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ORIGINAL ARTICLE

Autonomic Response to Face-Mask-Wearing in Individuals with Anxiety Disorders

Respon Otonom Terhadap Penggunaan Masker Pada Individu Dengan Gangguan cemas

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ABSTRACT

Background
Medical masks, commonly known as surgical masks, are designed to inhibit the spread of microorganisms. While masks offer numerous benefits, they also have side effects, including anxiety. N95 respirators have several additional side effects compared to surgical masks. This study aimed to examine the relationship between N95 mask use and autonomic responses in individuals with anxiety disorders, a relatively understudied area.

Methods
This is an analytic experimental study on 140 respondents. Assessment of anxiety disorders was carried out by completing the DASS-42 questionnaire and psychiatric interviews by a psychiatrist. Autonomic responses are assessed using heart rate variability (HRV), the fluctuation in the time intervals between adjacent heartbeats. Short-term root mean square of successive differences (RMSSD) HRV parameters were measured using the Polar H10. HRV was measured when the respondent was not wearing a mask, when wearing an N95 mask, and when wearing an N95 mask with a valve opened (sham).

Results
HRV in respondents with anxiety disorders had a significantly lower value than in respondents non-anxiety disorders. HRV values were significantly lower in respondents with anxiety disorders compared to those without, both at baseline (median: 16.33 vs 23.35, p=0.004), while using an N95 mask (median: 16.47 vs 22.01, p=0.008), and while using a sham N95 mask (median: 16.94 vs 22.24, p=0.005). However, there was no relationship between the use of N95 masks and HRV in respondents with anxiety disorders (RMSSD baseline vs. N95: median 16.33 vs. 16.47, p=0.979).

Conclusions
There is no relationship between the use of N95 masks and HRV in individuals with anxiety disorders. These findings suggest that N95 use is safe even for individuals with anxiety disorders.

Keywords: anxiety disorders; heart rate variability; N95 mask.

ABSTRAK

Latar Belakang

Masker medis, yang umumnya dikenal sebagai masker bedah, dirancang untuk mencegah penyebaran mikroorganisme. Meskipun menawarkan banyak manfaat, masker juga memiliki efek samping, termasuk kecemasan. Respirator N95 memiliki beberapa efek samping tambahan dibandingkan masker bedah. Penelitian ini bertujuan untuk mengkaji hubungan antara penggunaan masker N95 dan respons otonom pada individu dengan gangguan kecemasan, suatu bidang yang relatif kurang diteliti.

Metode

Penelitian menggunakan desain analitik eksperimental dengan jumlah sampel 140 orang. Penilaian gangguan cemas pada responden dilakukan dengan pengisian kuesioner DASS 42 dan wawancara psikiatri oleh dokter spesialis kesehatan jiwa. Respons otonom dinilai dengan mengukur *heart rate variability* (HRV), yaitu fluktuasi interval waktu antara detak jantung yang berdekatan. Dilakukan pengukuran parameter HRV jangka pendek *root mean square of successive differences* (RMSSD) dengan menggunakan alat Polar H10. HRV diukur pada saat responden tidak mengenakan masker, saat mengenakan masker N95 dan saat mengenakan masker N95 berkatup dengan katup yang telah dibuka (sham).

Hasil

HRV pada responden dengan gangguan cemas secara significant memiliki nilai yang lebih rendah dibanding responden tanpa gangguan cemas. Baik pada saat baseline (median: 16,33 vs 23,35, p=0,004), saat menggunakan N95 (median: 16,47 vs 22,01, p=0,008) maupun saat menggunakan sham N95 (median: 16,94 vs 22,24, p=0,005). Namun tidak terdapat hubungan antara penggunaan masker N95 dengan HRV pada responden dengan gangguan cemas (RMSSD baseline vs N95: median 16,33 vs 16,47, p=0,979).

Kesimpulan

Tidak terdapat hubungan antara penggunaan masker N95 dengan HRV pada individu dengan gangguan cemas. Temuan ini menunjukkan bahwa penggunaan N95 aman bahkan bagi individu dengan gangguan kecemasan.

Kata Kunci: gangguan cemas; variabilitas denyut jantung; masker N95.

INTRODUCTION

During and after the COVID-19 pandemic, the use of masks is recommended, or even required in some circumstances, to prevent virus transmission and break the chain of transmission. As we know, the primary mode of transmission of COVID-19 is contact between the SARS-CoV-2 virus contained in respiratory droplets of a sick individual and the nasal mucosa of another person.[1] The use of masks is intended to inhibit droplet formation by the wearer and protect them from droplets produced by others.[2]

Wearing a mask increases the temperature and humidity around the mouth and nose, which can cause discomfort.[3] The direct effect of mask use, particularly filtering facepiece (FFP) types, such as N95 respirators, on blood oxygen and carbon dioxide levels remains controversial. In healthy individuals, the effect is thought to be minimal, especially when the respirator is used for light or moderate activity.[4] However, in individuals with underlying medical conditions, significant decreases in pO_2 and increases in pCO_2 can occur.[5] Therefore, through both biological and psychological mechanisms, mask use can trigger the body's stress response (fight-or-flight), accompanied by activation of the autonomic nervous system. Physiological symptoms resulting from autonomic nervous system activation, particularly sympathetic activation, vary. These include palpitations, shortness of breath, increased heart rate, chest discomfort, and even panic attacks. The sympathetic response can also be activated by an individual's pre-existing anxiety disorder and can produce similar physiological symptoms.[6] Pre-existing anxiety disorders can be further triggered by changes in lifestyle, fear of disease, and the discomfort caused by wearing a mask.

Therefore, in individuals with anxiety disorders, the sympathetic nervous system may be further activated by mask use. Short-term sympathetic activation is a normal response the body requires to cope with stress or threats. However, chronic and persistent sympathetic activation is known to increase cardiovascular risk and morbidity/mortality.[7,8]

One way to assess autonomic system activity is by observing heart rate. The time interval between heartbeats is normally not fixed but fluctuates with sympathetic and parasympathetic stimulation. This fluctuation in the time between heartbeats, called heart rate variability (HRV), can be used to assess the autonomic system.[9] Decreased heart rate variability, or HRV, indicates an autonomic imbalance, namely increased sympathetic activity and decreased parasympathetic activity. Decreased HRV is a cardiovascular risk factor in both individuals with and without pre-existing cardiovascular disease.[10] N95 masks cause complex physiological changes in the autonomic nervous system. To date, no specific studies have assessed changes in objective heart rate variability in individuals with clinically diagnosed anxiety disorders while using N95 respirators. Current data are restricted to healthy individuals or studies that exclusively evaluate subjective anxiety measures. This gap is important to explore, especially during the pandemic.

Based on the aforementioned considerations, this study will investigate whether the utilization of N95 respirators is correlated with sympathetic activation, as measured by heart rate variability (HRV). Additionally, we will examine whether there is a relationship between N95 respirator use and HRV in respondents with anxiety disorders. The results of this study are expected to provide additional data in assessing the risk of mask use on increased sympathetic responses, which can negatively impact cardiovascular disease, particularly in psychologically vulnerable groups.

METHODS

The study used an experimental analytical method. Respondents were 140 adults aged 18 or older, employees of the Faculty of Medicine, Universitas Trisakti, selected using consecutive nonrandom sampling. Exclusion criteria included factors that could affect HRV, such as pacemaker users, those with arrhythmias or those taking antiarrhythmic medications, pregnancy, those using psychoactive drugs and alpha/beta agonists, and those unable to use an N95.

Anxiety disorders were assessed using the Depression Anxiety Stress Scales (DASS-42) questionnaire and interviews with mental health specialists. The DASS-42 questionnaire has excellent reliability and validity, even when used outside clinical settings.[11,12] Autonomic system responses were assessed by measuring HRV using a Polar H10 chest strap heart rate monitor.[13] The HRV parameter used was the root mean square of successive differences (RMSSD), a measure of short-term HRV.[14,15] Following the psychiatric interview, HRV was measured for 5 minutes without a mask in respondents. The procedure continued with 5 minutes of HRV measurement while respondents wore an N95 mask with a valve (8210V), followed by 5 minutes of HRV measurement while wearing an N95 mask with the valve removed (sham N95), which provided relatively little breathing resistance.

The analysis was conducted on two groups of respondents: those with anxiety disorders and those without anxiety disorders. In both groups, HRV was compared while not wearing a mask, while wearing an N95 mask, and while wearing a sham N95 mask.

RESULTS

Table 1 displays the baseline data for the study respondents. Of the 140 respondents, 38 people (27.1%) had anxiety disorders. There were no significant differences in gender and age variables between the anxiety and non-anxiety groups. The distribution of RMSSD was not normal, with the median baseline RMSSD of all respondents being 20.16 (range: 2.6-212.21). The median RMSSD when using N95 and sham N95 was 20.30 (range: 5.44-223) and 20.57 (range: 2.01-223). Analysis using the

Wilcoxon signed-rank test showed no significant difference between baseline RMSSD, N95, and sham N95 (Table 2).

Table 1. Baseline Characteristics

Variables	Anxiety	
	Yes (n=38)	No (n=102)
Male (%)	14.0 (36.84)	44.0 (43.14)
Female (%)	24.0 (63.16)	58.0 (56.86)
Age (mean; range)	33.5 (20-53)	33.5 (21-64)
Heart rate (median; range)		
Baseline	96.0 (74-133)	89.0 (64-124)
N95	94.5 (77-124)	86.5 (65-116)
Sham	95.0 (77-124)	86.0 (65-114)
RMSSD (median; range)		
Baseline	16.33 (4.5-117.34)	23.35 (2.6-212.21)
N95	16.47 (5.44-57.91)	22.01 (6.25-223)
Sham	16.94 (5.19-54.44)	22.24 (2.01-223)

* The distributions of age, HR, and HRV data are not normal. Data are presented as median (range).

Table 2. Comparison of median RMSSD baseline, N95, and Sham

Variables	Median	p value
RMSSDb vs RMSSDn	20.16 vs 20.30	0.364
RMSSDb vs RMSSDs	20.16 vs 20.57	0.812
RMSSDn vs RMSSDs	20.30 vs 20.57	0.126

Wilcoxon signed rank

The median RMSSD in anxiety and non-anxiety individuals was compared using the Mann-Whitney U test due to non-normal distributions. RMSSD in the anxiety and non-anxiety groups showed consistently significant differences across all RMSSD measurements, both at baseline, during N95 use, and during sham N95 (Table 3).

Table 3. Comparison of median RMSSD baseline, N95, and sham between anxiety and non-anxiety.

Variables	Anxiety		p value
	Yes	No	
RMSSDb	16.33	23.35	0.004*
RMSSDn	16.47	22.01	0.008*
RMSSDs	16.94	22.24	0.005*

Independent-samples Mann-Whitney U Test

* $p<0.05$

Bivariate analysis in the non-anxiety group showed no significant differences between baseline RMSSD vs. N95, baseline RMSSD vs. sham N95, or N95 RMSSD vs. sham N95 (Table 4). Similarly, in the anxiety group, there were no significant differences between baseline RMSSD and N95, baseline RMSSD and sham N95, or N95 RMSSD and sham N95 (Table 5).

Table 4. Comparison of median RMSSD baseline, N95, and Sham in the anxiety group

Variables	Median	p value
RMSSDb vs RMSSDn	16.33 vs 16.47	0.979
RMSSDb vs RMSSDs	16.33 vs 16.94	0.791
RMSSDn vs RMSSDs	16.47 vs 16.94	0.091

Wilcoxon signed rank

Table 5. Comparison of median RMSSD baseline, N95, and sham in the non-anxiety group

Variables	Median	p value
RMSSDb vs RMSSDn	23.35 vs 22.01	0.366
RMSSDb vs RMSSDs	23.35 vs 22.24	0.737
RMSSDn vs RMSSDs	22.01 vs 22.24	0.309

Wilcoxon signed rank

DISCUSSION

Subject characteristics data showed that 38 (27.1%) of the 140 subjects experienced anxiety disorders. This prevalence is significantly higher than WHO estimates, which indicate that 4.4% of the global population currently experiences anxiety disorders. Data collection during the pandemic may have contributed to the high prevalence of anxiety in this study. Research by Santomauro et al.,[16] published in The Lancet, reported an increase in anxiety prevalence due to the COVID-19 pandemic, reaching 25.6%.

Characteristic data showed that more female subjects experienced anxiety than male subjects (63.16% vs. 36.84%). This is consistent with global WHO data, which states that the prevalence of anxiety disorders is much higher in women than in men.[17] The serotonin transporter, encoded by the SLC6A4 gene, is responsible for gender-based differences in mental health. Furthermore, numerous studies have confirmed the presence of hormonal fluctuations in women (progesterone, estrogen, and oxytocin), which may contribute to differences in anxiety between men and women.[18]

The group of anxiety subjects was found to have a higher heart rate than the non-anxiety group, both at baseline and using N95S or sham masks. Theory suggests a relationship between heart rate and anxiety. Under anxiety, the sympathetic nervous system becomes hyperactive. Recent evidence suggests that anxiety, as a personality trait, is positively associated with muscle sympathetic nerve activity (MSNA).[19] Cognitive stress, also known as mental stress, is a key factor linking physiological and psychological well-being to mental health conditions such as depression and anxiety.[20] The complex interaction among heart activity, stress, and cognitive function has been extensively studied, demonstrating links among cognitive decline, vascular health, and mental well-being.[21] Recently, HRV has emerged as a focal point, particularly in its correlation with depression and anxiety.[21-23] Research consistently demonstrates that heart rate variability (HRV), indicative of the autonomic nervous system's responsiveness to diverse psychological and physiological stimuli, is significantly associated with mental health disorders and cognitive load.[24]

As shown in Table 3, HRV was lower in the group with anxiety disorders than in the group without anxiety disorders. This finding is consistent with previous research indicating that individuals with anxiety disorders have low vagally mediated HRV.[16,17] HRV reflects the autonomic nervous system's (ANS) regulatory capacity over heart rate, including interactions between the sympathetic and parasympathetic nervous systems.[25] Higher HRV, particularly related to parasympathetic function, is associated with good health, as it reflects the flexibility and adaptability of the autonomic nervous system.[26] Conversely, low HRV can be associated with cardiovascular disease, psychological stress, anxiety, depression, and other problems.[26] Psychological stress and emotional states can directly affect autonomic nervous system activity, thereby influencing HRV levels.[27]

This study aimed to determine whether there was a relationship between mask use, specifically N95 masks, and autonomic activation, as measured by HRV. However, this study found no relationship between N95 mask use and HRV. N95 use was not associated with HRV in either respondents with or without anxiety disorders (Tables 4 and 5). Several previous studies have found similar findings with the use of surgical masks. Langrish, et al. even found that athletes who wore surgical masks during exercise showed increased HRV. The study was conducted in 2009 in Beijing, which at the time had high levels of pollution. The study reported an increase in overall heart rate variability (SDNN) when subjects wore masks, which can, at least partially, mitigate the adverse effects of air pollution exposure on heart rate variability.[28]

The use of N95 masks may also be associated with decreased HRV due to discomfort.[29] The results of this study differ from those of Kim et al., who reported that wearing an N95 mask for 1 hour increased heart rate from 5.7 to 10.6 beats per minute.[29] The vacuum in an N95 mask without a valve can cause CO2 (carbon dioxide) accumulation. Roberge et al[4], stated that decreased O_2 and increased CO_2 result in increased heart rate and blood pressure. The increase in heart rate during mask use is also influenced by the duration of mask use, workload, physical ability, and anxiety.[29] Pakanati et al.[31], also showed a decrease in MSSD after wearing an N95 for 1 hour. The difference in results from previous studies may be due to HRV measurements being conducted for a short period, namely, 5 minutes. This short duration is thought to be insufficient to capture the medium- and long-term HRV changes observed when an N95 mask is worn for a longer period.

Anxiety disorders increase the risk of cardiovascular disease (CHD) and mortality, even after controlling for confounding factors such as smoking, lifestyle, and socioeconomic status, and regardless of a history of medical disorders. Conversely, impaired vagal function, indicated by decreased heart rate variability (HRV), may be one mechanism linking anxiety disorders to CHD.[32] HRV is a physiological measure that reflects the dynamic interplay between the sympathetic and parasympathetic nervous systems. Deficient HRV may serve as an endophenotype of pathological anxiety and as a non-invasive index of prefrontal cortex control over the amygdala, potentially aiding in predicting treatment outcomes in anxiety. Overall, HRV shows promise as a physiological biomarker of pathological anxiety, potentially transdiagnostic and linked to heart-brain connections, thus providing a novel approach to advancing the development of anxiety treatments.

CONCLUSION

This study found no association between N95 mask use and HRV in either respondents with or without anxiety disorders. Short-term N95 mask use was not found to have any effect on autonomic activation in individuals with anxiety disorders. Further research with longer durations of N95 mask use is needed to assess medium- and long-term changes in HRV.

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AUTHORS CONTRIBUTION

The authors' contributions to this research are as follows: Research concept and design: AK and EI. Statistical analysis: VS, RK, and HW.

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CONFLICT OF INTEREST

There is no conflict of interest.

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ABSTRACT

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Methods
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Results
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Conclusions
There is no relationship between the use of N95 masks and HRV in individuals with anxiety disorders. These findings suggest that N95 use is safe even for individuals with anxiety disorders.

Keywords: anxiety disorders; heart rate variability; N95 mask.

ABSTRAK

Latar Belakang

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Metode

Penelitian menggunakan desain analitik eksperimental dengan jumlah sampel 140 orang. Penilaian gangguan cemas pada responden dilakukan dengan pengisian kuesioner DASS 42 dan wawancara psikiatri oleh dokter spesialis kesehatan jiwa. Respons otonom dinilai dengan mengukur *heart rate variability* (HRV), yaitu fluktuasi interval waktu antara detak jantung yang berdekatan. Dilakukan pengukuran parameter HRV jangka pendek *root mean square of successive differences* (RMSSD) dengan menggunakan alat Polar H10. HRV diukur pada saat responden tidak mengenakan masker, saat mengenakan masker N95 dan saat mengenakan masker N95 berkatup dengan katup yang telah dibuka (sham).

Hasil

HRV pada responden dengan gangguan cemas secara significant memiliki nilai yang lebih rendah dibanding responden tanpa gangguan cemas. Baik pada saat baseline (median: 16,33 vs 23,35, p=0,004), saat menggunakan N95 (median: 16,47 vs 22,01, p=0,008) maupun saat menggunakan sham N95 (median: 16,94 vs 22,24, p=0,005). Namun tidak terdapat hubungan antara penggunaan masker N95 dengan HRV pada responden dengan gangguan cemas (RMSSD baseline vs N95: median 16,33 vs 16,47, p=0,979).

Kesimpulan

Tidak terdapat hubungan antara penggunaan masker N95 dengan HRV pada individu dengan gangguan cemas. Temuan ini menunjukkan bahwa penggunaan N95 aman bahkan bagi individu dengan gangguan kecemasan.

Kata Kunci: gangguan cemas; variabilitas denyut jantung; masker N95.

INTRODUCTION

During and after the COVID-19 pandemic, the use of masks is recommended, or even required in some circumstances, to prevent virus transmission and break the chain of transmission. As we know, the primary mode of transmission of COVID-19 is contact between the SARS-CoV-2 virus contained in respiratory droplets of a sick individual and the nasal mucosa of another person.[1] The use of masks is intended to inhibit droplet formation by the wearer and protect them from droplets produced by others.[2]

Wearing a mask increases the temperature and humidity around the mouth and nose, which can cause discomfort.[3] The direct effect of mask use, particularly filtering facepiece (FFP) types, such as N95 respirators, on blood oxygen and carbon dioxide levels remains controversial. In healthy individuals, the effect is thought to be minimal, especially when the respirator is used for light or moderate activity.[4] However, in individuals with underlying medical conditions, significant decreases in pO_2 and increases in pCO_2 can occur.[5] Therefore, through both biological and psychological mechanisms, mask use can trigger the body's stress response (fight-or-flight), accompanied by activation of the autonomic nervous system. Physiological symptoms resulting from autonomic nervous system activation, particularly sympathetic activation, vary. These include palpitations, shortness of breath, increased heart rate, chest discomfort, and even panic attacks. The sympathetic response can also be activated by an individual's pre-existing anxiety disorder and can produce similar physiological symptoms.[6] Pre-existing anxiety disorders can be further triggered by changes in lifestyle, fear of disease, and the discomfort caused by wearing a mask.

Therefore, in individuals with anxiety disorders, the sympathetic nervous system may be further activated by mask use. Short-term sympathetic activation is a normal response the body requires to cope with stress or threats. However, chronic and persistent sympathetic activation is known to increase cardiovascular risk and morbidity/mortality.[7,8]

One way to assess autonomic system activity is by observing heart rate. The time interval between heartbeats is normally not fixed but fluctuates with sympathetic and parasympathetic stimulation. This fluctuation in the time between heartbeats, called heart rate variability (HRV), can be used to assess the autonomic system.[9] Decreased heart rate variability, or HRV, indicates an autonomic imbalance, namely increased sympathetic activity and decreased parasympathetic activity. Decreased HRV is a cardiovascular risk factor in both individuals with and without pre-existing cardiovascular disease.[10] N95 masks cause complex physiological changes in the autonomic nervous system. To date, no specific studies have assessed changes in objective heart rate variability in individuals with clinically diagnosed anxiety disorders while using N95 respirators. Current data are restricted to healthy individuals or studies that exclusively evaluate subjective anxiety measures. This gap is important to explore, especially during the pandemic.

Based on the aforementioned considerations, this study will investigate whether the utilization of N95 respirators is correlated with sympathetic activation, as measured by heart rate variability (HRV). Additionally, we will examine whether there is a relationship between N95 respirator use and HRV in respondents with anxiety disorders. The results of this study are expected to provide additional data in assessing the risk of mask use on increased sympathetic responses, which can negatively impact cardiovascular disease, particularly in psychologically vulnerable groups.

METHODS

The study used an experimental analytical method. Respondents were 140 adults aged 18 or older, employees of the Faculty of Medicine, Universitas Trisakti, selected using consecutive nonrandom sampling. Exclusion criteria included factors that could affect HRV, such as pacemaker users, those with arrhythmias or those taking antiarrhythmic medications, pregnancy, those using psychoactive drugs and alpha/beta agonists, and those unable to use an N95.

Anxiety disorders were assessed using the Depression Anxiety Stress Scales (DASS-42) questionnaire and interviews with mental health specialists. The DASS-42 questionnaire has excellent reliability and validity, even when used outside clinical settings.[11,12] Autonomic system responses were assessed by measuring HRV using a Polar H10 chest strap heart rate monitor.[13] The HRV parameter used was the root mean square of successive differences (RMSSD), a measure of short-term HRV.[14,15] Following the psychiatric interview, HRV was measured for 5 minutes without a mask in respondents. The procedure continued with 5 minutes of HRV measurement while respondents wore an N95 mask with a valve (8210V), followed by 5 minutes of HRV measurement while wearing an N95 mask with the valve removed (sham N95), which provided relatively little breathing resistance.

The analysis was conducted on two groups of respondents: those with anxiety disorders and those without anxiety disorders. In both groups, HRV was compared while not wearing a mask, while wearing an N95 mask, and while wearing a sham N95 mask.

RESULTS

Table 1 displays the baseline data for the study respondents. Of the 140 respondents, 38 people (27.1%) had anxiety disorders. There were no significant differences in gender and age variables between the anxiety and non-anxiety groups. The distribution of RMSSD was not normal, with the median baseline RMSSD of all respondents being 20.16 (range: 2.6-212.21). The median RMSSD when using N95 and sham N95 was 20.30 (range: 5.44-223) and 20.57 (range: 2.01-223). Analysis using the

Wilcoxon signed-rank test showed no significant difference between baseline RMSSD, N95, and sham N95 (Table 2).

Table 1. Baseline Characteristics

Variables	Anxiety	
	Yes (n=38)	No (n=102)
Male (%)	14.0 (36.84)	44.0 (43.14)
Female (%)	24.0 (63.16)	58.0 (56.86)
Age (mean; range)	33.5 (20-53)	33.5 (21-64)
Heart rate (median; range)		
Baseline	96.0 (74-133)	89.0 (64-124)
N95	94.5 (77-124)	86.5 (65-116)
Sham	95.0 (77-124)	86.0 (65-114)
RMSSD (median; range)		
Baseline	16.33 (4.5-117.34)	23.35 (2.6-212.21)
N95	16.47 (5.44-57.91)	22.01 (6.25-223)
Sham	16.94 (5.19-54.44)	22.24 (2.01-223)

* The distributions of age, HR, and HRV data are not normal. Data are presented as median (range).

Table 2. Comparison of median RMSSD baseline, N95, and Sham

Variables	Median	p value
RMSSDb vs RMSSDn	20.16 vs 20.30	0.364
RMSSDb vs RMSSDs	20.16 vs 20.57	0.812
RMSSDn vs RMSSDs	20.30 vs 20.57	0.126

Wilcoxon signed rank

The median RMSSD in anxiety and non-anxiety individuals was compared using the Mann-Whitney U test due to non-normal distributions. RMSSD in the anxiety and non-anxiety groups showed consistently significant differences across all RMSSD measurements, both at baseline, during N95 use, and during sham N95 (Table 3).

Table 3. Comparison of median RMSSD baseline, N95, and sham between anxiety and non-anxiety.

Variables	Anxiety		p value
	Yes	No	
RMSSDb	16.33	23.35	0.004*
RMSSDn	16.47	22.01	0.008*
RMSSDs	16.94	22.24	0.005*

Independent-samples Mann-Whitney U Test

* p<0.05

Bivariate analysis in the non-anxiety group showed no significant differences between baseline RMSSD vs. N95, baseline RMSSD vs. sham N95, or N95 RMSSD vs. sham N95 (Table 4). Similarly, in the anxiety group, there were no significant differences between baseline RMSSD and N95, baseline RMSSD and sham N95, or N95 RMSSD and sham N95 (Table 5).

Table 4. Comparison of median RMSSD baseline, N95, and Sham in the anxiety group

Variables	Median	p value
RMSSDb vs RMSSDn	16.33 vs 16.47	0.979
RMSSDb vs RMSSDs	16.33 vs 16.94	0.791
RMSSDn vs RMSSDs	16.47 vs 16.94	0.091

Wilcoxon signed rank

Table 5. Comparison of median RMSSD baseline, N95, and sham in the non-anxiety group

Variables	Median	p value
RMSSDb vs RMSSDn	23.35 vs 22.01	0.366
RMSSDb vs RMSSDs	23.35 vs 22.24	0.737
RMSSDn vs RMSSDs	22.01 vs 22.24	0.309

Wilcoxon signed rank

DISCUSSION

Subject characteristics data showed that 38 (27.1%) of the 140 subjects experienced anxiety disorders. This prevalence is significantly higher than WHO estimates, which indicate that 4.4% of the global population currently experiences anxiety disorders. Data collection during the pandemic may have contributed to the high prevalence of anxiety in this study. Research by Santomauro et al.,[16] published in The Lancet, reported an increase in anxiety prevalence due to the COVID-19 pandemic, reaching 25.6%.

Characteristic data showed that more female subjects experienced anxiety than male subjects (63.16% vs. 36.84%). This is consistent with global WHO data, which states that the prevalence of anxiety disorders is much higher in women than in men.[17] The serotonin transporter, encoded by the SLC6A4 gene, is responsible for gender-based differences in mental health. Furthermore, numerous studies have confirmed the presence of hormonal fluctuations in women (progesterone, estrogen, and oxytocin), which may contribute to differences in anxiety between men and women.[18]

The group of anxiety subjects was found to have a higher heart rate than the non-anxiety group, both at baseline and using N95S or sham masks. Theory suggests a relationship between heart rate and anxiety. Under anxiety, the sympathetic nervous system becomes hyperactive. Recent evidence suggests that anxiety, as a personality trait, is positively associated with muscle sympathetic nerve activity (MSNA).[19] Cognitive stress, also known as mental stress, is a key factor linking physiological and psychological well-being to mental health conditions such as depression and anxiety.[20] The complex interaction among heart activity, stress, and cognitive function has been extensively studied, demonstrating links among cognitive decline, vascular health, and mental well-being.[21] Recently, HRV has emerged as a focal point, particularly in its correlation with depression and anxiety.[21-23] Research consistently demonstrates that heart rate variability (HRV), indicative of the autonomic nervous system's responsiveness to diverse psychological and physiological stimuli, is significantly associated with mental health disorders and cognitive load.[24]

As shown in Table 3, HRV was lower in the group with anxiety disorders than in the group without anxiety disorders. This finding is consistent with previous research indicating that individuals with anxiety disorders have low vagally mediated HRV.[16,17] HRV reflects the autonomic nervous system's (ANS) regulatory capacity over heart rate, including interactions between the sympathetic and parasympathetic nervous systems.[25] Higher HRV, particularly related to parasympathetic function, is associated with good health, as it reflects the flexibility and adaptability of the autonomic nervous system.[26] Conversely, low HRV can be associated with cardiovascular disease, psychological stress, anxiety, depression, and other problems.[26] Psychological stress and emotional states can directly affect autonomic nervous system activity, thereby influencing HRV levels.[27]

This study aimed to determine whether there was a relationship between mask use, specifically N95 masks, and autonomic activation, as measured by HRV. However, this study found no relationship between N95 mask use and HRV. N95 use was not associated with HRV in either respondents with or without anxiety disorders (Tables 4 and 5). Several previous studies have found similar findings with the use of surgical masks. Langrish, et al. even found that athletes who wore surgical masks during exercise showed increased HRV. The study was conducted in 2009 in Beijing, which at the time had high levels of pollution. The study reported an increase in overall heart rate variability (SDNN) when subjects wore masks, which can, at least partially, mitigate the adverse effects of air pollution exposure on heart rate variability.[28]

The use of N95 masks may also be associated with decreased HRV due to discomfort.[29] The results of this study differ from those of Kim et al., who reported that wearing an N95 mask for 1 hour increased heart rate from 5.7 to 10.6 beats per minute.[29] The vacuum in an N95 mask without a valve can cause CO2 (carbon dioxide) accumulation. Roberge et al[4], stated that decreased O_2 and increased CO_2 result in increased heart rate and blood pressure. The increase in heart rate during mask use is also influenced by the duration of mask use, workload, physical ability, and anxiety.[29] Pakanati et al.[31], also showed a decrease in MSSD after wearing an N95 for 1 hour. The difference in results from previous studies may be due to HRV measurements being conducted for a short period, namely, 5 minutes. This short duration is thought to be insufficient to capture the medium- and long-term HRV changes observed when an N95 mask is worn for a longer period.

Anxiety disorders increase the risk of cardiovascular disease (CHD) and mortality, even after controlling for confounding factors such as smoking, lifestyle, and socioeconomic status, and regardless of a history of medical disorders. Conversely, impaired vagal function, indicated by decreased heart rate variability (HRV), may be one mechanism linking anxiety disorders to CHD.[32] HRV is a physiological measure that reflects the dynamic interplay between the sympathetic and parasympathetic nervous systems. Deficient HRV may serve as an endophenotype of pathological anxiety and as a non-invasive index of prefrontal cortex control over the amygdala, potentially aiding in predicting treatment outcomes in anxiety. Overall, HRV shows promise as a physiological biomarker of pathological anxiety, potentially transdiagnostic and linked to heart-brain connections, thus providing a novel approach to advancing the development of anxiety treatments.

CONCLUSION

This study found no association between N95 mask use and HRV in either respondents with or without anxiety disorders. Short-term N95 mask use was not found to have any effect on autonomic activation in individuals with anxiety disorders. Further research with longer durations of N95 mask use is needed to assess medium- and long-term changes in HRV.

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AUTHORS CONTRIBUTION

The authors' contributions to this research are as follows: Research concept and design: AK and EI. Statistical analysis: VS, RK, and HW.

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CONFLICT OF INTEREST

There is no conflict of interest.

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