# Strict association between development of psychological conditions and hypertension incidence: A cross-sectional study 

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#### Abstract

Background/Aims: Previous studies indicated a significant association between mental disorders and cardiovascular diseases, including heart failure (HF) and coronary artery disease (CAD) with comorbidity hypertension (HTN), and vice versa, leading to a challenge in the final decision. To resolve this issue, we aimed to exclude comorbidities and further assessed to better find any association between mental disorders and cardiovascular diseases (CVD).

Methods: The cross-sectional study involved 300 participants: 100 with HTN (without HF or CAD), 100 with HF (without HTN or CAD), 100 with CAD (without HTN or $H F)$, and 100 healthy individuals as a control group. To evaluate depression, anxiety, and stress levels, the Depression, Anxiety, and Stress Scale - 21 (DASS-21) was applied. For further analysis, the SPSS ver. 20 was used.

Results: The analysis showed that the score of depression, anxiety, and stress was higher in the HTN patients compared to the control ( $p<0.001$ ), CAD ( $p<0.001$ ), and HF ( $p<0.001$ ) groups, respectively. However, no significant differences were observed between the other study groups. Notably, patients with HF and CAD without concurrent HTN had similar psychological distress levels to healthy participants. Conclusion: The present study emphasized the higher prevalence of psychological distress in HTN patients and suggests a requirement for further research regarding the etiology involved in this association.


## KEYWORDS

anxiety, coronary artery disease, depression, heart failure, hypertension, stress

## 1 | INTRODUCTION

Despite recent advances in healthcare and therapeutics, cardiovascular diseases (CVDs) remain one of the leading causes of morbidity and mortality worldwide. ${ }^{1,2}$ It has been reported that CVDs cause over 18 million mortalities per year, which will rise to
23.3 million by $2030 .{ }^{3}$ Besides, CVDs impose a heavy social and financial burden on the global economy, particularly in low- and middle-income countries. ${ }^{4}$ Aging, obesity, inadequate preventive strategies, and suboptimal management of risk factors increase the burden of CVDs. ${ }^{4}$ However, it is noteworthy that well-known cardiac risk factors such as aging and obesity can explain only half

[^0]of the causes of clinical CVDs. ${ }^{5}$ On the other hand, a growing body of evidence has emphasized the substantial role of psychological disorders, especially depressive disorder, anxiety states, including panic disorder, post-traumatic psychological symptoms, and mental stress in the development of CVDs. ${ }^{6-8}$ To some extent, poor outcomes of patients with CVDs and concomitant psychological disorders have made them the subjects of much recent research in this era. ${ }^{9,10}$ Depression in patients with congestive heart failure (CHF) has an independent prognostic role in patients' outcomes and can promote about two to three-fold higher rates of re-hospitalization and mortality. ${ }^{9,10}$ Also, anxiety is reported to be significantly associated with mortality in patients with coronary artery disease (CAD). ${ }^{11}$

Likewise, it has been reported that higher stress states such as social isolation or work-related stress can lead to a poor prognosis in patients with established CAD. ${ }^{12}$ Although the underlying mechanisms are not well-defined, studies using electrophysiological and neurochemical techniques, demonstrated that the sympathetic nervous system activation in psychological disorders seems to have an important role in CVD development. ${ }^{5}$

To explain the underlying mechanisms jointly involved in psychological disorders and CAD development, it is worth noting that following depression, both hemostatic factors and acute phase proteins increase, promoting thrombus formation and subsequently resulting in ischemic heart diseases. ${ }^{13}$ Besides, inflammatory responses are instigated in patients with depression, following increased levels of pro-inflammatory cytokines, including interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ), accompanied by activation of the sympathetic nervous system, sympathetic outflow, and endothelial dysfunction.

In this context, there is also an association between systolic and diastolic blood pressures with serum levels of IL-6. In other words, hypertension is known as one of the main risk factors to stimulate inflammatory responses, leading to atherosclerotic events. Furthermore, mounting evidence showed a relationship between depression and metabolic disorders, consisting of hypercholesterolemia and hypertriglyceridemia. ${ }^{13}$

Noteworthy, a high prevalence of psychological disorders is reported among hypertensive patients in whom the numbers vary greatly among previous studies. ${ }^{14-17}$ In addition, there are contradictory reports regarding the subset of patients with HF or CAD suffering from concurrent psychological disorders. However, it should be noted that of the subjects with HF or CAD, there is a majority of patients with concomitant hypertension (HTN). ${ }^{18-20}$ Considering that the patients with HTN experience a higher rate of psychological disorders, ${ }^{21,22}$ the presumable bias regarding the intrusively higher prevalence of psychological disorders among the patients with HF and CAD would be expected due to the presence of HTN as a predisposing factor in this subgroup. ${ }^{23,24}$

Therefore, to resolve this issue we aimed to exclude those patients with HF and CAD who have a history or concomitant HTN and investigated the possible association between the considered CVDs and three important psychological conditions.

## 2 METHODS

This study was designed as a cross-sectional study on patients aged $\geq 18$ years, who were referred to the outpatient clinics (the name of the center was disclosed for peer review), from January 2019 to January 2020 using a combination of convenience sampling and medical records review. Inclusion criteria for the HTN, HF, and CAD groups included a confirmed diagnosis by a qualified healthcare professional based on established clinical guidelines (explained briefly below). A total of 300 patients were consecutively included, of whom 100 patients had HTN (without a history or concomitant HF or CAD), 100 patients had HF (without a history or concomitant HTN or CAD), and 100 patients had CAD (without a history or concomitant HTN or HF). A total number of 100 healthy participants was also considered as the control group. Written informed consent for participation was obtained and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research ethics committee.

The diagnosis of HF, HTN, and CAD was assigned by an attending cardiologist. The HF diagnosis was based on the Framingham criteria, in which the patients meet either at least two major criteria or one major + two minor criteria along with the $<40 \%$ ejection fraction (EF). ${ }^{25}$ Patients with systolic blood pressure of $\geq 140 \mathrm{~mm} \mathrm{Hg}$ and diastolic blood pressure of $\geq 90 \mathrm{~mm} \mathrm{Hg}$ or who receive antihypertensive drugs were considered hypertensive according to the Eighth Joint National Committee (JNC 8) guideline. ${ }^{26}$ Regarding CAD, it was also diagnosed based on a history of confirmed myocardial infarction (MI) or a previous angiography report demonstrating more than 50\% luminal narrowing of coronary arteries. ${ }^{25}$ The exclusion criteria for all groups were individuals with other significant cardiovascular conditions, severe comorbidities, inability to provide informed consent, pregnancy, substance abuse disorders, inadequate language proficiency, terminal illness, or non-compliance with the study protocol.

Demographic characteristics, including age, gender, marital status, place of residence, education, number of children, and occupation status were also recorded. The average rate of sleeping (hours), self-reported sleep disorders, and incidence of spontaneous crying were asked, as well. Depression Anxiety Stress Scale 21 (DASS-21) was used as a value of the three traits of depression, anxiety, and stress. DASS-21 scale, consisting of 21 questions, each question needs to be answered on a 4-point scale. The internal consistency scores for this scale in terms of Cronbach's alpha scores rate are high (0.96-0.97 for Depression, 0.84-0.92 for Anxiety, and 0.90-0.95 for Stress). ${ }^{27,28}$ The patients' scores were interpreted by converting them to $z$-scores and comparing them to the normative values contained in the DASS manual. The scores obtained from the DASS-21 were converted to the DASS normative data and multiplied the scores by two ( $\times 2$ ). A $z$-score of 0.5 was considered normal, $0.5-1.0$ was mild, 1.0-2.0 was moderate, 2.0-3.0 was severe, and $z$-scores over 3.0 were considered extremely severe depression, anxiety, or stress status. In this study, a translated version of the DASS-21(in Persian) was used. The validity and reliability of the Persian translation of

DASS-21 have also been verified previously (Cronbach Alphas of $0.77,0.79$, and 0.78 for the depression, anxiety, and stress subscales, respectively). ${ }^{29}$ Furthermore, a significant correlation of DASS21 with well-known criteria such as Beck's Depression Inventory ( $r=0.70$ ), Zung's Anxiety Inventory ( $r=0.67$ ), and Perceived Stress Inventory ( $r=0.49$ ) has also been demonstrated. ${ }^{29}$

## 2.1 | Statistical data analysis

The Normal distribution of all variables was tested by the Kolmogorov-Smirnov test. The quantitative variables were calculated as mean and standard deviation (mean $\pm$ SD)/median, while the qualitative variables were expressed as frequency and percentage (\%). Student's $t$-test or Mann-Whitney $U$ was used to compare quantitative variables between two groups, and one-way ANOVA or the Kruskal-Wallis to compare the means of more than two groups. Chisquare or Fisher's exact test was used for qualitative variables. Also, the ANCOVA test was used to compare the scores between groups with adjustment for patients' demographics (age, gender, marriage status, education, residence place, and occupation), sleep duration, sleep disorder, and spontaneous crying with analysis of covariance (after logarithmic transformation). Finally, a post-hoc Tukey test was also performed to determine significant differences between groups. Data analysis was performed by SPSS software vs. 20.0. A $p$-value $<0.05$ was considered statistically significant.

## 3 | RESULTS

A total of 400 participants, including 213 women (53.2\%) and 187 men ( $46.8 \%$ ), with a mean age of $55.1 \pm 14.1$ years old, were included. The majority of the participants were married (95.8\%), illiterate $(34.7 \%)$, and urban residents ( $80.5 \%$ ), and employed ( $77 \%$ ). The participants had a median number of 3 children ( $0-11$ ). The demographic characteristics of participants within each study group are summarized in Table 1; in detail, the study groups were significantly different in age, gender, marriage status, children number, education, residence place, and occupation (Table 1, $p<0.001$ ).

As shown in Table 1, the study groups were highly varied in terms of sleep duration ( $p=0.035$ ) and sleep disorder ( $p<0.001$ ). While $70 \%$ of participants in the control group reported having adequate daily sleep (defined as 6-8h of sleep), $49 \%, 63 \%$, and $62 \%$ of patients with HTN, CAD, and HF reported having adequate daily sleep, respectively (Table 1). Although only $38 \%$ of participants in the control group suffered from a sleep disorder, it was as much as $71 \%$ in the HTN group, $43 \%$ in the CAD group, and $57 \%$ in the HF group (Table 1). In addition, the status of spontaneous crying was statistically different between the groups ( $p<0.001$ ), in which $12 \%$, $53 \%, 20 \%$, and $10 \%$ of control, HTN, CAD, and HF subjects reported experiencing spontaneous crying, respectively (Table 1).

Based on our findings, insufficient daily sleep, sleep disorder, and spontaneous crying were more common among HTN patients
when compared to other groups. As mentioned earlier, the depression, anxiety, and stress scores were classified by the DASS manual's normative values. Regarding the depression levels, the frequency of normal versus (vs.) severe levels in control, HTN, CAD, and HF groups were $90 \%$ vs. $1 \%, 43 \%$ vs. $9 \%, 91 \%$ vs. $1 \%$, and $94 \%$ vs. $2 \%$, respectively. Moreover, the prevalence of normal vs. severe anxiety levels in control, HTN, CAD, and HF groups were $86 \%$ vs. $1 \%, 24 \%$ vs. $44 \%, 85 \%$ vs. $2 \%$, and $92 \%$ vs. $2 \%$, respectively. Finally, the prevalence of normal vs. severe stress levels in control, HTN, CAD, and HF groups were $92 \%$ vs. $2 \%, 54 \%$ vs. $10 \%, 94 \%$ vs. $1 \%$, and $96 \%$ vs. $2 \%$, respectively (Table 2 ).

The total scores of depression in the study groups had an average of 4.6 in the control group, and 9.1, 3.7, and 4.4 in the patients with HTN, CAD, and HF, respectively (Table 2, Figure 1). As shown in Table 2, the depression scores between the study groups were significantly different ( $p<0.001$, Table 2). In the subgroup analysis, the depression scores of HTN patients were considerably higher in comparison with other study groups ( $p<0.001$; Table 3).

The estimations for anxiety scores revealed overall averages of 3.9, 11.1, 4.1, and 3.6 for control, HTN, CAD, and HF groups, respectively (Table 2). In addition, the study groups showed a remarkable difference in anxiety scores ( $p<0.001$, Table 2); in which, a higher amount of anxiety scores was reported among the HTN patients ( $p<0.05$, Table 3).

Regarding the total scores of stress, which were significantly different between the groups ( $p<0.001$ ), the overall averages of 6.5, 13.6, 5.2, and 5.4 , were estimated for control, HTN, CAD, and HF groups, respectively (Table 2). Similar to depression and anxiety scores, the stress scores of HTN patients were significantly higher when compared with other groups ( $p<0.05$ ), while the other scores did not show significant differences during sub-group analysis (Table 3).

## 4 | DISCUSSION

The association of cardiovascular diseases (CVDs) such as heart failure (HF), coronary artery disease (CAD), and hypertension (HTN) with psychological disorders, especially depression, anxiety, and mental stress are topics of great interest for recent investigations. The general belief is that HF, CAD, and HTN all can individually result in depression, anxiety, and mental stress and vice versa. However, we detected by excluding those patients with a history of HTN from HF and CAD groups that HF and CAD are not individually associated with depression, anxiety, and mental stress and only the HTN group had significantly worse conditions than the control group in terms of higher depression, anxiety, and mental stress. Also, a large number of HTN patients had sleeping disorders and spontaneous crying, whereas the patients with HF and CAD showed similar results to healthy participants in terms of the status of anxiety, stress, sleep duration, sleep disorders, and spontaneous crying regardless of depression which was even lower in HF patients when compared with the control group.

TABLE 1 The demographics of participants ( $n=400$ ).

|  | Study groups |  |  |  | $p \text {-Value }$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Control ( $n=100$ ) | HF ( $n=100$ ) | HTN ( $n=100$ ) | CAD ( $n=100$ ) |  |
| Age (years) ${ }^{\text {a }}$ | 43.5 (13.0) | 62.8 (11.5) | 55.8 (12.3) | 58.3 (12.3) | $<0.001{ }^{\text {d }}$ |
| $S e x^{b}$ |  |  |  |  |  |
| Male | 37 (37.0) | 66 (66.0) | 21 (21.0) | 63 (63.0) | $<0.001{ }^{\text {e }}$ |
| Female | 63 (63.0) | 34 (34.0) | 79 (79.0) | 37 (37.0) |  |
| Marriage status ${ }^{\text {b }}$ |  |  |  |  |  |
| Married | 89 (89.0) | 100 (100) | 95 (95.0) | 99 (99.0) | $<0.001{ }^{\text {e }}$ |
| Single | 11 (11.0) | 0 | 5 (5.0) | 1 (1.0) |  |
| Children (number) ${ }^{\text {c }}$ | 2 (0-8) | 4 (1-11) | 3 (0-10) | 3 (0-9) | $<0.001^{\text {f }}$ |
| Education ${ }^{\text {b }}$ |  |  |  |  |  |
| Illiterate | 13 (13.0) | 59 (59.0) | 31 (31.0) | 36 (36.0) | $<0.001{ }^{\text {e }}$ |
| Middle school | 22 (22.0) | 35 (35.0) | 35 (35.0) | 34 (34.0) |  |
| Diploma | 24 (24.0) | 6 (6.0) | 15 (15.0) | 16 (16.0) |  |
| University degree | 41 (41.0) | 0 | 19 (19.0) | 14 (14.0) |  |
| Residence place ${ }^{\text {b }}$ |  |  |  |  |  |
| Urban | 90 (90.0) | 61 (61.0) | 90 (90.0) | 81 (81.0) | $<0.001{ }^{\text {e }}$ |
| Rural | 10 (10.0) | 39 (39.0) | 10 (10.0) | 19 (19.0) |  |
| Occupation ${ }^{\text {b }}$ |  |  |  |  |  |
| Unemployed | 6 (6.0) | 28 (28.0) | 5 (5.0) | 7 (7.0) | $<0.001{ }^{\text {e }}$ |
| Employee | 21 (21.0) | 0 | 11 (11.0) | 12 (12.0) |  |
| Businessman | 25 (25.0) | 34 (34.0) | 9 (9.0) | 29 (29.0) |  |
| Retired | 10 (10.0) | 6 (6.0) | 11 (11.0) | 19 (19.0) |  |
| Housekeeper | 38 (38.0) | 32 (32.0) | 64 (64.0) | 33 (33.0) |  |
| Sleep duration ${ }^{\text {b }}$ |  |  |  |  |  |
| 6-8h | 70 (70.0) | 62 (62.0) | 49 (49.0) | 63 (63.0) | $0.035^{\text {e }}$ |
| 3-6h | 28 (28.0) | 38 (38.0) | 48 (48.0) | 35 (35.0) |  |
| $<3 \mathrm{~h}$ | 2 (2.0) | 0 | 3 (3.0) | 2 (2.0) |  |
| Sleep disorder ${ }^{\text {b }}$ | 38 (38.0) | 57 (57.0) | 71 (71.0) | 43 (43.0) | $<0.001{ }^{\text {e }}$ |
| Spontaneous crying ${ }^{\text {b }}$ | 12 (12.0) | 10 (10.0) | 53 (53.0) | 20 (20.0) | $<0.001{ }^{\text {e }}$ |

${ }^{\text {a }}$ Data are presented as Mean (SD).
${ }^{\text {b }}$ Data are presented as $n$ (\%).
${ }^{\text {c }}$ Data are presented as Median (min-max).
${ }^{\mathrm{d}}$ Analysis of variance (ANOVA).
${ }^{e}$ Fisher's exact test.
${ }^{\mathrm{f}}$ Kruskal-Wallis test.

Overall, these results confirm the evidence demonstrating a significant association between psychological disorders and HTN. ${ }^{14-17}$ Similarly, Ginty et al. revealed a significant association between symptoms of depression and anxiety and a diagnosis of HTN followed up for 5 years. ${ }^{7}$ However, they did not consider other CV comorbidity and their additional impacts on the progression of psychological disorders. Maatouk et al., in a recent study, have also confirmed the relationship between depression and a higher risk of HTN. ${ }^{14}$ Of note, some studies have recently questioned the above-mentioned findings, proposing that depression and anxiety can lead to lower BP. ${ }^{16,17,30}$ In this regard, two studies attempted to explain these discrepancies and presumed an
age-related pattern more common in middle-aged patients than in young or elderly individuals. ${ }^{6,31}$ In parallel with this finding, we also reported the HTN group mainly consisted of middle-aged patients (half of the patients aged between 48 and 65 years). However, the underlying mechanisms involved in the age-related pattern remain to be determined. Intriguingly, a possible association between mental illness, such as anxiety or depressive symptoms in elderly hypertensive patients, all-cause mortality, and the development of newly diagnosed cardiovascular events (CVE) was investigated in a cohort study at 8 years follow-up. The results uncovered a significant association between psychological distress and new coronary events but not all-cause mortality. ${ }^{32}$

TABLE 2 The levels of depression, anxiety, and stress in study groups ( $n=400$ ).

|  | Study groups |  |  |  | $p$ Value |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Control ( $n=100$ ) | HF ( $n=100$ ) | HTN ( $n=100$ ) | CAD ( $n=100$ ) |  |
| Depression level ${ }^{\text {a }}$ |  |  |  |  |  |
| Normal | 90 (90.0) | 94 (94.0) | 43 (43.0) | 91 (91.0) | <0.001 |
| Mild | 8 (8.0) | 4 (4.0) | 28 (28.0) | 5 (5.0) |  |
| Moderate | 1 (1.0) | 0 | 20 (20.0) | 3 (3.0) |  |
| Severe | 1 (1.0) | 0 | 7 (7.0) | 1 (1.0) |  |
| Very severe | 0 | 2 (2.0) | 2 (2.0) | 0 |  |
| Anxiety level ${ }^{\text {a }}$ |  |  |  |  |  |
| Normal | 86 (86.0) | 92 (92.0) | 24 (24.0) | 85 (85.0) | <0.001 |
| Mild | 7 (7.0) | 2 (2.0) | 7 (7.0) | 6 (6.0) |  |
| Moderate | 6 (6.0) | 4 (4.0) | 25 (25.0) | 7 (7.0) |  |
| Severe | 1 (1.0) | 0 | 25 (25.0) | 1 (1.0) |  |
| Very severe | 0 | 2 (2.0) | 19 (19.0) | 1 (1.0) |  |
| Stress level ${ }^{\text {a }}$ |  |  |  |  |  |
| Normal | 92 (92.0) | 96 (96.0) | 54 (54.0) | 94 (94.0) | <0.001 |
| Mild | 4 (4.0) | 2 (2.0) | 16 (16.0) | 1 (1.0) |  |
| Moderate | 2 (2.0) | 0 | 20 (20.0) | $4(4.00$ |  |
| Severe | 2 (2.0) | 2 (2.0) | 9 (9.0) | 1 (1.0) |  |
| Very severe | 0 | 0 | 1 (1.0) | 0 |  |
| Mean scores (95\% confidence interval) |  |  |  |  |  |
| Depression score | 4.6 (4.0-5.4) | 4.4 (3.5-5.3) | 9.1 (7.8-10.5) | 3.7 (3.1-4.5) | $<0.001^{\text {b }}$ |
| Anxiety score | 3.9 (3.3-4.6) | 3.6 (3.0-4.2) | 11.1 (9.6-12.8) | 4.1 (3.5-4.8) | <0.001 ${ }^{\text {b }}$ |
| Stress score | 6.5 (5.5-7.6) | 5.4 (4.7-6.2) | 13.6 (12.2-15.1) | 5.2 (4.5-6.0) | $<0.001^{\text {b }}$ |

${ }^{a}$ Data are presented as $n$ (\%).
${ }^{\mathrm{b}}$ Analysis of covariance (ANCOVA) adjusted for patients' demographics, sleep duration, sleep disorder, and spontaneous crying with analysis of covariance (after logarithmic transformation).

Some underlying mechanisms have been proposed regarding the association between psychological distress and HTN. Both unhealthy behaviors and physiological dysregulation in patients with psychological disorders are assumed to contribute to the development of HTN. Some of the possible physiological dysregulations include altered hypothalamic-pituitary-adrenal axis, ${ }^{33}$ deregulated autonomic function, ${ }^{34}$ and altered brain activity (i.e., hypometabolism of dorsal cortical regions and ventral limbic structures). ${ }^{35}$ Besides, an increased postganglionic sympathetic fibers activation passing to blood vessels of skeletal muscle results in vasoconstriction and increased blood pressure in patients with borderline or established hypertension. ${ }^{5,36,37}$

Although previous studies indicated that there is an association between HF and CAD with psychological disorders, ${ }^{18-20}$ our results did not support this finding. One possible reason for this discrepancy could be the inclusion of HF/CAD patients with concomitant HTN. Garfield et al. also reported a significant association between anxiety disorders and depression with incident HF. Although the results of this study were adjusted to HTN at baseline due to existing depression/anxiety disorders over the course of the study, it was not considered in the final analysis as a confounding factor. ${ }^{18}$

It is also worth noting that some studies did not mention managing the HTN confounding effect in the progression of depression in HF patients. ${ }^{19,38}$ Abramson et al. revealed that depression could lead to a two-fold higher rate of HF incidence in patients with HTN. Furthermore, they corroborated that HTN may play a critical role in this association. ${ }^{24}$

Conclusively, it can be thought that despite the higher prevalence of depression among HF patients, this phenomenon could be mainly related to HTN. Interestingly, once the HF patients with a history of HTN were excluded, no higher rate of depression was observed. Similar results could also find a cross-talk between HF and anxiety/stress. ${ }^{18,38,39}$ A recent cross-sectional study also evaluated the prevalence of psychological distress in hypertensive patients. According to the results, the highest rate was followed by anxiety (21.3\%), depression (16.2\%), and stress symptoms (13.9\%), respectively. However, the uncontrolled hypertensive population showed a different trend upon performing logistic regression, including depressive, anxiety, and stress symptoms. ${ }^{40}$ In this context, Eghbali et al. also designed a study to determine psychological distress, selfcare, and medication adherence on HTN control. They found a negative relationship between psychological distress score, self-care,

FIGURE 1 The results of three dimensions of DASS-21 included CAD

TABLE 3 The post-hoc differences in depression, anxiety, and stress scores $(n=400)$.

| Study groups | Mean difference (95\% CI) |
| :--- | :--- |
| HF vs. control | $0.5(-1.7$ to 2.7$)$ |
| HTN vs. control | $5.7(3.7$ to 7.7$)$ |
| CAD vs. control | $0.3(-1.6$ to 2.3$)$ |
| HTN vs HF | $5.2(3.1$ to 7.3$)$ |
| CAD vs. HF | $-0.1(-2.0$ to 1.7$)$ |
| CAD vs HTN | $-5.3(-7.3$ to -3.4$)$ |
| HF vs. control | $1.2(-0.9$ to 3.3$)$ |
| HTN vs. control | $8.7(6.8$ to 10.6$)$ |
| CAD vs. control | $1.5(-0.4$ to 3.4$)$ |
| HTN vs. HF | $7.5(5.5$ to 9.5$)$ |
| CAD vs. HF | $0.3(-1.4$ to 2.1$)$ |
| CAD vs HTN | $-7.2(-9.0$ to -5.3$)$ |
| HF vs. control | $1.6(-0.9$ to 4.1$)$ |
| HTN vs. control | $7.9(5.6$ to 10.1$)$ |
| CAD vs. control | $1.0(-1.3$ to 3.3$)$ |
| HTN vs. HF | $6.3(3.8$ to 8.7$)$ |
| CAD vs. HF | $-0.6(-2.7$ to 1.5$)$ |
| CAD vs. HTN | $-6.9(-9.1$ to -4.6$)$ |

Abbreviation: 95\% CI: 95\% confidence interval.
${ }^{\text {a }}$ The post-hoc Tukey test.
and subsequent HTN management. ${ }^{41}$ It has been finally highlighted that psychological intervention would be warranted in the HTN therapeutic schedule. In this line, Ang and his colleagues recently
documented that using a hypertension care cascade accompanied by mental health interventions would substantially aid in providing mental health support to hypertensive patients. ${ }^{42}$ Beyond the strong cross-talk between the occurrence of HTN and mental illness, Hert et al. emphasized bidirectional links between mental illness and coronary heart disease (CHD), in which severe mental illness (e.g., major depression, schizophrenia, and bipolar disorder) exerted an increased risk of developing CHD when compared with healthy individuals [adjusted hazard ratio $(\mathrm{HR})=1.54 ; 95 \%$ confidence interval (CI): 1.30-1.82, $p<0.0001$ ], while, with a lesser extent, anxiety (Relative Risk $(R R)=1.41,95 \% \mathrm{Cl}: 1.23-1.61, p<0.0001$ ), as well as experience of stress ( $\mathrm{HR}=1.27,95 \% \mathrm{Cl}: 1.08-1.49$ ) were independently associated with CHD developing. ${ }^{43}$ Notably, a prospective cohort study revealed that the higher rate of psychological distress among women with CAD was directly associated with a higher incidence of upcoming CVD events. ${ }^{44}$

In the case of HF, it has also been well-established that some psychological problems, especially depression, contribute to promoting adverse outcomes under cardiovascular conditions. However, we could not find any significant adverse effects regarding the development of psychological distress in patients with HF. ${ }^{45}$

Although this cross-sectional study may not allow us to argue more about the involved factors in the relationship between psychological disorders and HTN, the low rate of psychological disorders among HF and CAD patients without concomitant HTN leads us to suppose that the psychological distress in HTN is more likely to be a physical response rather than an emotional behavior. However, this issue must be proved by further longitudinal studies and preventive intervention research.

## 4.1 | Study limitations

Our study also had some limitations. First, this study was designed as a cross-sectional rather than a cohort study. Second, the analysis of demographic characteristics demonstrated significant differences among the study groups, possibly due to the consecutive inclusion of patients without considering their demographic characteristics. A previous study in Iran indicated no significant association between DASS-21 scale scores and demographic variables (i.e., age, gender, education, and marital status). ${ }^{46}$ Therefore, differences in demographic characteristics may not stop us from considering our data for comparing the results of DASS-21 between HTN, HF, and CAD patients. However, possible confounding effects of these variables were controlled in the final analysis.

## 5 | CONCLUSION

Our study demonstrated a significantly higher rate of psychological distress (including stress, anxiety, and depression) among patients with HTN. However, the rate of psychological disorders in patients with HF and CAD without concomitant HTN was similar to those in healthy participants. Therefore, we can also conclude that (1) the confounding effect of HTN needs to be considered in future studies, and evaluated the possible association between psychological disorders and HF/CAD. (2) Due to the higher rate of incident psychological disorders among HTN patients and subsequent negative implications, more attention should be paid to mental disorders in these patients. (3) Given that we found higher rates of psychological disorders among patients with HTN but not HF and CAD, it can pave the way for broader investigations to find the exact pathophysiology that uniquely links HTN to mental disorders.

## AUTHOR CONTRIBUTIONS

Hossein Namdar, designed the study, Fatemeh Jamshidi, collected the data; Aysa Rezabakhsh, prepared the first draft; Davoud Ezzati, contributed to data analysis, Raana Zakeri, interpreted the results; Seyyed-Reza Sadat-Ebrahimi, supervised the work.

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## CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

## DATA AVAILABILITY STATEMENT

All data and material collected during this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

Ethics approval statement: The protocol of this study was approved by the medical ethics committee of our institution.

Patient consent statement: Informed consent was obtained from the participants.

Permission to reproduce material from other sources: Consent for publication was granted.

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## REFERENCES

1. Smith SC, Collins A, Ferrari R, Holmes DR, Logstrup S, McGhie DV, et al. Our time: a call to save preventable death from cardiovascular disease (heart disease and stroke). J Am Coll Cardiol. 2012;60(22):2343-8.
2. Bansilal S, Castellano JM, Fuster V. Global burden of CVD: focus on secondary prevention of cardiovascular disease. Int J Cardiol. 2015;201 Suppl 1:S1-S7.
3. World Health Organization Cardiovascular diseases (CVDs). Available from: https://www.who.int/news-room/fact-sheets/de-tail/cardiovascular-diseases-(cvds). Accessed 3 Jun 2023.
4. Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. Health Aff. 2007;26(1):38-48.
5. Esler M, Kaye D. Sympathetic nervous system activation in essential hypertension, cardiac failure and psychosomatic heart disease. J Cardiovasc Pharmacol. 2000;35:S1-S7.
6. Gangwisch JE, Malaspina D, Posner K, Babiss LA, Heymsfield SB, Turner JB, et al. Insomnia and sleep duration as mediators of the relationship between depression and hypertension incidence. Am J Hypertens. 2010;23(1):62-9.
7. Ginty A, Carroll D, Roseboom T, Phillips A, De Rooij S. Depression and anxiety are associated with a diagnosis of hypertension 5 years later in a cohort of late middle-aged men and women. J Hum Hypertens. 2013;27(3):187-90.
8. Darabi Z, Najafi F, Safari-Faramani R, Salimi Y. Controlled direct effect of psychiatric disorders on cardiovascular disease: evidence from a large Kurdish cohort. BMC Cardiovasc Disord. 2020;20(1):501.
9. Jiang W, Alexander J, Christopher E, Kuchibhatla M, Gaulden LH, Cuffe MS, et al. Relationship of depression to increased risk of mortality and Rehospitalization in patients with congestive heart failure. Arch Intern Med. 2001;161(15):1849-56.
10. Freedland KE, Carney RM, Rich MW. Effect of depression on prognosis in heart failure. Heart Fail Clin. 2011;7(1):11-21.
11. Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ. Tension and anxiety and the prediction of the 10-year incidence of coronary heart disease, atrial fibrillation, and total mortality: the Framingham offspring study. Psychosom Med. 2005;67(5):692-6.
12. Steptoe A, Kivimäki M. Stress and cardiovascular disease. Nat Rev Cardiol. 2012;9(6):360-70.
13. Ho RCM, Chua AC, Tran BX, Choo CC, Husain SF, Vu GT, et al. Factors associated with the risk of developing coronary artery disease in medicated patients with major depressive disorder. Int J Environ Res Public Health. 2018;15(10):2073.
14. Maatouk I, Herzog W, Bohlen F, Quinzler R, Lowe B, Saum KU, et al. Association of hypertension with depression and generalized anxiety symptoms in a large population-based sample of older adults. J Hypertens. 2016;34(9):1711-20.
15. Ohmori Y, Ito H, Morita A, Deura K, Miyachi M. Associations between depression and unhealthy behaviours related to metabolic syndrome: a cross sectional study. Asia Pac J Clin Nutr. 2017;26(1):130-40.
16. Jackson CA, Pathirana T, Gardiner PA. Depression, anxiety and risk of hypertension in mid-aged women: a prospective longitudinal study. J Hypertens. 2016;34(10):1959-66.
17. Bhat SK, Beilin LJ, Robinson M, Burrows S, Mori TA. Relationships between depression and anxiety symptoms scores and blood pressure in young adults. J Hypertens. 2017;35(10):1983-91.
18. Garfield LD, Scherrer JF, Hauptman PJ, Freedland KE, Chrusciel T, Balasubramanian S, et al. Association of anxiety disorders and depression with incident heart failure. Psychosom Med. 2014;76(2):128-36.
19. Jani BD, Mair FS, Roger VL, Weston SA, Jiang R, Chamberlain AM. Comorbid depression and heart failure: a community cohort study. PLoS One. 2016;11(6):e0158570.
20. Rosenman RH, Brand RJ, Jenkins CD, Friedman M, Straus R, Wurm M. Coronary heart disease in the Western collaborative group study: final follow-up experience of $81 / 2$ years. JAMA. 1975;233(8):872-7.
21. Taraghi Z, Akbari Kamrani A-A, Foroughan M, Yazdani J, Mahdavi A, Baghernejad SK. Cognitive impairment among elderly patients with chronic heart failure and related factors. Iran J Psychiatry Behav Sci. 2016;10(2):e4500.
22. Zuccala G, Marzetti E, Cesari M, Lo Monaco MR, Antonica L, Cocchi A, et al. Correlates of cognitive impairment among patients with heart failure: results of a multicenter survey. Am J Med. 2005;118(5):496-502.
23. Serafini G, Pompili M, Innamorati M, Iacorossi G, Cuomo I, Della Vista M, et al. The impact of anxiety, depression, and suicidality on quality of life and functional status of patients with congestive heart failure and hypertension: an observational cross-sectional study. Prim Care Companion J Clin Psychiatry. 2010;12(6):PCC.09m00916.
24. Abramson J, Berger A, Krumholz HM, Vaccarino V. Depression and risk of heart failure among older persons with isolated systolic hypertension. Arch Intern Med. 2001;161(14):1725-30.
25. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. Braunwald's heart disease a textbook of cardiovascular medicine. Philadelphia: Elsevier Health Sciences; 2018.
26. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-20.
27. Clara IP, Cox BJ, Enns MW. Confirmatory factor analysis of the de-pression-anxiety-stress scales in depressed and anxious patients. J Psychopathol Behav Assess. 2001;23(1):61-7.
28. Page AC, Hooke GR, Morrison DL. Psychometric properties of the depression anxiety stress scales (DASS) in depressed clinical samples. Br J Clin Psychol. 2007;46(3):283-97.
29. Sahebi A, Asghari MJ, Salari RS. Validation of depression anxiety and stress scale (DASS-21) for an Iranian population. Iran Psychol. 2005;4(1):299-313.
30. Hildrum B, Romild U, Holmen J. Anxiety and depression lowers blood pressure: 22-year follow-up of the population based HUNT study, Norway. BMC Public Health. 2011;11(1):601.
31. Nabi H, Chastang J-F, Lefèvre T, Dugravot A, Melchior M, Marmot MG, et al. Trajectories of depressive episodes and hypertension over 24 years: the Whitehall II prospective cohort study. Hypertension. 2011;57(4):710-6.
32. de Hartog-Keyzer JML, Pedersen SS, El Messaoudi S, Nijveldt R, Pop VJM. Psychological distress is independently related to new
coronary events at 8 years' follow-up in elderly primary care patients with hypertension. J Psychosom Res. 2022;160:110980.
33. Brown ES, Varghese FP, McEwen BS. Association of depression with medical illness: does cortisol play a role? Biol Psychiatry. 2004;55(1):1-9.
34. Kibler JL, Ma M. Depressive symptoms and cardiovascular reactivity to laboratory behavioral stress. Int J Behav Med. 2004;11(2):81-7.
35. Taylor WD, Aizenstein HJ, Alexopoulos GS. The vascular depression hypothesis: mechanisms linking vascular disease with depression. Mol Psychiatry. 2013;18:963-74.
36. Esler M. Sympathetic activity in experimental and human hypertension. Handbook Hypertens. 1997;17:628-73.
37. Julius S. Changing role of the autonomic nervous system in human hypertension. J Hypertens Suppl. 1990;8(7):S59-S65.
38. Haworth JE, Moniz-Cook E, Clark AL, Wang M, Waddington R, Cleland JGF. Prevalence and predictors of anxiety and depression in a sample of chronic heart failure patients with left ventricular systolic dysfunction. Eur J Heart Fail. 2005;7(5):803-8.
39. Jiang W, Babyak M, Krantz DS, Waugh RA, Coleman RE, Hanson MM, et al. Mental stress-induced myocardial ischemia and cardiac events. JAMA. 1996;275(21):1651-6.
40. Loke WH, Ching SM. Prevalence and factors associated with psychological distress among adult patients with hypertension in a primary care clinic: a cross-sectional study. Malays Fam Physician. 2022;17(2):89-98.
41. Eghbali M, Akbari M, Seify K, Fakhrolmobasheri M, Heidarpour M, Roohafza H, et al. Evaluation of psychological distress, self-care, and medication adherence in association with hypertension control. Int J Hypertens. 2022;2022:7802792.
42. Ang CW, Tan MM, Bärnighausen T, Reininghaus U, Reidpath D, Su TT. Mental distress along the cascade of care in managing hypertension. Sci Rep. 2022;12(1):15910.
43. De Hert M, Detraux J, Vancampfort D. The intriguing relationship between coronary heart disease and mental disorders. Dialogues Clin Neurosci. 2018;20(1):31-40.
44. Pimple P, Lima BB, Hammadah M, Wilmot K, Ramadan R, Levantsevych O, et al. Psychological distress and subsequent cardiovascular events in individuals with coronary artery disease. J Am Heart Assoc. 2019;8(9):e011866.
45. Moser DK, Arslanian-Engoren C, Biddle MJ, Chung ML, Dekker RL, Hammash MH, et al. Psychological aspects of heart failure. Curr Cardiol Rep. 2016;18(12):119.
46. Asghari A, Saed F, Dibajnia P. Psychometric properties of the depression anxiety stress Scales-21 (DASS-21) in a non-clinical Iranian sample. Int J Psychol. 2008;2(2):82-102.

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