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Treatment adherence as a mediator of blood pressure control in Chinese older adults with depression

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Abstract

Objectives: Both depression and hypertension (HTN) are prevalent, costly and destructive, and frequently coexist among the aging population of China. This study aimed to examine the role that treatment adherence plays in blood pressure control in older adult Chinese with depression.

Methods: Data for these analyses were taken from a randomized control trial of a collaborative depression care management intervention conducted in rural villages of Zhejiang Province, China with older adults who had comorbid depression and HTN. They included baseline assessments of 2362 subjects ages 60 years, whose blood pressure and depression were measured using a calibrated manual sphygmomanometer and the Chinese version of the 17-item Hamilton

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Conflict of Interest
None.

Depression Rating Scale (HDRS-17) respectively. Treatment adherence was identified by a single question asking whether patients on occasion did not take their medicine.

Results: Uncontrolled HTN was associated with older age ($t=3.10$, $p<0.01$), higher HDRS-17 score ($t=5.76$, $p<0.01$), and higher rates of non-adherence to HTN treatment ($\chi^2=21.34$, $p<0.01$). Logistic regression models indicated that adherence accounted for 39.4% of the total effect between depression and HTN. Specifically, those with poor adherence were at 1.417 greater odds of having their HTN uncontrolled compared to those with good adherence.

Conclusions: HTN control in older adults with depression is complicated by nonadherence to treatment. In addition to diagnosing and treating depression in their older adult patients, primary care physicians can optimize blood pressure control by identifying and addressing their patients' adherence to recommendations for HTN management.

Keywords

Hypertension; Depression; Adherence; Mediation; Elderly

Introduction

Hypertension (HTN) is one of the most common chronic diseases among older adults. As the underlying cause of two-thirds of all strokes and half of all ischemic heart disease¹, it is a major risk factor for cardiovascular morbidity and mortality^{2,3}. Approximately one-quarter of individuals have been diagnosed with HTN worldwide, with estimates that in China almost 30% will have the diagnosis by 2025^{4,5}. HTN is estimated to affect about 57% of Chinese people aged ≥ 65 years⁶, and is poorly recognized and inadequately treated. In one recent study⁷ of rural Chinese older adults, only 45% of cases of HTN were recognized, and while over 94% of diagnosed patients were being treated, blood pressure (BP) was controlled in only 5%.

Depression is one of the leading causes of disability worldwide⁸, with approximately 350 million people affected⁹. Patients suffering from depression may experience multiple medical comorbidities with functional impairment¹⁰, poor clinical outcomes¹¹, and increased health care expenditures¹². At its worst, depression can lead to increased all-cause mortality and suicide^{13,14}. Like HTN, depression is common in the aging population of China, where 8% of its residents aged 60 or more were diagnosed with depression, and only 5% of them preferred to seek treatment from mental health professionals¹⁵.

As the first and second disorders in the WHO's list of greatest expected causes of global illness burden by 2020¹⁶, depression and HTN often coexist, and each complicates the management of the other^{17–21}. Depression is well recognized as a risk factor for HTN and may impact its treatment adherence²⁰. As well, HTN and its sequelae are risk factors for depression, complicating help-seeking, diagnosis, treatment and prognosis²¹. We recently reported that 13% of rural Chinese primary care patients aged 60 or more with HTN had clinically significant depressive symptoms, and that the presence of depressive symptoms was associated with poor BP control – 70% of those with depressive symptoms had uncontrolled HTN compared to 21% of those without²².

Given the strong evidence of an association between depression and HTN, our further interest was to explore in greater depth the nature of this association. In this article we focused on treatment adherence as a mediator to uncontrolled HTN in depression. Adherence, defined as “the extent to which a person’s behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice”²³, is highly variable in chronic disease management, with estimates for levels of medication adherence range from 20% to 80%^{24,25}. As well, adherence is a potent determinant of treatment outcome. Approximately 50% of treatment failures are ascribable to non-adherence²⁶. Recent studies demonstrate that poor adherence is associated with increased hospitalizations²⁷, higher costs²⁸ and higher rates of mortality^{29–31} in chronic diseases. Despite the clear benefits of antihypertensive medications on blood pressure control and cardiovascular outcomes, up to 50% of patients do not take their antihypertensive medications as prescribed and only 50% of treated individuals reach their blood pressure goals²⁶. That depression may complicate adherence is also fairly well established. Cukor and colleagues found that depression is an important contributor to low medication adherence in hemodialysis and transplant recipients³², and Ettinger and colleagues reported that depression was correlated with an increased risk of antiepileptic drug nonadherence³³. Moreover, a meta-analysis reported that depressed patients are 1.8 times more likely to be nonadherent with medical treatment recommendations for their chronic diseases than individuals who are not depressed³⁴.

Despite the frequency with which depression and HTN coexist and the importance of both adherence and depression to BP control, no study has yet examined the role that treatment adherence plays in the association between depression and HTN. As part of an ongoing study of management of comorbid depression and HTN among older adults cared for in rural Chinese primary care clinics, we tested the hypothesis that poor BP control is accounted for partly by poor treatment adherence in patients with depression. Understanding the role that adherence plays in HTN treatment outcome will give primary care providers (PCPs) additional guidance with which to manage HTN in their older depressed patients and improve treatment outcomes.

Methods

Setting and participants

Data for this analysis were taken from baseline assessments of the Depression/HTN in Chinese Older Adults—Collaborations in Health (COACH) Study, an ongoing project funded by the U. S. National Institute of Mental Health (NIMH) designed to compare collaborative depression care management with care as usual for the treatment of comorbid depression and HTN in Chinese older rural village residents³⁵.

Ten towns with a total of 219 villages were included in the COACH study (see Fig.1). Their total population aged ≥ 60 years was 101,318, of whom 29,659 (29%) has a diagnosis of HTN registered in their electronic medical records (EMR). PCPs for these patients screened 26,677 (89%) for depressive symptoms using the Patient Health Questionnaire-9 (PHQ-9), of whom 2,899 had a total PHQ-9 score ≥ 10, indicative of clinically significant depression³⁶, and were invited to participate in the study. Written informed consent was provided by 2,365

participants, of whom three had missing data on the blood pressure measurement. The remaining 2,362, therefore, constitute the sample for these analyses. The study was approved by the institutional review boards of Zhejiang University, the University of Rochester, and the NIMH.

Measurements

Blood pressure

BP measurements were made in the subjects' homes or village clinics by PCPs trained in the study procedures using a calibrated manual sphygmomanometer and stethoscope according to standards developed by Center for Disease Control and Prevention in China (auscultation with cuff deflation method after seated quietly for 5 minutes in the proper position; no caffeine, exercise or smoking in preceding 30 minutes; appropriately sized cuff; average of three measurements is recorded.). The BP readings distinguished two HTN conditions: controlled HTN vs. uncontrolled HTN. The latter was defined as systolic BP ≥ 130 or diastolic BP ≥ 80 for patients with diabetes mellitus, coronary heart disease or renal disease, and BP ≥ 140 or diastolic BP ≥ 90 for all others^{3,37}.

Depressive symptoms

Patients' depressive symptoms were assessed by research assistants, who were masked to the results of BP and adherence and trained in the administration of the 17-item Hamilton Depression Rating Scale (HDRS-17), during the same period of BP and adherence measurements. The Chinese version of HDRS-17 has been shown to have acceptable validity and reliability³⁸.

Treatment adherence

Adherence was identified by PCPs using a simple self-report item, "Do you sometimes forget to take your antihypertensive pills?" designed to reflect one's compliance to HTN treatment regardless of the reason. Responses were specified to be "Yes" or "No". This item has been frequently used to detect treatment adherence in older patients with HTN in China, where forgetting to take pills is a leading contributor to poor adherence^{39–41}.

Data analysis

Descriptive statistics (frequency distributions, T-test and Chi-square) were used to examine the basic characteristics of our sample divided into controlled and uncontrolled HTN subgroups.

Given that both the HTN and adherence were binary variables, we adopted the analytic strategy for testing mediation effects of categorical variables developed by Iacobucci⁴² by establishing three logistic regression models. The first and second models used depression as a predictor for uncontrolled HTN and adherence respectively, while the third model used depression and adherence as predictors for uncontrolled HTN. Age was included as a covariate in the analysis due to its significant association with adherence and HTN control. Box-Tidwell tests⁴³ were applied to examine the linearity of depression and age as continuous variables in the logit fitting processes before establishing these models, and

Hosmer and Lemeshow Tests⁴³ were conducted to test their goodness-of-fit. The statistic Z_{ab} derived from the three models was examined to determine whether the mediation effect of adherence was significant.

Uncontrolled HTN was code as “1” while controlled HTN was coded as “0”, and poor medication adherence (response “Yes”) was coded as “1” while the another was coded “0” in the analysis. Depression was treated as a continuous variable identified by the total score of HDRS-17. All analyses were performed using the Predictive Analytics Software Statistics, version 18.

Results

Demographic characteristics

In the analyzed sample, 1648 (71.3%) had uncontrolled HTN. Demographic characteristics in these two subgroups are listed in Table 1. Older patients with uncontrolled HTN had an older mean age than those with controlled HTN, but no significant differences were found on gender and literacy between the two groups. In addition, patients with uncontrolled HTN had a higher mean HDRS-17 score than those with controlled HTN. A significantly lower proportion of those with uncontrolled HTN endorsed being nonadherent to their medications as well.

Logistic Regression Model I using depression to predict HTN control

Before doing the logistic regression analyses, the Box-Tidwell tests⁴³ indicated acceptable linearity of depression and age as continuous variables in the logit fitting processes, which supported the linearity assumption of establishing logistic regression models.

All the results of logistic regression models were demonstrated in Table 2. The regression coefficient of depression in model I was 0.062, $p < 0.01$, indicating that depression was significantly associated with uncontrolled HTN. The Hosmer and Lemeshow Test for the goodness-of-fit of this model had a $\chi^2 = 18.35$, $df = 8$, $p = 0.02 < 0.05$, showing poor model fitness, which implied that other factors such as adherence should be included to better predict HTN control.

Logistic Regression Model II using depression to predict adherence

Logistic regression model II was designed to estimate the effect of depression in predicting treatment adherence. The regression coefficient of depression in this model was 0.063, $p < 0.01$, suggesting depression also contributed to poor adherence of HTN treatment. The Hosmer and Lemeshow Test for this model had a $\chi^2 = 7.85$, $df = 8$, $p = 0.449 > 0.05$, showing acceptable model fitness.

Logistic Regression Model III using depression and adherence to predict HTN control

The regression coefficients of depression and adherence were 0.057 and 0.349 respectively, both $p < 0.01$. The Hosmer and Lemeshow Test for this model had a $\chi^2 = 11.38$, $df = 8$, $p = 0.181 > 0.05$, indicating a good fitness of this model, with the relationships that depression and treatment adherence were significant predictors of one's blood pressure control.

Specifically, the odds ratio of adherence implied that nonadherent patients with depression were at about 1.417 greater odds of having uncontrolled HTN compared to those who were adherent.

Mediation of the association of depression and hypertension by treatment adherence

According to Iacobucci's (2012)⁴² suggestion, the examination of the mediation effect on categorical variables equals to the examination of the statistic Z_{ab} , which was calculated to be 3.095, $p < 0.01$ in this case.

Given the coefficient of depression in model III and the statistic Z_{ab} were significant^{42,44}, there existed a partial mediation of medication adherence between depression and uncontrolled HTN. The estimate of this mediation effect⁴⁴ was 39.4%, meaning that the mediation effect of adherence accounted for 39.4% of the total effect of depression on uncontrolled HTN.

Discussion

Both depression and HTN are prevalent and commonly coexist in older adults, complicating the management of one another with adverse health outcomes^{14,28}. Depression may impact HTN by both direct and indirect pathways. Direct effects may include some depression-caused and hypertension-related physiological process, such as increased sympathetic tone⁴⁵. Indirect means by which depression can exacerbate HTN include poor diet⁴⁶, decreased activity⁴⁷, smoking and alcohol abuse⁴⁸, and poor treatment adherence³⁴. However, few studies have examined the mediation effect of adherence in the association between depression and HTN, including in the aging population of China.

The main aim of present study was to explore the relationships among depression, HTN and adherence in Chinese older adults, and examine the mediation effect of adherence between depression and uncontrolled HTN.

Main findings

We found that more than two thirds of the study sample had their BP uncontrolled, and depression was significantly associated with higher risk of poor adherence and uncontrolled HTN. The results of mediation analyses supported our hypothesis that HTN control was mediated partially by treatment adherence in patients with HTN. These findings are consistent with previous work^{21,22}.

The unique contribution here is that a single question for adherence measurement explains in part the observed association between depression and uncontrolled HTN. Asking this single adherence question as the first level screen, therefore, may be an efficient means by which PCPs can identify a modifiable barrier to HTN control in their depressed patients.

Implications and limitations

Uncontrolled HTN is a risk factor of stroke, coronary heart disease, congestive heart failure, and mortality^{3,49}. In the present study we found that depression was significantly associated with higher risk of uncontrolled HTN, which underscores the importance of managing the

two disorders simultaneously in order to optimize treatments and achieve better health outcomes. Primary care-based collaborative care approaches, which have been developed and well tested in Western nations, are a promising strategy for management of depression^{50–52} and comorbid chronic conditions^{52,53} in primary care, testing of which in China is the objective of the COACH study.

We have demonstrated that adherence, determined by a simple, single item that is easily understood by rural elders, is an intermediate on the pathway to BP control in patients with depression, accounting for about one third of the total effect. An important implication of this finding is that by improving adherence, which is an especially common problem in people with depression, HTN control may be in turn improved. Nonadherence risk can be managed by means such as simplifying dosing regimens, motivational strategies, patient education or even complex approaches that overcome patient-specific barriers^{54,55}. Future studies are recommended to determine the effectiveness of these strategies on improving adherence and HTN control.

Furthermore, given the mediation effect is partial, other contributions such as the direct effect of depression on BP control or other unmeasured factors, are anticipated to effect HTN control. Thus, even with improving HTN treatment adherence, untreated depression may still lead to poor HTN treatment response. Therefore, while PCPs need to explore and address adherence to HTN treatment, they are also recommended to diagnose and treat depression and its other health related behavioral sequelae.

Our use of a single item of adherence is both a strength and a limitation. Since it is simple and general, PCPs can not know exactly why the person did not on occasion take their medicines. There are myriad potential reasons including poor health literacy (knowledge of consequences of untreated HTN), skepticism about the drug's efficacy, concerning about side effects, cost, memory decline and so on^{56,57}. In that sense, the single item is highly sensitive but nonspecific, characteristics of a useful first level screen. To then determine the underlying reason that one's patient may be nonadherent, further inquiry will be needed. PCPs should follow up a positive response to the single item with other questions in order to find out what the adherence problem is, and then work effectively with the patients to change their habits. In that case, PCPs may require additional training in psychoeducation and motivational interviewing techniques. Nonetheless, one easy to administer question sensitive to the potential for nonadherence is an effective first level screen with which to begin the process.

Other limitations of this study include that the focus here is solely on older adults with depression and HTN, a group at very high risk for both non-adherence and poor BP control. Nonetheless, the issue of adherence likely applies to older adults with depression and any chronic condition. Another concern is the exclusion of individuals who reported no significant depression, thus comparisons of adherence and HTN control can not be made between those with and without depression, which is also very interesting. Future studies are recommended to examine these associations.

The data in this study are cross-sectional, which prevented analysis of the longitudinal associations between depression, adherence and HTN. And finally, the sample is from rural villages in China, so our findings may have limited generalizability to higher income and better resourced areas. However, because depression and nonadherence to treatment are common problems worldwide, the findings may lend insights to HTN management in a wide range of cultures and primary care treatment settings.

Conclusion

To our best knowledge, the present study was the first attempt to examine the mediation effect of medication adherence on uncontrolled HTN in rural Chinese older adults with depression, adding new evidence to the literature on the relationships between patients' depression, adherence and HTN control. Uncontrolled HTN was found to be very common among older patients with depression, with their association partially mediated by adherence. PCPs are recommended to routinely use a brief question about treatment adherence as the first level screen in their older patients with depression as a basis for further inquiry and potential interventions to improve HTN treatment outcomes.

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Key Points:

1. Depression and hypertension commonly coexist among older people. However, the mechanism of their association has received little attention.
2. The current study found a partial mediation effect of adherence linking depression to hypertension control.
3. In addition to diagnosing and treating depression in their older patients, primary care physicians can optimize blood pressure control by identifying and addressing their patients' adherence to recommendations for hypertension management.
4. This finding may also need to be addressed by an integrated care model managing comorbid depression and hypertension.

Figure. 1. Participants procedure

HTN, hypertension; EMR, electronic medical record system; PHQ-9, nine item Patient Health Questionnaire.

Table 1

Demographic characteristics of participants

Demographic characteristics	Controlled HTN	Uncontrolled HTN	Statistics
N	678	1684	¥
Mean age, y $\pm$ SD	73.6 $\pm$ 8.3	74.8 $\pm$ 8.2	t=3.10, p <0.01
Women, n (%)	463 (68.3)	1111 (66.0)	χ^2 =1.17, p >0.05
Education, n (%)			
Illiteracy	357 (52.7)	938 (55.7)	
Primary school (1–5 yrs)	270 (39.8)	655 (38.9)	χ^2 =4.53, p >0.05
High school or higher ($\geq$ 6yrs)	51 (7.5)	91 (5.4)	
Mean HDRS-17 score, y $\pm$ SD	21.2 $\pm$ 3.5	22.2 $\pm$ 4.3	t=5.76, p <0.01
Poor adherence, n (%)	224 (33.0)	730 (43.3)	χ^2=21.34, p<0.01

Note: HTN, hypertension; HDRS-17, 17 item-Hamilton Depression Rating Scale.

Table 2

Estimates from logistic regression models

Model	Parameter	df	B	SE	Wald	Sig.	Exp(B)	95% CI for EXP(B)	
								Lower	Upper
I	HDRS-17	1	0.062	0.012	26.203	0.000	1.064	1.039	1.090
	Age	1	0.016	0.006	8.247	0.004	1.016	1.005	1.028
	Constant	1	-1.634	0.486	11.325	0.001	0.195	¥	¥
II	HDRS-17	1	0.063	0.010	36.438	0.000	1.065	1.043	1.087
	Age	1	0.038	0.005	53.014	0.000	1.039	1.028	1.050
	Constant	1	-4.639	0.458	102.674	0.000	0.010	¥	¥
III	HDRS-17	1	0.057	0.012	21.728	0.000	1.058	1.033	1.084
	Adherence	1	0.349	0.097	12.811	0.000	1.417	1.171	1.716
	Age	1	0.013	0.006	5.425	0.020	1.013	1.002	1.025
	Constant	1	-1.437	0.490	8.597	0.003	0.238	¥	¥

Note: HDRS-17, 17 item-Hamilton depression rating scale

Model I: HDRS-17 and age as predictors for uncontrolled hypertension

Model II: HDRS-17 and age as predictors for nonadherence

Model III: HDRS-17, adherence and age as predictors for uncontrolled hypertension.