Markers of loss of control of hypertension

Richard Ian Casson, MD, MSC, CCFP(EM) Will D. King, MSC, PHD
Noah Marshall S. Godwin, MD, MSC, CCFP, FCFP

ABSTRACT

OBJECTIVE To identify markers for loss of control of hypertension.

DESIGN Questionnaire administered to patients who had been monitored for 18 months and had had their blood pressure (BP) measured many times.

SETTING Fifty family practices in southeastern Ontario.

PARTICIPANTS Three hundred eighty-five adults with essential hypertension that was initially stable and controlled by medication.

MAIN OUTCOME MEASURES Change in BP (from baseline to mean of three measurements over 18 months) and proportion of patients with BP exceeding threshold values at most follow-up visits.

RESULTS Higher income was associated with an increase in diastolic BP; poor adherence to medication regimens and higher life stress were associated with increases in systolic BP. Stress also led to a twofold increase in risk of exceeding BP thresholds. Other factors under study were not related to loss of control.

CONCLUSION Adherence to medication regimens, higher income, and life stress were the only factors associated with elevated BP or loss of control in previously controlled hypertension.

RÉSUMÉ

OBJECTIF Identifier des facteurs prédictifs d'une perte de contrôle de l'hypertension.

TYPE D'ÉTUDE Questionnaire administré à des patients suivis depuis 18 mois et dont la tension artérielle (TA) avait été mesurée de nombreuses fois.

CONTEXTE Cinquante établissements de médecine familiale du sud-est de l'Ontario.

PARTICIPANTS Trois cent quatre-vingt-cinq adultes suivis pour une hypertension essentielle initialement stable et contrôlée par la médication.

PRINCIPAUX PARAMÈTRES À L'ÉTUDE Changement de la TA (différence entre le niveau de base et la moyenne de trois valeurs mesurées sur une période de 18 mois) et proportion des patients ayant des TA supérieures aux valeurs seuils à la plupart des visites.

RÉSULTATS Une association existe entre un revenu élevé et une augmentation de la TA diastolique; on a associé un défaut de fidélité au traitement ou un niveau élevé de stress à une augmentation de la TA systolique. Le facteur stress double le risque d'avoir des TA supérieures aux niveaux seuils. Les autres facteurs examinés ne sont pas reliés à la perte de contrôle.

CONCLUSION Un défaut de fidélité à la médication, des revenus élevés et un haut niveau de stress quotidien sont les seuls facteurs associés à une TA élevée ou à une perte de contrôle chez ceux dont la TA était jusque-là bien contrôlée.

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Successful hypertension management involves awareness, treatment, and control. Most people with hypertension are aware of the condition,[1,2] and evidence-based treatment guidelines are available.[3,4] Control, however, continues to be elusive for most hypertensive patients, even those who are treated.[1] Poor adherence to treatment regimens[5] and undertreatment[6] have been investigated as reasons for lack of control.

This study aimed to identify other factors that might be associated with lack of control among treated patients: sociodemographic variables (age, sex, education, occupational activity, marital status), clinical variables (parental hypertension, duration of hypertension, target organ damage, and number of antihypertensive medications and comorbid conditions), and lifestyle variables (smoking, at-risk drinking, salt intake, and body mass index). These factors are potential markers for risk of loss of control because they can be assessed in primary care and some have a known association with hypertension.[7-20]

Patients whose hypertension was initially controlled under the care of their family physicians are an important group to study. Losing control could put them again at risk of adverse outcomes, and hypertension is very costly to the health care system, given its prevalence and lifelong nature. Recommendations suggest regularly monitoring it.[3]

Loss of control was measured by combining blood pressure (BP) measurements over time; this summary measure was chosen because BP varies considerably.[21,22] Identifying the characteristics of those at risk of losing control could suggest why these patients have uncontrolled hypertension. Even if risk factors are not modifiable, knowing the associations (and lack of associations) might help family physicians individualize their care of these patients.

METHODS

The physicians in this study were volunteers from 50 family practices of various types in southeastern Ontario. The patients were also volunteers in a randomized controlled trial (the Hypertension Follow-up Interval Study [personal communication from Dr R. Birtwistle, principal investigator]) of 3- versus 6-month follow-up intervals for hypertensive adults. The HFIS included patients with essential hypertension who were 30 to 70 years old; were under the care of their family physicians; were being treated with medication to lower BP; had controlled hypertension as assessed by their family physicians; had had no change in antihypertensive medication for at least 3 months before study onset; and had initial BP of ≤140/90 mm Hg (30 to 40 years old), ≤150/95 mm Hg (41 to 59 years old), and ≤160/95 (60 to 70 years old). These values were chosen in 1995 as reasonable thresholds for a study of patients with controlled, stable hypertension. Current recommendations are to keep BP below 140/90 mm Hg in patients without diabetes or kidney disease, regardless of age.

In the HFIS, other than the suggested intervals for routine follow up, physicians and patients decided on management of hypertension. Physicians were given guidelines for measurement technique.[23] Change in BP was calculated as the difference between baseline measurements (on family physicians' charts before enrolment into the study) and the mean of three measurements at about 6, 12, and 18 months later. Loss of control was defined as exceeding HFIS entry thresholds on either systolic or diastolic BP on at least two of three follow-up visits.

At about 18 months after enrolment in the HFIS, patients, with the help of a nurse, completed a questionnaire developed for this study, had their weight and height recorded, and had their antihypertensive pills counted. Adherence to medication was calculated as the number of pills gone from patients' current containers divided by the number that should have been missing if patients had taken all the medicine as prescribed.

Questionnaire

Questions regarding salt intake were suggested by a consensus guideline[21] and the Canada Health Survey.[24] Subjects answering "often (usually daily)" to one or more of three questions about use of prepared foods or salty snacks or adding salt to food at the table were considered at higher risk of increased salt intake than those who indicated less frequent use. Questions on frequency and quantity[25] of alcohol intake were used to produce the categories "at risk" and "not at risk" for problem drinking, according to Canadian guidelines.[19] Questions on smoking[26] identified current smokers. A question about self-perceived

Dr Casson *is an Assistant Professor in the Department of Family Medicine,* **Dr King** *is an Associate Professor in the Department of Community Health and Epidemiology, and* **Dr Godwin** *is a Professor in the Departments of Family Medicine and Community Health and Epidemiology, all at Queen's University in Kingston, Ont.*

stress in life[26] was used to identify "very" or "fairly" versus "not very" and "not at all" stressful lives. Income, education, marital status, and employment data were collected using single questions with several response levels, as used in the Ontario Health Survey.[27]

Chart review

Clinical data collected by chart review when patients entered the HFIS were used in this study: comorbidity (from a list of 10 general conditions), antihypertensive drugs prescribed, duration of hypertension, and target organ damage. Physical activity and cardiorespiratory fitness are not reported here; they are addressed in a separate paper.[28]

Statistical analysis

For the continuous outcome (change in BP), clinical significance was determined in advance to be a difference of 5 mm Hg in diastolic BP between groups with and without particular risk markers. The sample size had adequate power to show such a difference, if it was there, for the characteristics studied.

Stepwise procedures in multiple regression (with a liberal criterion of F score = 0.10) were used to select parsimonious sets of predictive factors for each outcome that could then be used to determine adjusted estimates of the effect of each variable on the respective outcome. Age and sex were included in the models a priori because of their potential importance.

Multiple linear regression was used to estimate adjusted mean change for continuous outcomes, and log binomial regression was used to calculate adjusted ratios for risk of exceeding thresholds.[29] Only adjusted differences and risks are presented in the tables because, in general, they did not differ from crude results (obtained from *t* tests, one-way analysis of variance, and contingency tables, depending on outcome and factor involved). The Research Ethics Board of Queen's University in Kingston, Ont, approved the study.

RESULTS

Of 481 patients invited to participate in the study, 425 agreed and of these, 385 had had at least three office visits for follow up of hypertension. Mean age was 57 years, 46% were male, and their mean entry BP was 137/84 mm Hg (standard deviation 13/7). Half had had their hypertension diagnosed for more than 5 years, 14% had target organ damage, and 60% had two or more comorbid conditions (7% had diabetes, and 1% had chronic renal disease). About a third were taking two or more antihypertensive medications; 28% were poorly adherent, measured as having taken ≤80% of their pills as prescribed. Those excluded or who refused to participate were not different in any characteristics from those included (at $P = .05$).

Overall, 16% of patients (95% confidence interval [CI] 13 to 20) had increases of >20 mm Hg systolic BP or >10 mm Hg diastolic BP, and 41% of patients (95% CI 36 to 46) had increases of >10 and/or >5 mm Hg. On at least two of their three follow-up visits, 14% of patients (95% CI 11 to 18) exceeded HFIS entry thresholds.

Table 1 shows relationships between diastolic BP change and lifestyle, clinical, and sociodemographic predictors adjusted for age, sex, and income. The only significant predictor of change was income. Patients with household incomes <$30 000 had decreases in diastolic BP; those on higher incomes had increases. The difference between the changes was 2.5 mm Hg (95% CI 0.5 to 4.5). Age, sex, and income explained only 4% of the variation in diastolic BP change.

Table 2 shows relationships between systolic BP change and predictors adjusted for age, sex, stress, adherence, and income. Low adherence was associated with higher systolic BP increases; the difference in change between low-adherence and high-adherence groups was 4.6 mm Hg (95% CI 1.4 to 7.8, $P = .005$). Higher levels of life stress were associated with systolic BP increases; the adjusted difference in increase between high- and low-stress groups was 3.7 mm Hg (95% CI 0.25 to 7.1, $P = .04$). This model explained only 6% of the variation in systolic BP change.

Table 3 shows relationships between the dichotomous outcome (exceeding thresholds or not) and various patient characteristics adjusted for age, sex, smoking, adherence, and stress. Those reporting high levels of stress had twice the risk of exceeding thresholds compared with those reporting low stress levels (relative risk 2.03, 95% CI 1.1 to 3.7, $P = .02$).

DISCUSSION

The literature, with one exception,[30] does not distinguish loss of control in previously controlled hypertension from lack of control among hypertensive patients in general. So comparisons for the results of this study must come from what is known about the characteristics of hypertensive patients in general. Among these patients, poor adherence to medication regimens is associated with lower rates of goals.[5,31]

Table 1. Change in diastolic blood pressure from entry to follow up

CHARACTERISTICS	N (%)	MEAN (MEAN OF STANDARD ERROR)	ADJUSTED DIFFERENCE*	95% CONFIDENCE INTERVAL
LIFESTYLE				
Current smoking				
• Yes	78 (20)	1.36 (0.85)	-0.27	-2.48, 1.93
• No	306 (80)	0.67 (0.48)		
At-risk drinking				
• Yes	30 (8)	0.77 (1.63)	0.11	-3.14, 3.36
• No	335 (92)	1.04 (0.45)		
Life stress				
• Higher	166 (43)	0.92 (0.63)	0.10	-1.81, 2.01
• Lower	219 (57)	0.72 (0.56)		
Body mass index				
• ≥30	189 (50)	0.58 (0.57)	0.05	-1.71, 1.81
• <30	189 (50)	1.02 (0.63)		
Salt intake				
• At risk	241 (63)	0.06 (0.47)	-1.78	-3.60, 0.04
• Not	144 (37)	2.05 (0.79)		
CLINICAL FACTORS				
Parental hypertension				
• Yes	232 (77)	0.78 (0.53)	-0.05	-2.40, 2.31
• No	70 (23)	1.16 (0.88)		
Duration of hypertension				
• ≤5 y	196 (51)	1.32 (0.58)	-0.80	-2.57, 0.97
• >5 y	188 (49)	0.24 (0.61)		
Target organ damage				
• Yes	55 (14)	0.58 (1.04)	0.28	-2.24, 2.80
• No	330 (86)	0.84 (0.46)		
Hypertension medications at entry				
• ≥2	135 (36)	-0.04 (0.69)	-1.12	-2.95, 0.71
• 1	244 (64)	1.28 (0.54)		
Comorbid conditions				
• ≥2	228 (59)	0.57 (0.55)	-0.04	-2.22, 1.35
• 0-1	157 (41)	1.15 (0.65)		
Adherence to pills at 18 months				
• ≤80%	116 (35)	1.32 (0.71)	1.19	-0.76, 3.14
• >80%	220 (65)	0.58 (0.58)		
DEMOGRAPHIC FACTORS				
Age (per 10 years)	-	-	-0.17	-1.08, 0.73
Sex				
• Male	175 (46)	0.92 (0.64)	0.42	-1.31, 2.14
• Female	210 (54)	0.71 (0.56)		
Education†				
• Lower	186 (48)	0.74 (0.65)	-2.11	-5.10, 0.89
• Higher	199 (52)	0.86 (0.55)		
Occupation‡				
• Housework	54 (15)	0.69 (1.23)	1.48	1.66, 4.61
• Working at a job	179 (49)	0.61 (0.59)	-0.13	-2.67, 2.41
• Retired	132 (36)	0.30 (0.72)		
Income				
• <$30 000	85 (26)	-1.26 (0.94)	-2.50	-4.46, 0.54
• ≥$30 000	238 (74)	1.31 (0.48)		
Marital status				
• Single, widowed, divorced	75 (20)	0.39 (1.05)	0.77	-1.55, 3.10
• Married, common law	310 (80)	0.91 (0.46)		

**Adjusted for age, sex, and income, which is the parsimonious model for diastolic blood pressure change. The difference is for first listed level compared with second; except for occupation, where differences are compared with retired.*

†Higher is at least some university or college; lower is all others.

‡Differences in housework and working at a job are in comparison to retired.

Table 2. Change in systolic blood pressure from entry to follow up

CHARACTERISTICS	N (%)	MEAN (MEAN OF STANDARD ERROR)	ADJUSTED DIFFERENCE*	95% CONFIDENCE INTERVAL
LIFESTYLE				
Current smoking				
• Yes	78 (20)	3.88 (1.48)	-1.54	-5.42, 2.34
• No	306 (80)	3.97 (0.74)		
At-risk drinking				
• Yes	30 (8)	3.40 (2.43)	0.87	-5.08, 6.82
• No	335 (92)	4.16 (0.71)		
Life stress				
• Higher	166 (43)	5.52 (1.05)	3.67	0.25, 7.10
• Lower	219 (57)	2.71 (0.84)		
Body mass index				
• ≥30	189 (50)	3.83 (0.89)	0.94	-2.12, 3.40
• <30	189 (50)	4.04 (1.00)		
Salt intake				
• At risk	241 (63)	3.62 (0.80)	-0.08	-3.26, 3.10
• Not	144 (37)	4.47 (1.14)		
CLINICAL FACTORS				
Parental hypertension				
• Yes	232 (77)	4.00 (0.85)	2.26	-1.84, 6.35
• No	70 (23)	3.64 (1.54)		
Duration of hypertension				
• ≤5 y	196 (51)	4.43 (0.82)	-0.87	-3.94, 2.20
• >5 y	188 (49)	3.38 (1.05)		
Target organ damage				
• Yes	55 (14)	4.29 (1.95)	-2.22	-6.48, 2.04
• No	330 (86)	3.88 (0.70)		
Hypertension medications at entry				
• ≥2	135 (36)	3.27 (1.10)	-1.84	-5.00, 1.32
• 1	244 (64)	4.28 (0.84)		
Comorbid conditions				
• ≥2	228 (59)	4.62 (0.88)	1.24	-1.95, 4.42
• 0-1	157 (41)	2.96 (0.99)		
Adherence to pills at 18 months				
• ≤80%	116 (35)	6.52 (1.20)	4.60	1.44, 7.78
• >80%	220 (65)	2.80 (0.82)		
DEMOGRAPHIC FACTORS				
Age (per 10 years)	-	-	1.08	-0.70, 2.85
Sex				
• Male	175 (46)	3.84 (0.97)	-0.28	-3.28, 2.73
• Female	210 (54)	4.02 (0.90)		
Education†				
• Lower	186 (48)	3.45 (0.95)	-1.18	-4.29, 1.93
• Higher	199 (52)	4.40 (0.92)		
Occupation‡				
• Housework	54 (15)	2.82 (1.54)	1.27	-4.13, 6.67
• Working at a job	179 (49)	3.69 (0.99)	1.30	-3.13, 5.73
• Retired	132 (36)	3.54 (1.13)		
Income				
• <$30 000	85 (26)	1.47 (1.51)	-2.74	-6.28, 0.79
• ≥$30 000	238 (74)	4.39 (0.83)		
Marital status				
• Single, widowed, divorced	75 (20)	4.51 (1.65)	2.56	-1.52, 6.64
• Married, common law	310 (80)	3.80 (0.72)		

**Adjusted for age, sex, and income, which is the parsimonious model for systolic blood pressure change. The difference is for first listed level compared with second; except for occupation, where differences are compared with retired.*
†Higher is at least some university or college; lower is all others.
‡Differences in housework and working at a job are in comparison to retired.

Table 3. Relative risk of exceeding blood pressure thresholds

CHARACTERISTICS	N (%)	LOST CONTROL %	ADJUSTED RELATIVE RISK*	95% CONFIDENCE INTERVAL
LIFESTYLE				
Current smoking				
• Yes	78 (20)	19	1.61	0.92, 2.17
• No	306 (80)	13		
At-risk drinking				
• Yes	30 (8)	13	0.90	0.36, 2.30
• No	335 (92)	15		
Life stress				
• Higher	166 (43)	19	2.03	1.13, 3.67
• Lower	219 (57)	10		
Body mass index				
• ≥30	189 (50)	13	0.92	0.55, 1.55
• <30	189 (50)	16		
Salt intake				
• At risk	99 (26)	18	0.76	0.46, 1.34
• Not	286 (74)	12		
CLINICAL FACTORS				
Parental hypertension				
• Yes	232 (77)	16	1.92	0.80, 4.61
• No	70 (23)	9		
Duration of hypertension				
• ≤5 y	196 (51)	13	1.25	0.74, 2.11
• >5 y	188 (49)	14		
Target organ damage				
• Yes	55 (14)	11	0.64	0.29, 1.69
• No	330 (86)	14		
Hypertension medications at entry				
• ≥2	135 (36)	14	0.98	0.57, 1.68
• 1	244 (64)	14		
Comorbid conditions				
• ≥2	228 (59)	14	0.80	0.49, 1.37
• 0-1	157 (41)	15		
Adherence to pills at 18 months				
• ≤80%	116 (35)	20	1.64	0.98, 2.73
• >80%	220 (65)	11		
DEMOGRAPHIC FACTORS				
Age				
• ≥58 y	-	11	1.06	0.78, 1.46
• <58 y		17		
Sex				
• Male	175 (46)	15	1.20	0.72, 1.46
• Female	210 (54)	13		
Education†				
• Lower	186 (48)	14	0.91	0.55, 1.54
• Higher	199 (52)	14		
Occupation‡				
• Housework	54 (15)	6	0.26	0.14, 1.70
• Working at a job	179 (49)	16	1.28	0.56, 2.94
• Retired	132 (36)	12		
Income				
• <$30 000	85 (26)	14	0.94	0.49, 1.80
• ≥$30 000	238 (74)	13		
Marital status				
• Single, widowed, divorced	75 (20)	15	0.96	0.47, 1.97
• Married, common law	310 (80)	14		

**Adjusted for age, sex, adherence, smoking, and stress. The parsimonious model for exceeding thresholds: relative risk is for first level compared with second; except for occupation, where differences are compared with retired.*
†Higher is at least some university or college; lower is all others.
‡Differences in housework and working at a job are in comparison to retired.

In our study, poor adherence predicted greater increases in systolic BP, but not diastolic BP. There was also a suggested association (P = .06) between poor adherence and loss of control defined as exceeding thresholds.

In our study, higher household income was associated with larger increases in diastolic BP (and, at P = .13, with systolic BP). Canada Health Survey data show an increased odds ratio for hypertension among women in the highest income group compared with some, but not all, lower income groups, and no significant difference in risk of hypertension for men at any income level.[9] When we analyzed men and women separately, change in diastolic BP remained a significant association for women but not for men, although the interaction was not statistically significant. Although stress is a complex issue to measure and interpret, a higher number of both unfavourable and unexpected life events have been associated with loss of control among initially controlled hypertensive patients,[30] consistent with the finding of this study.

These associations (with adherence, stress, and income) are not strongly clinically significant nor are they robust in the sense of being consistently significant across all measures of loss of control used in this study or in the sense of explaining much of the outcome. Results of other characteristics studied did not show statistically significant differences between groups. Confidence intervals suggest that clinically significant differences (for example, a 5–mm Hg difference in diastolic BP between groups) are unlikely to have been found even with a larger sample size.

Other studies

For some of these characteristics, the lack of associations found in this study is consistent with the evidence found in other studies of hypertensive patients. Occupational status is not associated with prevalence of hypertension[9,10] or with control of hypertension.[15] Duration of hypertension is not associated with control.[32]

For other factors, however, the lack of associations seems inconsistent with results of other studies. Reduced salt intake leads to decreased BP in hypertensive patients;[21] obesity[18] and high alcohol consumption[19] are associated with high BP; and men are more likely than women to develop hypertension[7] and to have poor control.[11,33,34] Parental history of hypertension is related to development of hypertension.[9,35,36] In the Canada Health Survey, smokers were at lower risk of high BP compared with non-smokers.[9] In the literature, the effects of educational level and marital status on BP are mixed.[9,17,34] Increasing age is associated with decreasing diastolic and increasing systolic BP[3] and with increasing prevalence of hypertension,[9,10] but evidence about its importance as a predictor of control is contradictory.[10-13,15]

Limitations

The lack of associations found in this study could be due to its methodologic limitations. Although study subjects were a cohort defined by initial BP control and followed over time as their BP changed as in clinical practice, the independent variables were collected at a single point in time. As a result, change in independent variables was not measurable in this study. The inability to relate changes in patients' characteristics to changes in BP weakens conclusions about lack of association for those variables that might have changed over the course of the study.

Misclassification of patients with respect to outcomes was also possible. The 1-year interval during which follow-up BP measurements were made might have been too long or too short to correctly identify those out of control. The variability of BP poses a dilemma for research as well as for clinical practice.

The hypothesis that this group of hypertensive patients is different from others might also, however, explain the lack of associations. This is a study of risk factors for loss of control of hypertension, not for development of hypertension or for uncontrolled hypertension in general. Patients whose hypertension was controlled initially are likely to have been adherent to treatment; patients under the active care of physicians might have more knowledge and motivation than the general hypertensive population. At present, the differences between this group and those described in other literature on hypertension are hypothetical; the negative results of this study do not provide explanations.

Conclusion

Although knowledge of adherence to medication regimens, income, and stress might be marginally helpful to family physicians for identifying those at risk of loss of control, other risk markers, such as alcohol and salt intake and obesity, and patient characteristics, such as age, sex, and comorbidity, might not be helpful. Although this study provides only weak evidence for lack of association, this group of patients might be distinctive and, therefore, warrant further attention in trying to understand the problem of uncontrolled hypertension.

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Contributors

Dr Casson *contributed to conception and design of the study and analysis and interpretation of data, and drafted the article.* **Dr King** *contributed to conception and design of the study and analysis and interpretation of data.* **Dr Godwin** *contributed to analysis and interpretation of data.*

Competing interests

None declared

Correspondence to: *Dr Ian Casson, Family Medicine Centre, 220 Bagot St, PO Bag 8888, Kingston, ON K7L 5E9; telephone (613) 544-3400, extension 3964 or 3942; fax (613) 544-9899; e-mail* **ric@post.queensu.ca**

Editor's key points

- This study reports on characteristics of patients whose hypertension was initially managed by medication, but subsequently became more poorly controlled.
- Poor adherence to medication regimens, higher income, and higher stress levels were associated with increases in blood pressure, despite regular follow-up visits with family physicians.
- Other expected risk markers, such as obesity, high alcohol or salt intake, age, sex, and comorbidity, were not associated with increases in blood pressure.

Points de repère du rédacteur

- Cette étude décrit les caractéristiques de patients qui, au départ, avaient une hypertension bien contrôlée par la médication, mais chez qui il y a eu une perte subséquente de contrôle.
- Une association existe entre un défaut de fidélité à la médication, un revenu élevé ou un haut niveau de stress et une augmentation de la TA, même si le patient consulte régulièrement son médecin de famille.
- Les autres facteurs de risque étudiés, tels l'obésité, une forte consommation d'alcool ou de sel, l'âge, le sexe et la comorbidité, ne sont pas associés à une élévation de la TA.

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