


A Gap in Post-Stroke Blood Pressure Target Attainment at Entry to Cardiac Rehabilitation

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ABSTRACT: *Background:* Recurrent events account for approximately one-third of all strokes and are associated with greater disability and mortality than first-time strokes. Blood pressure (BP) is the most important modifiable risk factor. Objectives were to determine the proportion of post-stroke patients enrolled in cardiac rehabilitation (CR) meeting systolic and diastolic BP (SBP/DBP) targets and to determine correlates of meeting these targets. *Methods:* A retrospective study of 1,804 consecutively enrolled post-stroke patients in a CR program was conducted. Baseline data (database records 2006–2017) included demographics, anthropometrics, clinical/medication history, and resting BP. Multivariate analyses determined predictors of achieving BP targets. *Results:* Mean age was 64.1 ± 12.7 years, median days from stroke 210 (IQR 392), with most patients being male (70.6%; $n = 1273$), overweight (66.8%; $n = 1196$), and 64.2% diagnosed with hypertension ($n = 1159$), and 11.8% ($n = 213$) with sleep apnea. A mean of 1.69 ± 1.2 antihypertensives were prescribed, with 26% ($n = 469$) of patients prescribed 3–4 antihypertensives. SBP target was met by 71% ($n = 1281$) of patients, 83.3% ($n = 1502$) met DBP target, and 64.3% ($n = 1160$) met both targets. Correlates of meeting SBP target were not having diabetes, younger age, fewer prescribed antihypertensives, and more recent program entry. Correlates of meeting DBP target were not having diabetes, older age, fewer prescribed antihypertensives, and more recent stroke. *Conclusions:* Up to one-third of patients were not meeting BP targets. Patients with diabetes, and those prescribed multiple antihypertensives are at greater risk for poorly controlled SBP and DBP. Reasons for poor BP control such as untreated sleep apnea and medication non-adherence need to be investigated.

RÉSUMÉ : *Lacune dans l'atteinte de la pression artérielle cible chez des patients après un AVC au moment de l'admission à un programme de réadaptation cardiologique.* *Contexte :* Le tiers environ des accidents vasculaires cérébraux (AVC) sont en fait la répétition d'événements similaires, et ces derniers sont associés à une plus grande incapacité et à une mortalité plus élevée que les premiers. La pression artérielle (PA) est le facteur de risque modifiable le plus important. L'étude avait pour buts de déterminer la proportion de patients admis à un programme de réadaptation cardiologique après avoir subi un AVC, qui respectaient les valeurs cibles de pression systolique (PS) et de pression diastolique (PA); et d'établir des corrélations entre les résultats et les cibles en question. *Méthode :* Il s'agit d'une étude rétrospective, réalisée chez 1804 patients consécutifs, inscrits à un programme de réadaptation cardiologique après avoir subi un AVC. Les renseignements de base (base de données : 2006-2017) comprenaient des données démographiques et anthropométriques, les antécédents cliniques et pharmacologiques, et la PA au repos. Les facteurs prévisionnels d'atteinte des valeurs cibles de la PA ont été déterminés à l'aide d'analyses multifactorielles. *Résultats :* L'âge moyen était de $64,1 \pm 12,7$ ans, et le nombre médian de jours écoulés depuis l'AVC, de 210 (écart interquartile : 392). La plupart des patients étaient des hommes (70,6 %; $n = 1273$) et faisaient de l'embonpoint (66,8 %; $n = 1196$); 64,2 % étaient atteints d'hypertension ($n = 1159$) et 11,8 % ($n = 213$), d'apnée du sommeil. Le nombre d'antihypertenseurs prescrits s'élevait à $1,69 \pm 1,2$ en moyenne, et 26 % ($n = 469$) des patients prenaient 3-4 antihypertenseurs. Dans l'ensemble, 71 % ($n = 1281$) des patients avaient atteint la PS cible; 83,3 % ($n = 1502$), la PD cible; et 64,3 % ($n = 1160$), les deux cibles. L'absence de diabète, un âge moins avancé, un nombre moins élevé d'antihypertenseurs prescrits et une admission plus précoce au programme ont été corrélés à l'atteinte de la PS cible. Quant à l'atteinte de la PD cible, il y avait l'absence de diabète, un âge plus avancé, un nombre moins élevé d'antihypertenseurs prescrits et un AVC plus récent. *Conclusion :* Les valeurs cibles de la PA n'étaient pas atteintes chez environ le tiers des patients. Les personnes diabétiques et celles qui prennent plusieurs antihypertenseurs prescrits connaissent un risque accru de faible maîtrise de la PS et de la PD. Il faudrait approfondir les causes du manque de maîtrise de la PA, telles qu'une apnée du sommeil non traitée ou encore le non-respect de la prise de médicaments.

Keywords: Stroke, Blood pressure, Secondary prevention, Guideline adherence, Cardiac rehabilitation

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INTRODUCTION

In Canada, stroke is the fourth leading cause of death¹ and the tenth largest contributor to disability-adjusted life years,² making it a high priority for primary and secondary prevention.

Secondary prevention is of particular importance as having had a stroke substantially increases risk for another. Indeed, the cumulative risk of recurrent stroke is reported as 39.2% at 10 years.³ Recurrent stroke leads to higher disability and mortality

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compared to first-time stroke,⁴ leading to increased caregiver burden and health care utilization. Thus, prevention of recurrent stroke is critical to reduce the mortality and disability associated with stroke.

It is well established that blood pressure (BP) is the most important modifiable risk factor for recurrent stroke.⁵ Systolic hypertension is estimated to account for ~45% of the stroke burden in Canada.⁶ More recently, diastolic BP (DBP) and pulse pressure have emerged as important components of risk for coronary artery disease and stroke.^{7–9} The Canadian Stroke Best Practice Recommendations provide evidence-based guidelines for the prevention and management of stroke.⁵ Current secondary prevention guidelines recommend a BP target of <140/90 mmHg or <130/80 mmHg for patients with diabetes or small subcortical stroke.⁵ However, implementation of guidelines can prove challenging. Canadian cohort studies of patients with stroke in primary care and stroke prevention clinics have reported 46% to 83% of patients meet target for both systolic BP (SBP) and DBP.^{10–12} Thus, there remains a significant gap between guideline recommendations and real-world attainment.

Since 2006, the cardiac rehabilitation (CR) Program at Toronto Rehabilitation/University Health Network in Toronto, Canada, has amassed a database of over 20,000 patients who have entered outpatient CR. Retrospective analyses of this data were conducted to determine the proportion of patients with stroke enrolled in outpatient CR meeting secondary stroke prevention targets for DBP and SBP. A secondary objective was to determine the demographic and clinical factors associated with meeting BP targets.

METHODS

Setting

This study was a retrospective analysis of consecutive patients with a diagnosis of stroke, with or without cardiac disease, enrolled in a single CR program in Toronto, Canada. Participants were referred by neurologists, cardiologists, physiotherapists, and primary care physicians from 2006 to 2017.

Participants

To participate in CR, patients had to have no contraindications to exercise stress testing such as a recent significant change in resting ECG, uncontrolled severe hypertension, or uncontrolled metabolic disease such as diabetes.¹³ Patients had to (a) be able to walk ≥ 100 meters independently with or without an assistive device (no time restriction and rest breaks allowed) with no severe limitations due to pain, (b) be at least 10 weeks post-stroke, (c) not reliant on a wheelchair, and (d) be able to exercise at home independently or with assistance.

Study Design

Assessment at entry into the program included demographics, clinical and medication history, body mass index (BMI), and a cardiopulmonary assessment. Using the appropriately sized cuff, BP was measured after 4 to 5 minutes of rest prior to commencement of the cardiopulmonary assessment and then throughout the assessment using an automated device (SunTech Medical, US, Model 98/061-03) that allows the cardiac technologist to hear and record the Korotkoff sounds. Symptom-limited cardiopulmonary assessments with direct measurement of oxygen uptake ($\dot{V}O_2$),

BP and ECG tracings, previously described elsewhere,^{14,15} were conducted at baseline. Data were extracted from the institution's database. The study was approved by the University Health Network Research Ethics Board (REB number 13-6289).

Dependent Variables

The Canadian Stroke Best Practice Guidelines recommend achieving a SBP <140 mmHg or <130 mmHg for patients with diabetes and a DBP of <90 mmHg or <80 mmHg for patients with diabetes.⁵

Independent Variables for Logistic Regression Analyses

Measures previously shown to affect BP were chosen as candidate variables for entry into a logistic regression model. These included sex,¹⁶ age,¹⁷ marital status,¹⁸ employment status,^{19,20} stroke diagnosis as the reason for referral (most recent diagnosis),¹¹ year of entry to the program,²¹ BMI,²² $\dot{V}O_{2\text{peak}}$,²³ number of antihypertensive medications,²⁴ presence of coronary artery disease,²² diabetes,²² renal disease,²⁵ smoking,²⁶ sleep apnea,²⁷ and number of comorbidities.²⁸ Time since stroke was included as a candidate variable as adherence to antihypertensives decreases over time.²⁹

Statistical Analysis

Normal distribution of variables was confirmed through the Shapiro–Wilk statistic ($p > 0.05$). Elapsed time from stroke to start of CR data was positively skewed and thus was log-transformed to approximate normal distribution. Bivariate analysis to determine differences in patient characteristics between controlled BP and uncontrolled BP was conducted using χ^2 and Fisher's exact test for categorical variables as appropriate. Student's *t*-tests were used for continuous variables. A logistic regression analysis was conducted to determine correlates of meeting BP targets. Candidate factors for the multivariate logistic regression model were identified from the bivariate analysis as those with p -values ≤ 0.25 .³⁰ The final model maintained only variables reaching a criterion of $p < 0.05$, but forcing sex into the model when appropriate. All analyses were performed in SPSS (version 25). Missing data are reported in Table 1. For any variables without complete data, the *n* value is listed in the first column. Complete-case analysis was performed.

RESULTS

Participant Characteristics

There were 1853 consecutive patients with a stroke diagnosis enrolled in the CR program, and 1804 had complete resting BP data and were included in the study (Table 1). The majority of subjects were male ($n = 1273$, 70.6%), overweight ($n = 1196$ BMI ≥ 25 kg/m², 66.8%), with a mean age of 64.1 ± 12.7 years and median days from stroke 210 (interquartile range 392). Mean resting SBP was 125.8 ± 17.1 mmHg and mean resting DBP was 74.9 ± 9.8 mmHg. In the cohort, 64.2% had a diagnosis of hypertension ($n = 1159$) and this varied over time (60.3% 2006 to 2009 ($n = 527$); 67.5% 2010 to 2013 ($n = 597$); 64.4% 2014 to 2017 ($n = 68$); $p = 0.044$). Subjects were prescribed a mean of 1.69 ± 1.2 antihypertensive medications and 82.2% ($n = 1482$) were prescribed ≥ 1 antihypertensive. Of all patients, 32.4% ($n = 584$) were diagnosed with diabetes, 28.8%

Table 1: Characteristics of patients meeting versus not meeting systolic and diastolic blood pressure targets

	All subjects <i>n</i> = 1804	Meeting SBP target <i>n</i> = 1281	Not meeting SBP target <i>n</i> = 523	<i>p</i> -Value	Meeting DBP target <i>n</i> = 1502	Not meeting DBP target <i>n</i> = 302	<i>p</i> -Value
Age (years)	64.1 ± 12.7	63 ± 13.1	66.7 ± 11.3	<0.001	64.9 ± 12.8	60.1 ± 11.4	<0.001
Men, <i>n</i> (%)	1273 (70.6)	890 (69.5)	383 (73.2)	0.112	1048 (69.8)	225 (74.5)	0.1
Married, <i>n</i> (%) <i>n</i> = 1608	1182 (73.5)	830 (72.3)	352 (76.5)	0.083	990 (73.8)	192 (72.2)	0.591
Employment status <i>n</i> = 1460							
Employed, <i>n</i> (%)	250 (17.1)	179 (17.6)	71 (16)	0.3	195 (16.2)	55 (21.5)	<0.001
Retired, <i>n</i> (%)	746 (51.1)	505 (49.8)	241 (54.2)		655 (54.4)	91 (35.5)	
Unemployed, <i>n</i> (%)	464 (31.8)	331 (32.6)	133 (29.9)		354 (29.4)	110 (43)	
Median days since stroke (IQR), <i>n</i> = 1683	210 (392)	201(356)	238(468)		201(375)	261(460)	
Log-transformed days post-stroke	2.43 ± 0.55	2.43 ± 0.55	2.51 ± 0.54	0.01	2.43 ± 0.55	2.54 ± 0.54	0.002
Year of CR entry							
2006 to 2009, <i>n</i> (%)	527 (29.2)	352 (27.5)	175 (33.5)	0.004	430 (28.6)	97 (32.1)	0.267
2010 to 2013, <i>n</i> (%)	597 (33.1)	417 (32.6)	180 (34.4)		494 (32.9)	103 (34.1)	
2014 to 2017, <i>n</i> (%)	680 (37.7)	512 (40)	168 (32.1)		578 (38.5)	102 (33.8)	
Stroke most recent diagnosis, <i>n</i> (%)	1281 (71)	929 (72.5)	352 (67.3)	0.027	1069 (71.2)	212 (70.2)	0.734
VO _{2peak} (mL·kg ⁻¹ ·min ⁻¹), <i>n</i> = 1733	17 ± 6.05	17.5 ± 6.41	15.8 ± 4.95	<0.001	17.1 ± 6.12	16.8 ± 5.86	0.549
BMI (kg/m ²), <i>n</i> = 1790	27.7 ± 5.29	27.4 ± 5.14	28.5 ± 5.58	<0.001	27.5 ± 5.23	28.8 ± 5.4	<0.001
BMI ≥25 kg/m ² , <i>n</i> (%)	1196 (66.8)	825 (64.9)	371 (71.5)	0.007	975 (65.5)	221 (73.2)	0.010
BMI ≥30 kg/m ² , <i>n</i> (%)	498 (27.8)	337 (26.5)	161 (31.0)	0.054	382 (25.7)	116 (38.4)	<0.001
Hypertension, <i>n</i> (%)	1159 (64.2)	749 (64.6)	410 (35.4)	<0.001	930 (80.2)	229 (19.8)	<0.001
Diabetes, <i>n</i> (%)	584 (32.4)	300 (23.4)	284 (54.3)	<0.001	373 (24.8)	211 (69.9)	<0.001
Coronary artery disease, <i>n</i> (%)	520 (28.8)	333 (26.0)	187 (35.8)	<0.001	438 (29.2)	82 (27.2)	0.482
Renal disease, <i>n</i> (%)	62 (3.4)	36 (2.8)	26 (5)	0.022	50 (3.3)	12 (4)	0.575
Sleep apnea, <i>n</i> (%)	213 (11.8)	156 (12.2)	57 (10.9)	0.445	182 (12.1)	31 (10.3)	0.363
Current smoking, <i>n</i> (%)	27 (1.5)	18 (1.4)	9 (1.7)	0.619	20 (1.3)	7 (2.3)	0.203
Comorbidities							
0 or 1 <i>n</i> (%)	530 (29.4)	434 (33.9)	96 (18.4)	<0.001	480 (32)	50 (16.6)	<0.001
2 <i>n</i> (%)	457 (25.3)	316 (24.7)	141 (27)		359 (23.9)	98 (32.5)	
3 <i>n</i> (%)	333 (18.5)	221 (17.3)	112 (21.4)		271 (18)	62 (20.5)	
4 or 5 <i>n</i> (%)	484 (26.8)	310 (24.2)	174 (33.3)		392 (26.1)	92 (30.5)	
Number of antihypertensive medications	1.69 ± 1.15	1.54 ± 1.14	2.04 ± 1.11	<0.001	1.65 ± 1.16	1.89 ± 1.12	0.001
Number of antihypertensive medications							
0 <i>n</i> (%)	322 (17.8)	272 (21.2)	50 (9.6)	<0.001	286 (19.0)	36 (11.9)	0.014
1 <i>n</i> (%)	499 (27.7)	382 (29.8)	117 (22.4)		420 (28.0)	79 (26.2)	
2 <i>n</i> (%)	514 (28.5)	349 (27.2)	165 (31.5)		423 (28.2)	91 (30.1)	
3 <i>n</i> (%)	361 (20)	217 (16.9)	144 (27.5)		286 (19.0)	75 (24.8)	
4 <i>n</i> (%)	108 (6)	61 (4.8)	47 (9.0)		87 (5.8)	21 (7.0)	

Continuous data are represented as mean ± SD unless otherwise indicated. CR = cardiac rehabilitation; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure.

with coronary artery disease ($n = 520$), 3.4% with renal disease ($n = 62$), 11.8% ($n = 213$) with sleep apnea, and 1.5% ($n = 27$) were current smokers. Individual medications were prescribed as follows: β -blockers $n = 790$ (43.8%), Ca^{2+} channel antagonist $n = 553$ (30.7%), diuretics $n = 511$ (28.3%), angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers $n = 1175$ (65.1%), any diabetes medication $n = 495$ (27.4%), insulin $n = 132$ (7.3%), lipid-lowering medications $n = 1397$ (77.4%), antiplatelets $n = 1191$ (66%), and anticoagulants $n = 360$ (20%).

BP Target Attainment

In the cohort, 71% ($n = 1281$) of patients met the SBP target, 83.3% ($n = 1502$) met the DBP target, and 64.3% ($n = 1160$) met targets for both SBP and DBP. Of the patients without diagnosed hypertension ($n = 645$), 17.5% ($n = 113$) and 11.3% ($n = 73$) did not meet SBP and DBP targets, respectively, and 64% ($n = 413$) were prescribed at least one antihypertensive. Bivariate analyses to identify candidate variables to determine independent correlates of meeting BP targets are presented in Table 1. Figure 1 shows the proportion of patients meeting SBP and DBP targets by number of prescribed medications. Figure 2 shows the proportion of patients meeting the SBP target by year of CR program entry.

Patients with Diabetes

For patients with and without diabetes, mean SBP was 128.9 ± 17.4 mmHg and 124.4 ± 17.8 mmHg ($p < 0.001$), respectively, and mean DBP was 74.3 ± 10.1 mmHg and 75.2 ± 9.6 mmHg ($p = 0.07$), respectively. Among those with diabetes who were within the SBP target level versus those who were not, there was no significant difference in the proportion prescribed insulin (28.1%; $n = 68$ vs 27.7%; $n = 64$, $p = 0.924$, respectively), or prescribed at least one diabetes medication (81.7%; $n = 245$ vs 81.3%; $n = 231$, $p = 0.919$ respectively). Among those who were within the DBP target level versus those who were not, there was no significant difference in the proportion prescribed insulin (28.4%; $n = 87$ vs 26.9%; $n = 45$, $p = 0.731$, respectively), or prescribed at least one diabetes medication (82.6%; $n = 308$ vs 79.6%; $n = 168$, $p = 0.377$, respectively). Using non-diabetes target values (SBP < 140 mmHg and DBP < 90 mmHg), 72.1% ($n = 421$) of people with diabetes met the SBP target compared to 80.4% ($n = 981$) of people without diabetes ($p < 0.001$). For DBP, 93% ($n = 543$) of people with diabetes met the target compared to 92.5% ($n = 1129$) of people without diabetes ($p = 0.738$).

Independent Correlates of Controlled SBP

Correlates of meeting SBP targets were not having diabetes, younger age, not being prescribed any antihypertensives compared to two, three, or four antihypertensives, and more recent year starting the program (2014–2017 vs 2006–2009) (Table 2). A test of the full model compared with a constant-only or null model was statistically significant ($p < 0.001$), and the goodness of fit was assessed by the Hosmer–Lemeshow test ($p = 0.836$). As determined by the Nagelkerke R Square, 17.7% of the variance is explained with this model.

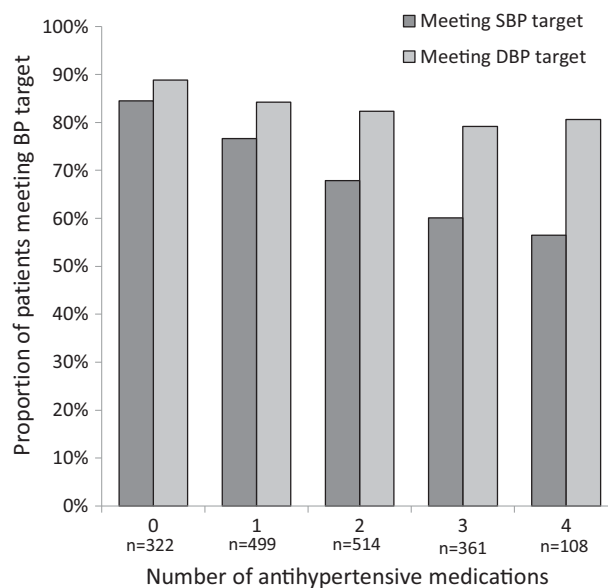


Figure 1: Proportion of patients meeting systolic blood pressure (SBP) and diastolic blood pressure (DBP) targets by number of prescribed medications.

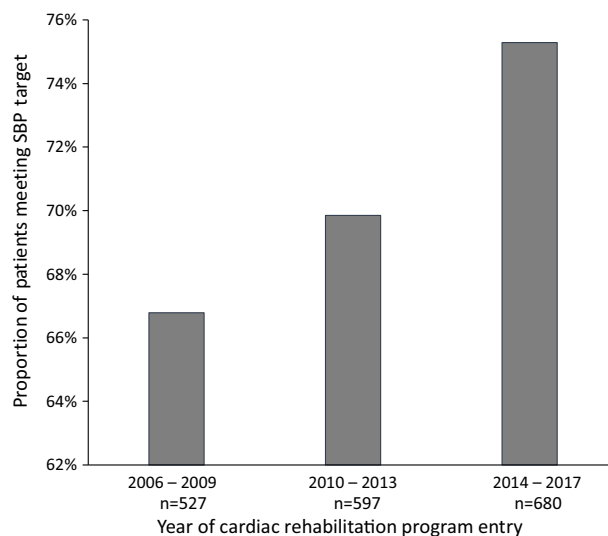


Figure 2: Proportion of patients meeting the systolic blood pressure (SBP) target by year of cardiac rehabilitation program entry.

Independent Correlates of Controlled DBP

Correlates of meeting DBP targets were not having diabetes, older age, not being prescribed any antihypertensives compared to two or three antihypertensives, and a more recent stroke (Table 3). A test of the full model compared with a constant-only or null model was statistically significant ($p < 0.001$), and the goodness of fit was assessed by the Hosmer–Lemeshow test ($p = 0.039$). As determined by the Nagelkerke R Square, 23.3% of the variance is explained with this model.

Table 2: Independent correlates of meeting systolic blood pressure target

Variable	Wald χ^2 test	Odds ratio	95% CI	p-Value
Diabetes	135.279	0.260	0.207–0.326	<0.001
Age	30.943	0.973	0.964–0.983	<0.001
Number of antihypertensives	25.006	–	–	<0.001
Reference 0 antihypertensives				
1 antihypertensive	1.628	0.779	0.530–1.143	0.202
2 antihypertensives	9.318	0.557	0.383–0.811	0.002
3 antihypertensives	15.414	0.457	0.309–0.676	<0.001
4 antihypertensives	12.063	0.398	0.236–0.669	0.001
Year of CR entry	11.670	–	–	0.003
Reference 2014–2017				
2006–2009	11.601	0.625	0.476–0.819	0.001
2010–2013	2.032	0.825	0.633–1.075	0.154
Sex, female	0.272	1.067	0.836–1.363	0.602

CR = cardiac rehabilitation.

Table 3: Independent correlates of meeting diastolic blood pressure target

Variable	Wald χ^2 test	Odds ratio	95% CI	p-Value
Diabetes	163.252	0.149	0.111–0.200	<0.001
Age	38.219	1.039	1.026–1.052	<0.001
Number of antihypertensives	6.718	–	–	0.152
Reference 0 antihypertensives				
1 antihypertensive	1.575	0.736	0.457–1.188	0.209
2 antihypertensives	4.780	0.585	0.361–0.946	0.029
3 antihypertensives	4.062	0.598	0.363–0.986	0.044
4 antihypertensives	0.119	0.888	0.453–1.742	0.730
Days post-stroke to CR entry	5.077	0.751	0.585–0.963	0.024
Sex, female	1.532	1.223	0.889–1.682	0.216

CR = cardiac rehabilitation.

DISCUSSION

This is the first study to identify independent correlates of meeting the secondary prevention targets for SBP and DBP in consecutively enrolled patients with a diagnosis of stroke entering an outpatient CR program. Of the 1,804 patients enrolled, 71% of patients met the SBP target, 83.3% met the DBP target, 64.3% met targets for both SBP and DBP, and 82.2% were prescribed at least one antihypertensive. Of the patients without diagnosed hypertension, 17.5% and 11.3% did not meet SBP and DBP targets respectively, suggesting hypertension may be underdiagnosed in this cohort. Correlates of meeting SBP targets were not having diabetes, younger age, being prescribed fewer antihypertensives, and more recent year starting the program (2014–2017 vs 2006–2009). Correlates of meeting DBP targets were not

having diabetes, older age, being prescribed fewer antihypertensives, and a more recent stroke. The most influential correlate of meeting the SBP and DBP target, respectively, was not having a diagnosis of diabetes.

A Gap Exists in BP Target Attainment in Canada

Our finding that 64.3% of patients met SBP and DBP targets is consistent with previously published Canadian studies that reported 46% to 83% of stroke patients meet target.^{10–12} Two studies of patients attending an initial visit at a stroke prevention clinic described 83% and 76% BP target attainment, respectively.^{10,12} A lower proportion of target attainment (46%) was reported in an outpatient study of patients with stroke or transient ischemic attack (TIA).¹¹ Unfortunately, none of these studies

reported time since stroke, making a comparison to our cohort of patients who were a median of 210 days post-stroke challenging. This significant gap in BP target attainment for secondary stroke prevention in Canada is critical to address as the odds of experiencing any stroke is 2.98 times higher for those with self-reported hypertension or BP $\geq 140/90$ mmHg.³¹ In addition, for individuals aged 40–69 years, every 20 mmHg increase in SBP or 10 mmHg increase in DBP is associated with more than a twofold increased risk of stroke mortality.³² In order to help understand and address the gap in BP target attainment, we examined correlates of meeting targets.

Diabetes Had the Strongest Association with not Achieving BP Targets

In the multivariate regression models, no diabetes was the strongest correlate for meeting SBP and DBP targets. Similarly, Chen et al. reported that in their multivariate logistic regression analysis a diagnosis of diabetes was independently associated with failing to meet BP targets.¹² When we examined DBP target attainment in patients with diabetes using the non-diabetes DBP target, there was no longer a significant difference between subjects with diabetes compared to those without. Thus, the greater proportion of people with diabetes not meeting the DBP target in this study is due, at least in part, to target levels that recommend tighter control. This was not the case for SBP. Poorer SBP target attainment in patients with diabetes is likely due in part to vascular remodeling and increased body fluid volume associated with diabetes.³³ In addition, the lack of significant difference in the proportion of patients with diabetes prescribed insulin who were meeting versus not meeting the SBP target indirectly suggests that inadequate glycemic control or diabetes treatment refractoriness may not be a predictor of BP control; however, this requires further investigation with direct measures of glycemic control.

Older Age Predicted DBP Control Whereas Younger Age Predicted SBP Control

In the multivariate regression analysis, older age predicted DBP control, whereas in the model for SBP, younger age predicted control. In Canada, 46.6% of adults aged 60 to 69 years and 70.4% of adults aged 70 to 79 years have hypertension.³⁴ Isolated systolic hypertension, a result of large artery stiffness causing widened pulse pressure, is the most common form of hypertension among older adults.¹⁷ After 50–60 years of age, DBP declines, pulse pressure rises steeply, while SBP continues to increase linearly.³⁵ Post-stroke, patients with normal or low DBP tend to be older.⁹ Our study is consistent with these findings. In addition, the divergence of DBP and SBP with age likely explains why a smaller proportion of subjects met the SBP target (71%) compared to the DBP target (83.3%) given that the mean age of the cohort was 64.1 ± 12.7 years. These results have important clinical implications as higher pulse pressure is an important component of risk for coronary artery disease and stroke.^{7–9}

More Recent Stroke Predicts DBP Control

Less elapsed time from stroke was independently associated with meeting the DBP target and in the bivariate analysis only was associated with meeting the SBP target. A cross-sectional study of primary care patients in England where the median time

since stroke/TIA was 2.5 years found that only 37% and 58% of patients were meeting the SBP and DBP targets, respectively.³⁶ This supports our finding of diminishing target attainment over time. This result may in part be related to reports that adherence with prescribed medications decreases over time²⁹ and poor adherence with prescribed antihypertensive medications is a common reason for inadequate BP control.^{37,38}

Lower Number of Prescribed Antihypertensives was Associated with Meeting BP Targets

Poor adherence to prescribed regimens may also explain why fewer prescribed antihypertensive medications were an independent correlate of meeting SBP and DBP targets, respectively. A study in Ghana examining post-stroke determinants of SBP control reported greater number of antihypertensives were independently associated with poor SBP control.³⁹ There are a number of possibilities to explain this finding. Medication adherence decreases with increased number of prescribed medications.⁴⁰ In addition, patients may overestimate their medication adherence⁴¹ due to recall bias, social desirability, and cognitive impairment post-stroke, leading to additional medication prescription despite inadequate optimization of their current regimen. Moreover, physicians may fail to adequately assess or recognize poor adherence prior to intensifying medication regimens.^{42,43} However, this finding requires further investigation.

BP Target Attainment Improved Over Time

Participants who commenced CR more recently (2014–2017) were more likely to meet the SBP target than those enrolled more remotely (2006–2009). In Canada, the prevalence of hypertension among 20- to 79-year-olds remained relatively stable from 2007–2009 to 2012–2015.³⁴ However, the proportion of patients diagnosed with hypertension who have controlled BP has increased with time.²¹ In our cohort, the proportion of patients diagnosed with hypertension did not increase linearly over time, suggesting improved control of BP rather than improved diagnosis of hypertension may have been the primary cause for improved target attainment over time. Public education programs, including national multidisciplinary efforts to generate and implement annually updated hypertension guidelines, may have contributed to the improvement in BP control over time in Canada.^{44–46}

Sleep Apnea may Have Been Underdiagnosed in this Cohort

Underdiagnosed sleep apnea may have played a role in some of the patients failing to meet BP targets. It is well established that untreated sleep apnea is a cause of hypertension⁴⁷ and undiagnosed sleep apnea is common in adults with resistant hypertension.⁴⁸ Studies have demonstrated a high prevalence of post-stroke sleep apnea, with up to 80% diagnosed with sleep-disordered breathing.²⁷ In contrast, only 11.8% of our sample were diagnosed with sleep apnea.

Women Who Have had a Stroke are Underrepresented in Outpatient CR

Our cohort had a much lower proportion of women at 29% compared to 57% in the general Canadian stroke population.⁴⁹ In a previous study, we followed 116 consecutively enrolled people

from an outpatient stroke rehabilitation program that is one of the primary referral sources to the CR program.⁵⁰ Of the 116 enrolled, only 36% were women. This disparity in outpatient stroke rehabilitation has also been demonstrated in the USA.⁵¹ Further, women were almost twice as likely to decline participation in CR than men, independent of age with no evidence of sex-related referral bias or difference in reasons for declining the CR program.⁵⁰ Stroke prevalence is higher in women and they are known to have worse outcomes post-stroke.^{52,53} Therefore, women are more likely to be discharged to chronic care facilities than men^{52,53} and thus less likely to be referred to CR.⁵⁴ This gap in women's participation in CR may be an important contributor to both poorer outcomes from the initial stroke and increased prevalence of recurrent stroke.

Future Directions

Internationally, it is recognized that BP target attainment for secondary stroke prevention is poor,^{55–58} leaving significant gaps that need to be addressed. A 2018 Cochrane systematic review and meta-analysis found there was moderate-quality evidence that organizational interventions resulted in improved BP target attainment post-stroke, with the largest BP reductions associated with a multidisciplinary approach and comprehensive patient education.⁵⁹ Many of these features are incorporated into CR programs and it has been shown that CR is feasible after stroke.^{60,61} CR programs include aerobic and resistance training, cardiac exercise assessments and screening, plasma glucose and lipid monitoring as well as psychosocial, nutrition, and risk factor modification education. In addition, a recent meta-analysis revealed that aerobic training following stroke resulted in significant reductions in SBP.⁶²

Existing CR programs in Canada⁶³ are an excellent platform for providing ongoing, comprehensive multidisciplinary support to patients who have had a stroke.⁶⁴ Studies have demonstrated superior CR program adherence in people following stroke compared to people with coronary artery disease even when matched by age and sex.^{50,60,65} Unfortunately, while 65% of Canadian CR programs accept referrals for people post-stroke, 63% of these report that <11 patients participated in the previous year.^{60,66} Yet over half of all CR programs were within a 25-km radius of an outpatient stroke rehabilitation program. Facilitators recommended by CR managers to increase referral of individuals with stroke to CR programs included collaboration with health care professionals from stroke rehabilitation units.⁶⁶ Indeed, a recent study by our group demonstrated that collaboration between CR and a single stroke rehabilitation program resulted in ~3/4 of eligible stroke patients participating in CR,⁵⁰ reaching the recommended target set by CR associations and national initiatives.⁶⁷ Future studies should examine the effect of CR–stroke rehabilitation partnerships nationally and the adoption of an automatic referral process where every patient post-stroke would be considered for referral to CR.

In addition to increasing referrals of stroke patients to CR, future studies should also examine CR adherence. Patients with increased medical comorbidities have lower participation in and adherence to CR programs.^{50,68} Home-based programs have been successful at increasing adherence to CR.⁶⁹ Future studies should investigate the effect of intensified and targeted exercise, nutrition and medication adherence strategies for people following stroke with comorbid diabetes and hypertension. In addition,

glycemic control in the post-stroke population as a possible predictor of BP control should be examined, as this was not addressed in the current study.

Limitations

With regard to generalizability, this was a single-center study. Our cohort is younger than the general Canadian population with stroke,⁴⁹ but consistent with the mean age of patients from the outpatient stroke rehabilitation program (mean age 65±14 years) that is the main referral source for the CR program in the current study.⁵⁰ Older patients have more severe deficits post-stroke and may not have been referred to CR due to actual or perceived ineligibility⁷⁰ or do not enter outpatient stroke rehabilitation or other potential referral pathways. Data on ethnicity were not available. Accuracy of BP measurement may have been strengthened by repeated measurement on more than one occasion.⁷¹ In addition, BP was measured 4 to 5 minutes prior to the cardiopulmonary assessment and thus anticipation of exercise may have resulted in elevation of the BP. This may account, in part, for some subjects without a previous hypertension diagnosis not meeting targets for DBP and/or SBP. There was no assessment of adherence to antihypertensive medications and no data with regard to the type of stroke. Finally, while the logistic regression models for independent correlates of DBP and SBP were significant, only 17.7% and 23.3% of the variance were explained, respectively. BP is a complex physiologic construct with innumerable clinical correlates. These clinical correlates are surrogate measures/determinants of the physiologic determinants of BP, mainly cardiac output and peripheral vascular resistance,⁷² and likely lack the sensitivity to detect subtle relationships.

CONCLUSIONS

In this retrospective cohort study of consecutive patients with stroke enrolled in a CR program, 71% of patients met the SBP target, 83.3% met the DBP target, and 64.3% met both targets for secondary stroke prevention. No diagnosis of diabetes, younger age, fewer prescribed antihypertensives, and later year of entry were independent correlates of meeting the SBP target. No diagnosis of diabetes, older age, fewer antihypertensives, and less time since stroke were independent correlates of meeting the DBP target. Medication non-adherence and underdiagnosed sleep apnea may have been contributing factors to poor BP control. Further research and quality improvement initiatives are needed to verify this and to address the gap in BP target adherence for secondary stroke prevention. Institutional, multidisciplinary, patient-centered programs, such as CR programs, provide the ideal environment to optimize risk factors for secondary stroke. Patients with stroke and comorbid diabetes should be closely monitored for elevated BP, medication adherence, and receive intensified CR and nutrition interventions.

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CONFLICTING INTERESTS

The authors declare that there is no conflict of interest.

STATEMENT OF AUTHORSHIP

CS contributed to the conception and design of the study, interpretation of the data, and drafting and revising the manuscript. PO contributed to the conception and design of the study, interpretation of the data, and critically revising the manuscript. SM contributed to the conception and design of the study, acquisition of data, analysis and interpretation of the data, and critically revising the manuscript.

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