but the question remains if they would be clinically significant. There is a need for further research into the long-term effects of those arrhythmia incidences and their correlations with AF and heart failure. Måneheim et al.'s study found an independent association between PVB recorded on 24-hour electrocardiogram monitoring and AF and heart failure, and this effect was altered by SPB frequency. The follow-up for that study was 17 years long and found that the coexistence of both PVBs and SPBs also accumulates the risk of occurrence of AF and/or HF, especially if PVBs were multiform [40]. Aizawa et al.'s study observed that some parameters of P-wave (P-wave durations greater than 130 ms), P-wave morphology, SPBs, PVBs, or runs could be associated with the significant risk of AF. However, the studies were not dedicated to people with obesity or who were overweight [41]. Our conclusions may indicate the adverse remodeling that, if given sufficient time, would eventually lead to clinically significant increases in hemodynamically impactful arrhythmia burden. Therefore, more studies should be performed on patients with class 2 and 3 obesity in the future.

The current study has some limitations. Firstly, the studied population was restricted to a relatively small sample group. Moreover, the participants came from only a small part of Poland, which means there is no ethnic diversity in the studied population. Due to this, the study results cannot be generalized to non-Caucasian people or Caucasian people from other world regions. Furthermore, we have not observed participants' examination results for an extended period, so we were limited to single-day observations. The short observation period likely underestimates the number of arrhythmias occurring in the patients. Another limitation is that the study included only normal-weight, overweight, and class 1 obesity patients. Due to this, we could not observe the prevalence of arrhythmias in patients with class 2 and 3 obesity and compare it to the BMI groups included in the study.

Additionally, echocardiography was not performed at the screening visit as it was not feasible in this study. Potentially, it could provide new information. If the Holter monitoring had been extended to 48 h, more arrhythmias, especially atrial fibrillation, could have been identified. Furthermore, BMI is a measurement that only accounts for a person's weight and height and does not differentiate between lean mass and fat mass. The study could have been improved by including additional bioelectrical impedance analysis (BIA) to consider body composition.

A similar study, with a larger group of participants, could provide more valuable data concerning arrhythmias in different BMI groups, including the influence of age, sex, and coexisting chronic diseases, e.g., hypertension. Furthermore, other populations also should be studied. A longitudinal study would be fascinating regarding the possibility of observing the incidence of arrhythmias with changing age, comorbidities, and BMI. In the age of wide usage of weight-loss medication, it seems crucial to study the relationship

between body mass and its distribution and arrhythmias, not only AF but also other supraventricular and ventricular arrhythmias, and to use that knowledge in clinical use. Adopting such information into a more individual approach and patient screening would be valuable. Due to its ease of access and non-invasive nature, electrocardiography is a valuable tool in stratifying the risk of life-threatening arrhythmias. It would be beneficial to find markers that could predict SCD early in different BMI groups to gain a chance to prevent it.

Clinicians should attempt to obtain the best knowledge on the prevalence of arrhythmia in those with obesity, as this group of patients is representative both in outpatients and in patients' clinical conditions. It could be beneficial to identify the subgroups with higher risk. In our study, we have shown that in class one, obesity and overweight, only less severe pathologies may occur, and we suggest the necessity for more studies in this aspect.

5. Conclusions

Obesity is a complex disorder that causes compensatory cardiovascular changes, including electromechanical dysfunction, and one of its complications may be the incidence of various types of arrhythmias. In the current study, it has been revealed that in a group with class 1 obesity, no life-threatening arrhythmias were found, and there were very few cases of atrial fibrillation, supraventricular tachycardia, and ventricular tachycardia. The main observation from this study was that in patients with class 1 obesity, there is a higher number of premature supraventricular beats and premature ventricular beats than in patients with normal body weight. Additionally, higher body mass was positively correlated with the number of premature supraventricular and ventricular beats, and similar correlations were present between waist circumference and SPB. Since the number of people with obesity still increases and, simultaneously, global health is burdened by its consequences, it is necessary to continue research in the field evaluating the relationship between obesity and arrhythmias. Especially in further studies, more patients with class 2 and class 3 obesity should be included in the analysis of the co-existing disorders.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Wroclaw Medical University (protocol code 710/2020 and date of approval 10 November 2020).

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

Data Availability Statement: The data are not publicly available due to patients' privacy.

Conflicts of Interest: The authors declare no conflicts of interest.

Appendix A

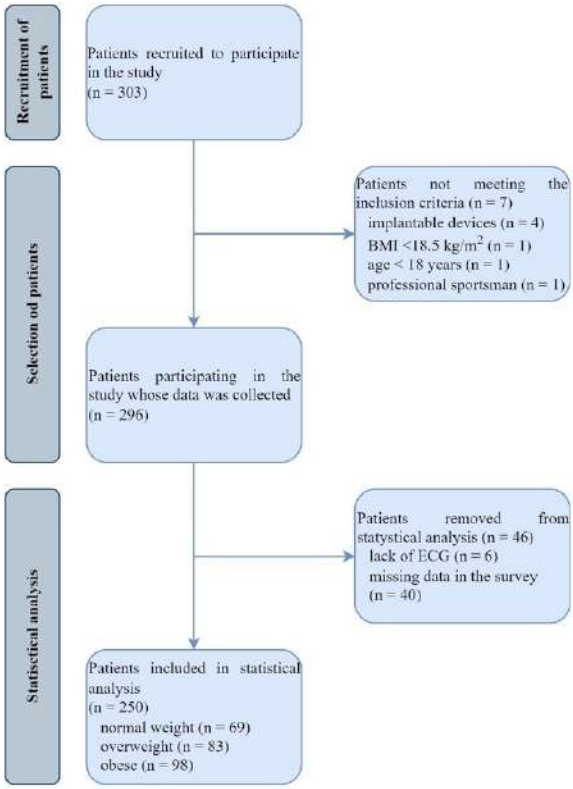

Figure A1. Flowchart presenting the selection of participants.

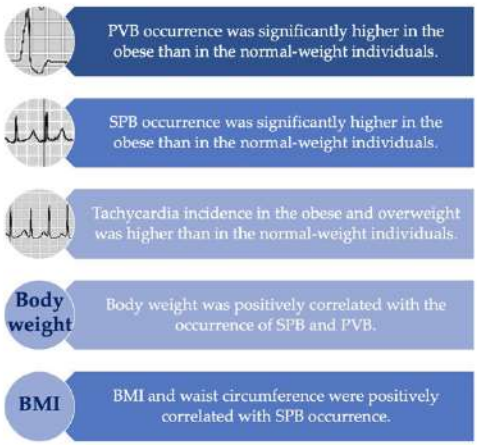

Figure A2. Key findings of this study.

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STRESZCZENIE

Nadwaga i otyłość, charakteryzujące się nieprawidłowym i nadmiernym odkładaniem się tkanki tłuszczowej w organizmie, są obecnie jednymi z najpoważniejszych problemów opieki zdrowotnej na świecie. Według Światowej Organizacji Zdrowia (WHO) w 2022 r. populacja z nadwagą i otyłością osiągnęła 2,5 miliarda osób na świecie. Około 43% wszystkich dorosłych na świecie zostało sklasyfikowanych jako osoby z nadwagą, a 16% jako osoby otyłe. Choroby układu krążenia należą do najważniejszych i narastających problemów opieki zdrowotnej. Związek chorób układu sercowo-naczyniowego i otyłości jest niepodważalny. Badania jednoznacznie wykazują, że nadmierna masa ciała stanowi istotny czynnik ryzyka śmiertelności i zachorowalności, w tym nagłej śmierci sercowej.

Celem prowadzonych badań była: - ocena elektrokardiograficzna wskaźników okresu repolaryzacji oraz dotyczących załamka P u osób z nadwagą i otyłością i ich powiązania z występowaniem zaburzeń rytmu serca, - analiza zapisów 24-godzinnych EKG metodą Holtera z oceną czasowych parametrów zmienności rytmu serca, w tym również określenie rozpowszechnienia nadkomorowych i komorowych zaburzeń rytmu serca oraz innych zmian w EKG u chorych z nadwagą i otyłością, - ocena zależności pomiędzy wybranymi czynnikami ryzyka chorób sercowo-naczyniowych a wskaźnikami okresu repolaryzacji i dotyczącymi załamka P. W dwóch pracach poglądowych, wchodzących w skład niniejszej rozprawy doktorskiej, omówiono z kolei aktualny stan wiedzy na temat epidemiologii otyłości i nadwagi, przed i po pandemii COVID-19 oraz dokonano przeglądu piśmiennictwa określającego związek pomiędzy wskaźnikiem Tpeak-Tend a chorobami układu krążenia.

Do badania zakwalifikowano 250 osób. Do grupy badanej należało 181 osób (90 kobiet i 91 mężczyzn), do grupy kontrolnej 69 osób (56 kobiet i 13 mężczyzn). Średnia wieku wszystkich uczestników badania wynosiła 59,94 lat. Wszyscy badani zostali poddani 12-odprowadzeniowemu badaniu EKG, jak również 24-godzinnemu badaniu EKG metodą Holtera. Wykonano szczegółową analizę 12-odprowadzeniowych zapisów EKG, uwzględniając zarówno nowe, jak i standardowe wskaźniki elektrokardiograficzne oraz analizę 24-godzinnego zapisu EKG metodą Holtera. Dodatkowo przeprowadzono czasową analizę zmienności rytmu serca (HRV, *heart rate variability*).

Na podstawie przeprowadzonych badań można stwierdzić, że nadwaga i otyłość mogą mieć wpływ na występowanie zmian w zapisie elektrokardiograficznym, zarówno spoczynkowym 12-odprowadzeniowym, jak i podczas całodobowej rejestracji EKG metodą Holtera. Wykazano znamiennie większe wartości niektórych standardowych jak i nowych wskaźników elektrokardiograficznych oceniających okres repolaryzacji oraz dotyczących załamka P u osób z nadwagą i otyłością w porównaniu do osób z prawidłową masą ciała. Podczas całodobowego monitorowania EKG metodą Holtera w grupie osób z otyłością wykazano znamiennie większą liczbę przedwczesnych pobudzeń nadkomorowych i przedwczesnych pobudzeń komorowych w porównaniu do osób o prawidłowej masie ciała. Poza tym stwierdzono, że większy wskaźnik masy ciała i większy obwód talii pozostawały w dodatniej zależności z występowaniem większej liczby przedwczesnych pobudzeń nadkomorowych. Nadwaga i otyłość mogą mieć wpływ na parametry zmienności rytmu serca. W przeprowadzonych badaniach wskaźnik mRR był znamiennie większy u osób z nadwagą i otyłością w porównaniu do grupy kontrolnej. Wykazano, że większe wartości wskaźnika JTpeak były powiązane z bardziej zaawansowanym wiekiem, większym wskaźnikiem talia-biodro, występowaniem cukrzycy typu 2 oraz paleniem papierosów.

Ze względu na występowanie zależności pomiędzy nadwagą i otyłością a stwierdzanymi zmianami w zapisach elektrokardiograficznych wskazane jest kontynuowanie dalszych badań w celu poszukiwania nowych wskaźników elektrokardiograficznych, pozwalających, w jeszcze bardziej precyzyjny sposób, dokonywać stratyfikacji ryzyka sercowo-naczyniowego.

SUMMARY

Overweight and obesity, characterized by abnormal and excessive accumulation of body fat, are currently some of the most severe healthcare problems in the world. According to the World Health Organization (WHO), in 2022, the overweight and obese population reached 2,5 billion people in the world. About 43% of all adults in the world were classified as overweight, and 16% as obese. Cardiovascular diseases are among the most important and growing healthcare problems. The link between cardiovascular diseases and obesity is indisputable. Studies clearly show that excess body weight is a significant risk factor for mortality and morbidity, including sudden cardiac death.

The aim of the conducted research was: - electrocardiographic assessment of the repolarization period and P wave indices in overweight and obese people and their association with the occurrence of cardiac arrhythmias, - analysis of 24-hour Holter ECG recordings with the time domain assessment of heart rate variability, including the determination of the prevalence of supraventricular and ventricular arrhythmias and other ECG changes in overweight and obese patients, - assessment of the relationship between selected risk factors of cardiovascular diseases and repolarization period and P wave indices. In two review papers included in this dissertation, the current state of knowledge on the epidemiology of obesity and overweight, before and after the COVID-19 pandemic, was discussed, and the literature describing the relationship between the Tpeak-Tend index and circulatory system diseases was reviewed.

250 people were qualified for the study. The study group consisted of 181 people (90 women and 91 men), and the control group consisted of 69 people (56 women and 13 men). The average age of all study participants was 59,94 years. All participants underwent a 12-lead ECG study, as well as a 24-hour Holter ECG study. A detailed analysis of the 12-lead ECG recordings was performed, considering both new and standard electrocardiographic indicators, as well as an analysis of the 24-hour Holter ECG recording. Additionally, a time-domain analysis of heart rate variability (HRV) was performed.

Based on the conducted studies, it can be concluded that overweight and obesity may affect changes in the electrocardiographic recording, both the resting 12-lead and during 24-hour Holter ECG recording. Higher values of some standard and new electrocardiographic indices assessing the repolarization period, and the P wave were demonstrated in overweight and obese individuals

compared to individuals with normal body weight. During 24-hour Holter ECG monitoring, a significantly higher number of premature supraventricular beats and premature ventricular beats were demonstrated in the group of obese individuals compared to individuals with normal body weight. In addition, it was found that a higher body mass index and a larger waist circumference were positively related to a more significant number of premature supraventricular beats. Overweight and obesity may affect heart rate variability parameters. In the conducted studies, the mRR index was significantly higher in overweight and obese individuals compared to the control group. It was shown that higher JTpeak values were associated with more advanced age, a higher waist-to-hip ratio, the occurrence of type 2 diabetes and cigarette smoking.

Due to the relationship between overweight and obesity and the changes observed in electrocardiographic recordings, it is advisable to continue further research to search for new electrocardiographic indicators that would allow for even more precise cardiovascular risk stratification.

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OŚWIADCZENIE

Oświadczam, że w pracy

1. Dykiert IA, Kraik K, **Jurczenko L,** Gać P, Poręba R, Poręba M. The Effect of Obesity on Repolarization and Other ECG Parameters. *J Clin Med.* 2024;13(12):3587. Published 2024 Jun 19. doi:10.3390/jcm13123587. 140 pkt, IF (3) mój udział polegał na współtworzeniu bazy danych, interpretowania zebranych wyników, zbieraniu piśmiennictwa naukowego oraz współredagowaniu merytorycznym publikacji.

2. Dykiert IA, Kraik K, **Jurczenko L,** Gać P, Poręba R, Poręba M. The Prevalence of Arrhythmias, Including Premature Supraventricular and Ventricular Beats and Other Electrocardiographic Patterns, in 24-Hour Holter Monitoring in Patients with Overweight and Obesity. *Life.* 2024;14(9):1140. Published 2024 Sep 09. doi.org/10.3390/life14091140. 70 pkt. IF(3,2) mój udział polegał na współtworzeniu bazy danych, interpretowania zebranych wyników, zbieraniu piśmiennictwa naukowego oraz współredagowaniu merytorycznym publikacji.

Podpis

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Wrocław, 05.09.2024

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ul. Borowska 213
50-556 Wrocław

OŚWIADCZENIE

Oświadczam, że w pracy

1. Dykiert I, Florek K, Kraik K, Gać P, Poręba R, Poręba M. Tpeak-Tend ECG Marker in Obesity and Cardiovascular Diseases: A Comprehensive Review. *Scientifica (Cairo)*. 2024;2024:4904508. Published 2024 Jun 26. doi:10.1155/2024/4904508. 40 pkt. IF (2,3) mój udział polegał na zbieraniu piśmiennictwa naukowego i współredagowaniu publikacji.

Podpis

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ZGODA KOMISJI BIOETYCZNEJ

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

OPINIA KOMISJI BIOETYCZNEJ Nr KB – 710 /2020

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 133/XV R/2017 z dnia 21 grudnia 2017 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. Jacek Daroszewski (choroby wewnętrzne, 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, prof. nadzw. (duchowny)
mgr prawa Luiza Műller (prawo)
dr hab. Sławomir Sidorowicz (psychiatria)
prof. dr hab. Leszek Szenborn, (pediatria, choroby zakaźne)
Danuta Tarkowska (pielęgniarstwo)
prof. dr hab. Anna Wiela-Hojeńska (farmakologia kliniczna)
dr hab. Andrzej Wojnar, prof. nadzw. (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

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.:

„Kompleksowa ocena elektrokardiograficznych parametrów okresu repolaryzacji oraz dotyczących załamka P u dorosłych z nadwagą i otyłością i ich powiazania z występowaniem zaburzeń rytmu w rożnych grupach wiekowych"

zgłoszonym przez **lek. Irenę Annę Wolińską,** uczestniczkę Szkoły Doktorskiej w Katedrze i Zakładzie Patofizjologii Uniwersytetu Medycznego im. Piastów Śląskich we Wrocławiu oraz złożonymi wraz z wnioskiem dokumentami, w tajnym głosowaniu postanowiła **wyrazić zgodę** na przeprowadzenie badania w Katedrze i Zakładzie Patofizjologii UMW pod nadzorem dr hab. Małgorzaty Poręby, prof. nadzw. **pod warunkiem zachowania anonimowości uzyskanych danych**.

Uwaga: Badanie to zostało objęte ubezpieczeniem odpowiedzialności cywilnej Uniwersytetu Medycznego we Wrocławiu z tytułu prowadzonej działalności.

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 projektu badawczego będącego podstawą rozprawy doktorskiej.

Wrocław, dnia 10 listopada 2020 r.

Uniwersytet Medyczny we Wrocławiu
KOMISJA BIOETYCZNA
przewodniczący
prof. dr hab. Jan Kornafel