Lack of Association Between Hypertension and Hypothyroidism in Postmenopausal Women Seen in a Primary Care Setting

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***Background*: Several studies undertaken in hospital-based specialty clinics have reported an association between hypertension and hypothyroidism. This work examines the association between these two common disorders in postmenopausal women seen within a primary care office setting.**

***Methods:* Seven hundred seven postmenopausal women aged 50 years and older were studied using a cross-sectional design. Data on thyroid status, hypertension and risk factors, and patient demographics were collected from the office medical record.**

***Results:* Overall, 45.4 percent of the population studied had hypertension and 10.9 percent had hypothyroidism. Compared with normotensive women, hypertensive women were significantly older (66.4 years versus 63.0 years, $P < 0.0001$) and had a higher body mass index (29.2 kg/m^2 versus 26.2 kg/m^2, $P < 0.0001$). Hypertension was significantly associated with diabetes mellitus and the use of NSAIDs (odds ratios [ORs] = 1.77 and 2.63, respectively). We did not find a significant association between hypertension and hypothyroidism (OR 1.04, 95 percent confidence interval 0.64 to 1.76).**

***Conclusions:* In this population of postmenopausal women we did not find hypertension to be associated with hypothyroidism. (J Am Board Fam Pract 1997;10:185-91.)**

Hypothyroidism has been described as a cause of hypertension in many[1-5] but not all[6-8] medical textbooks. Several researchers have reported an association between hypertension and hypothyroidism in clinical settings, but these studies have been undertaken in specialty clinics largely using referred patients.[9-14] A community-based study, however, found no differences in mean blood pressures or the prevalence of hypertension in hypothyroid and euthyroid women.[15]

Both hypothyroidism and hypertension are common, and their occurrence increases with age. In the community setting, overt hypothyroidism occurs in 1.5 to 2.0 percent of women and 0.2 percent of men.[16] Subclinical hypothyroidism, defined as an elevated thyroid-stimulating hormone (TSH) (up to 10 U/L) but with a normal free thyroxine, is common among persons older than 60 years; it has been documented in 5.9 percent of an unselected population of community-dwelling elderly persons[17] and 14.6 percent of elderly women in a primary care geriatrics clinic.[18] The prevalence of hypertension (defined as a blood pressure of 140/90 mmHg or greater) increases from less than 30 percent for white women aged 35 to 44 years to more than 50 percent for white women aged 65 to 74 years.[19] Because hypertension and hypothyroidism are both common, their coexistence in patients might not indicate an association. A causative association would be clinically important if subsequent studies showed that early recognition and treatment of hypothyroidism prevent chronic hypertension from developing. Prevention of hypertension could prevent stroke and myocardial infarction.

The purpose of our project was to examine the association between hypertension and hypothyroidism in postmenopausal women seen in a primary care office setting. This group was selected because both diseases occur widely in this population. We hypothesized that if an association existed, then a diagnosis of hypothyroidism should occur in a greater percentage of hyper-

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Table 1. Comparison of Hypertensive and Normotensive Women, by Patient Characteristics.

Characteristics	Hypertensive (n = 321)	Normotensive (n = 386)	*P* Value
Patients (age distribution)			< 0.0001
50 to 59 years	96	174	
60 to 69 years	102	103	
70 to 79 years	78	76	
80 to 89 years	40	31	
90 years and older	5	2	
Age, mean years (SD)	66.4 (11.0)	63.0 (10.4)	< 0.0001
Body mass index, mean kg/m^2 (SD)	29.2 (6.3)	26.2 (5.2)	< 0.0001
Median number of visits 2 years before index visit	4	2	< 0.0001
Median number of visits year after index visit	3	2	< 0.0001

tensive women than in that of their normotensive peers.

Methods

All postmenopausal women aged 50 years and older who were seen at the family practice office between 1989 and 1993 and who used this facility for their primary health care were eligible for this study. The office is in a university community in the Midwest and records more than 20,000 visits per year. The office was considered to be a woman's source of primary health care if she received her preventive health care at this office, as indicated by at least one cervical cytologic smear during the study period. During the study period it was the recommendation of this office that all adult women, regardless of age and hysterectomy status, undergo routine cytologic screening.

Data were collected by chart review using a cross-sectional design. There was at least 1 year between the visit for preventive care and the chart review. Patient charts were reviewed by research assistants using a standard data-collection instrument. Data on hypertension, hypothyroidism, diabetes mellitus, smoking, nonsteroidal anti-inflammatory drug (NSAID) use, estrogen use, coronary artery disease, congestive heart failure, and chronic renal failure, as well as height, weight, and number of office visits 2 years before and 1 year after the index visit were extracted from the charts. A patient's index visit was the first visit during the study period at which she underwent cervical cytologic screening. Reliability was checked by having the research assistants re-extract data from 80 randomly selected charts initially reviewed by the other reviewer. Agreement was excellent, with kappas greater than 0.95 for both hypertension and hypothyroidism.

Classification Criteria

Patients were classified as having hypothyroidism if either of the following was recorded in the chart:

1. Elevated TSH or low free thyroxine (both as defined by the laboratory performing the test) preceding the index visit or within 1 year following the index visit.
2. Thyroid replacement prescribed by the index visit or within 1 year following the index visit.

Patients were classified as having hypertension if any of the following were recorded in the chart:

1. Elevated blood pressures in the office, as defined by diastolic blood pressure greater than 90 mmHg, on at least 3 occasions within 1 year of the index office visit.
2. Taking medications for treatment of hypertension, as documented by any mention in the chart of the patient having been prescribed a diuretic, β–blocker, α–blocker, calcium channel blocker, or angiotensin-converting enzyme inhibitor at the time of the index visit or within 1 year of that visit. Documentation of these drugs did not satisfy this criterion if the medication was prescribed for another condition, such as migraine, idiopathic edema, congestive heart failure, angina, or renal protection in the face of diabetes mellitus.
3. Any record within the office chart of the diagnosis of hypertension in a progress note, problem list, health summary questionnaire, hospital discharge note, or consultant's note preceding the index visit.

Data Analysis

When the variables were dichotomous, we performed a univariate analysis using chi-square, and

Table 2. Comparison of Hypertensive and Normotensive Women, by Percentage with Study Variable.

Variable	Hypertensive (n = 321)	Normotensive (n = 386)	*P* Value
Obesity (BMI ≥ 30 kg/m^2)	38.0	18.9	< 0.0001
Coronary artery disease	17.8	7.0	< 0.0001
Diabetes mellitus	11.8	3.4	< 0.0001
NSAID use	26.8	15.3	0.0002
Congestive heart failure	9.0	3.9	0.005
Estrogen use	19.0	23.3	0.16
Ever smoker	34.4	38.3	0.31
Current smoker	15.1	17.4	0.40
Hypothyroidism	11.5	10.4	0.62

BMI - body mass index, NSAID - nonsteroidal anti-inflammatory drug.

when they were continuous, we used the Student t-test or Mann-Whitney U test. Statistical analyses were performed with the Solo, Version 4, statistical software.[20] The level of significance was set at 0.05.

Multivariate analyses were undertaken using logistic regression with hypertension as the dependent variable and hypothyroidism as an independent variable. Independent variables found to be significant in the univariate analysis at the 0.10 level and additional variables of concern were included in the model. For ease of interpretation, age was entered into the model by decade and body mass index was entered into the model by increments of 5 kg/mg^2. Power analysis was performed with Solo Power Analysis.[21]

Results

Seven hundred forty-two women, aged 50 years and older, obtained their primary health care at this office during the study period. Of these women, 35 were excluded because they were still menstruating or their charts could not be located, leaving 707 women in the study population. The mean age of the patients was 64.6 years (SD 10.8 years). Patients received care at the study site a median of 3 times during the 2 years before the index visit and 2 times during the year after the index visit.

Three hundred twenty-one of the women (45.4 percent) had hypertension and 77 women had hypothyroidism (10.9 percent). Hypothyroidism was diagnosed by abnormal laboratory findings in 49.4 percent of cases and by the use of thyroid replacement in 50.6 percent of cases.

Hypertensive women were significantly older than their normotensive peers and had a significantly higher mean body mass index. Hypertensive women were also more likely to have a history of congestive heart failure, a history of coronary artery disease, a history of diabetes mellitus, and to be chronic users of NSAIDs. The percentages of women who were current smokers or taking estrogen were similar in both groups. These univariate analyses are shown in Tables 1 and 2. The relations between hypertension and age and body mass index of the patients are shown in Figures 1 and 2, respectively.

The percentage of hypertensive women who also had hypothyroidism, 11.5 percent, was higher than the percentage found in the normotensive group, 10.4 percent, but this difference was not statistically significant ($P = 0.62$). The percentages of cases of hypothyroidism diagnosed by abnormal laboratory findings and by being on replacement therapy were similar in both groups of women ($P = 0.74$). No association was found between the two conditions when hypothyroidism was defined solely by an elevated TSH or low free thyroxine ($P = 0.925$). More women in the normotensive group also had a TSH level greater than 10 U/L than did women in the hypertensive group (10 versus 4, $P = 0.04$).

A logistic model was created with hypertension as the dependent variable and NSAID use, body mass index, hypothyroidism, age, and diabetes mellitus as independent variables. In this analysis the association between hypothyroidism and hypertension had an odds ratio of 1.04 (confidence interval 0.63 to 1.73). Age, body mass index, NSAID use, and diabetes mellitus were significantly associated with hypertension; the odds ratios for these associations are shown in Table 3.

Restricting the definition of hypothyroidism to either an elevated TSH or a low free thyroxine in the logistic model did not cause the association

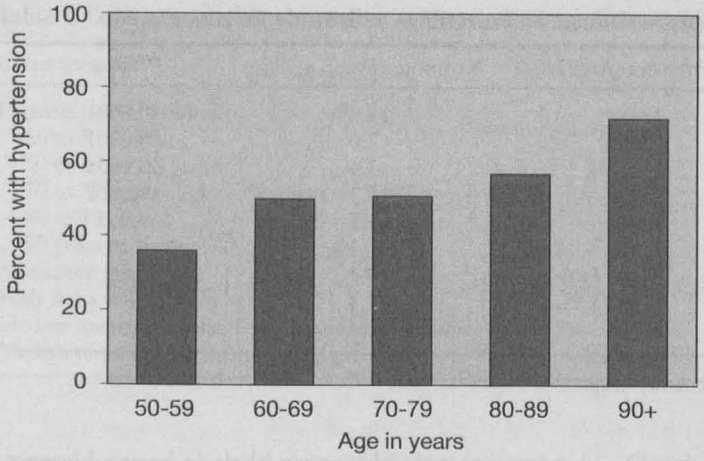

Figure 1. The percentage of women who had hypertension diagnosed, by age in decades.

between thyroid status and hypertension to become statistically significant ($P = 0.97$).

Discussion

Hypertension and hypothyroidism are common in postmenopausal women, but our office-based study did not detect an association between these two conditions. This lack of association contrasts with other reports about patients studied in specialty clinics. Bing et al[9] reported a case series of 6 hypothyroid patients with hypertension who became normotensive after treatment with thyroid replacement. Streeten and colleagues[10] studied 688 patients referred to a specialty clinic for evaluation and treatment of hypertension. Twenty-five of the patients (3.6 percent) were found to have hypothyroidism. After thyroid replacement therapy was initiated, 32 percent of the hypothyroid group became normotensive. Streeten et al[10] also reported that of 40 patients who became hypothyroid following treatment with radioiodine, 16 (40 percent) also developed hypertension, but after receiving thyroid replacement, 9 of the 16 (56 percent) returned to a normotensive condition. These studies lacked control groups, and it is possible that individual patients who became normotensive after thyroid replacement would have become normotensive without this intervention.

Saito et al[11] also found this association in a cross-sectional study of 477 patients with chronic thyroiditis seen in a hospital-based thyroid clinic. Less than 6 percent of the 308 euthyroid patients had hypertension compared with 14.8 percent of the 169 patients with hypothyroidism. Mean blood pressures were higher, and hypertension was more common only in hypothyroid patients who were aged 50 years and older. In the analysis patients were stratified by age, but not by other factors known to be associated with hypertension, such as body mass index, NSAID use, and diabetes mellitus. Response to thyroid replacement was reported for a subset of 18 patients. Although 13 (72 percent) of the treated patients had a decline in blood pressure after being prescribed L-thyroxine, the authors acknowledged that the drop in blood pressure could represent a placebo response.[22]

An additional problem common to most of the previous research is that referred populations were used to study the association between hypertension and hypothyroidism. The reported association could be due to selection and referral bias and not apply to patients seen in a primary care setting.[23] Referral patterns influence the characteristics of patients with hypertension seen by physicians; therefore, studies undertaken in specialty clinics do not always generalize to hypertensive patients seen in another setting.[24,25]

Although we did not find an association between hypertension and hypothyroidism, our methods correctly found factors that are well known to be related to hypertension. These include age,[26] body mass index,[26] NSAID use,[27] and diabetes mellitus.[28] It is possible that our inability to find an association between hypertension and hypothyroidism is due to imprecision in the classifications of thyroid status. About one half of the women in this study with the diagnosis of hypothyroidism did not have their condition confirmed by laboratory studies. Additionally, some of the women with documented elevation in TSH had, in fact, subclinical hypothyroidism (an elevated TSH less than 10 U/L and a normal free thyroxine). To assess misclassification bias, we started with a liberal definition of hypothyroidism (abnormal laboratory findings or being on thyroid replacement) and then used a more restrictive definition of hypothyroidism in additional analyses. Regardless of our definition of hypothyroidism, we were unable to show a significant association with hypertension.

Our inability to find an association between these two disorders is in agreement with the findings of a study by Endo et al,[15] in which 81 hypothyroid women were compared with 73 euthyroid women drawn from the surrounding community. No significant differences in the mean blood pressures or in the prevalence of hypertension were detected after stratifying the patients by age.

There are several weaknesses in our study design that should be addressed. A primary concern is that our data were not prospectively collected but were obtained by retrospective review of office records. This design is susceptible to bias from a systematic underreporting of hypothyroidism in hypertensive women when compared with their normotensive peers, which would obscure a relation between the two conditions. Patients with hypertension, however, had more physician visits before and after the index visits than did their normotensive peers. The increased contact with medical providers should have increased the opportunities for detecting hypothyroidism, so that our data would be biased to show an association between hypertension and hypothyroidism when one did not actually exist. We found a greater percentage of hypertensive women had TSH measurements in their charts than did their normotensive peers (43.9 percent versus 37.6 percent), although this difference did not reach statistical significance ($P = 0.09$). Because of these findings we think it unlikely that misclassification resulting from a detection bias is obscuring a relation between hypertension and hypothyroidism.

It is also possible that some of the women with hypertension had their hypothyroidism diagnosed and treated at another medical care site. We attempted to avoid this problem by studying only a population of women who obtained their preventive health care at the primary care office used for the study. Additionally, we reviewed all medical data available to us in the office record, including consultations, office notes, a self-administered health questionnaire, and hospital admission and discharge notes. It is likely that either a new or previous diagnosis of hypothyroidism at another site would have been uncovered by the primary care physician during visits for preventive health care. Although our selection criteria could have biased our findings, as only 52 percent of all women aged 50 years and older obtained cervical cytologic screening in our office during the study period, the data on the prevalence of hypertension in the studied group are consistent with that found in unselected populations.[19]

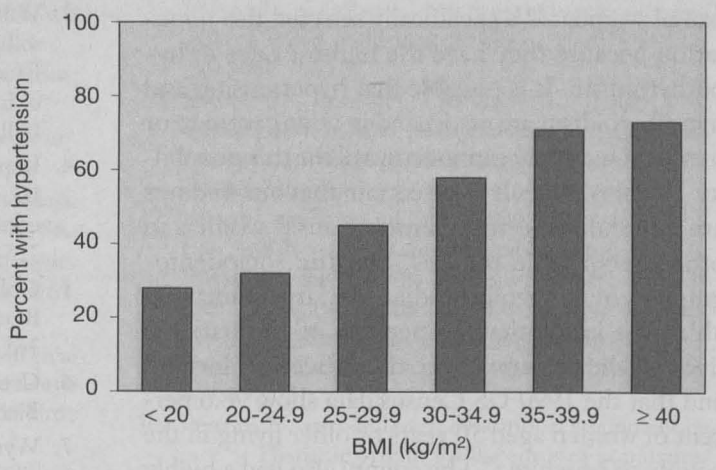

Figure 2. The percentage of women who had hypertension diagnosed, by body mass index (BMI) in increments of 5 kg/m².

A third concern should focus on our sample size. It might be argued that we had an insufficient number of patients to detect a clinically significant association between hypertension and hypothyroidism. With 707 patients and a 10.9 percent prevalence of hypothyroidism, however, we had a power of 0.8 for detecting an odds ratio of 1.37 for the association between hypothyroidism and hypertension by the logistic regression model. The odds ratio for the association of these two conditions in the Saito et al study was 2.98.[11]

Lastly, our findings pertain only to postmeno-

Table 3. Logistic Modeling of the Associations Between Hypertension and Selected Factors.

Variable	Odds Ratio (95% CI)	*P* Value
BMI (in 5-kg/m² increments)	1.58 (1.37 - 1.81)	< 0.0001
Age (in decades)	1.41 (1.20 - 1.65)	< 0.0001
NSAID use	1.77 (1.19 - 2.62)	0.005
Diabetes mellitus	2.63 (1.33 - 5.19)	0.006
Hypothyroidism	1.04 (0.63 - 1.73)	0.87

CI - confidence interval, BMI - body mass index, NSAID - nonsteroidal anti-inflammatory drug.

pausal women. We specifically selected this population because they have the highest rates of hypothyroidism. It is possible that hypertension and hypothyroidism are associated in young women or in men. Our study cannot control for this possibility. It is also difficult to be certain that our findings are generalizable to postmenopausal women in other geographic regions. Specific sociodemographics of the group studied are largely unavailable. We know that 76 percent of the patients lived in the county where the office was located and that the 1990 US Census data show 98.6 percent of women aged 50 years or older living in the county to be white.[29] The county also had a highly educated population, with 69.3 percent of the population aged 25 years or older having education beyond high school.[30] We also know that approximately 10 percent of the women aged 50 to 64 years who obtained cervical cytologic screening at this office were on Medicaid or Medicare or were uninsured. At a minimum, our findings should apply to other groups of highly educated white women.

In summary, we investigated the association of hypertension and hypothyroidism in postmenopausal women receiving their health care in a family practice office setting. Although we found hypertension and hypothyroidism to be common in this population, we did not find evidence that these two conditions were directly associated. Instead, we found hypertension to be related to age, body mass index, NSAID use, and diabetes mellitus.

Our findings differ from those of previous reports, but the setting in which we collected our data differed from those in most of the earlier reports. Our study raises questions about whether reports linking hypertension and hypothyroidism in referred populations can be generalized to postmenopausal women seen in a primary care setting.

References

1. Hall WD, Wollman GL, Tuttle EP Jr. Diagnostic evaluation of the patient with systemic arterial hypertension. In: Schlant RC, Alexander RW, editors. The heart. Companion handbook. 8th ed. New York: McGraw-Hill, 1994:1405.
2. Frohlich ED. Pathophysiology of systemic arterial hypertension. In: Schlant RC, Alexander RW, editors. The heart. Companion handbook. 8th ed. New York: McGraw-Hill, 1994:1394.
3. Williams GH. Hypertensive vascular disease. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's principles of internal medicine. 13th ed. New York: McGraw-Hill, 1994:1117.
4. Kaplan NM. Endocrine hypertension. In: Wilson JD, Foster DW, editors. Williams textbook of endocrinology. 8th ed. Philadelphia: WB Saunders, 1992: 725-6.
5. Goldszer RC, Solomon HS. Hypertension. In Branch WT Jr, editor. Office practice of medicine. 3rd ed. Philadelphia: WB Saunders, 1994:117.
6. Grossman A, editor. Clinical endocrinology. Oxford: Blackwell Scientific Publications, 1992.
7. Wyngaarden JB, Smith LH, Bennet JC, editors. Cecil textbook of medicine. 19th ed. Philadelphia: WB Saunders, 1992.
8. Dale DC, Federman DD, editors. Scientific American medicine. New York: Scientific American, 1996.
9. Bing RF, Briggs RS, Burden AC, Russell GI, Swales JD, Thurston H. Reversible hypertension and hypothyroidism. Clin Endocrinol Oxf 1980;13:339-42.
10. Streeten DH, Anderson GH Jr, Howland T, Chiang R, Smulyn H. Effects of thyroid function on blood pressure. Recognition of hypothyroid hypertension. Hypertension 1988;11:78-83.
11. Saito I, Ito K, Saruta T. Hypothyroidism as a cause of hypertension. Hypertension 1983;5:112-5.
12. Thompson WO, Dickie LFN, Morris AE, Hilkevitch BH. The high incidence of hypertension in toxic goiter and in myxedema. Endocrinology 1931; 15:265-72.
13. Fuller H Jr, Spittell JA Jr, McConahey WM, Schirger A. Myxedema and hypertension. Postgrad Med 1966;40:425-8.
14. Menof P. The thyroid and atherosclerotic arterial disease. S Afr Med J 1973;47:2315-25.
15. Endo T, Komiya I, Tsukui T, Yamada T, Izumiyama T, Nagata H, et al. Re-evaluation of a possible high incidence of hypertension in hypothyroid patients. Am Heart J 1979;98:684-8.
16. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol Oxf 1977;7:481-93.
17. Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P. The aging thyroid. Thyroid deficiency in the Framingham study. Arch Intern Med 1985;145:1386-8.
18. Bemben DA, Winn P, Hamm RM, Morgan L, Davis A, Barton E. Thyroid disease in the elderly. Part 1. Prevalence of undiagnosed hypothyroidism. J Fam Pract 1994;38:577-82.
19. Drizd T, Dannenberg A, Engel A. Blood pressure levels in persons 18-74 years of age in 1976-80 and trends in blood pressure from 1960 to 1980 in the United States. Vital Health Statistics, series 11: data

from the National Health Survey. Vital Health Stat 11 1986;Jul:1-68.
20. Hintze J. Solo, version 4, statistical software [computer program]. Los Angeles: BMPD, 1993.
21. Hintze J. Solo power analysis [computer program]. Los Angeles: BMPD, 1993.
22. Saito I, Saruta T. Hypertension in thyroid disorders. Endocrinol Metab Clin North Am 1994;23:379-86.
23. Salive ME. Referral bias in tertiary care: the utility of clinical epidemiology. Mayo Clin Proc 1994;69:808-9.
24. Tucker RM, Labarthe DR. Frequency of surgical treatment for hypertension in adults at the Mayo Clinic from 1973 through 1975. Mayo Clin Proc 1977;52:549-55.
25. Giffod RW Jr. Evaluation of the hypertensive patient. Chest 1973;64:336-40.
26. Whelton PK. Epidemiology of hypertension. Lancet 1995;344:101-6.
27. Johnson AG, Nguyen TV, Day RO. Do nonsteroidal anti-inflammatory drugs affect blood pressure? A meta-analysis. Ann Intern Med 1994;121:289-300.
28. Sowers JR, Standley PR, Ram JL, Zemel MB, Resnick LM. Insulin resistance, carbohydrate metabolism, and hypertension. Am J Hypertens 1991;4:466S-72S.
29. Persons age by sex and race. 1990 census of population and housing: summary table. Tape file 3A, Iowa: Johnson County. Washington, DC: Department of Commerce, Bureau of the Census, 1992/3:10. (Burke SC, Goudy W, Hansen M. Ames, Iowa: Iowa State University, Department of Sociology, 1992/3.)
30. Persons 25 years and over: educational attainment by race or Hispanic origin. 1990: census of population and housing: summary table. Tape file 3A, Iowa: Johnson County. Washington, DC: Department of Commerce, Bureau of the Census, 1992/3:1. (Burke SC, Goudy W, Hansen M. Ames, Iowa: Iowa State University, Department of Sociology, 1992/3.)