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Editorial

Blood Pressure Control in Canada: The View From a Stroke Prevention Clinic

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See article by Gupta et al., pages 664-670 of this issue.

No doubt blood pressure control in Canada has improved dramatically since I opened one of the first hypertension clinics in Canada in 1977. In my first year in practice I saw 10 cases of hypertensive encephalopathy; malignant hypertension was a common cause of renal failure leading to dialysis, and on our Neurology service we were seeing approximately 200 patients per year with hypertensive intracerebral hemorrhage.

In 1978 the Department of Family Medicine at Western mounted a program to increase detection and treatment of hypertension in the community.[1] I assume that blood pressure control before the study was as bad in London as in the rest of North America, summarized by the rule of halves: half of the hypertensive individuals were detected, of those half (ie, 25%) were treated, and of those half (12.5%) were controlled. Five years later things had changed dramatically: a population survey found that 94% were detected, 72% were receiving treatment, and 70% were controlled. What that did for stroke was dramatic: strokes were reduced by half; strokes due to hypertensive small vessel disease (lacunar infarctions and hypertensive intracerebral hemorrhage) went from 50% to 7% of stroke.[2] Nowadays it is more common to see intracerebral hemorrhage from amyloid angiopathy than from hypertension—but the level of blood pressure control in the rest of the country was then nowhere near the levels obtained shortly after that study, and in London, Ontario, blood pressure control is not nearly as good now as it was in 1984. How quickly we forget!

In 1992 Joffres et al.[3] reported from the Canadian Heart Health Survey, a population-based survey of 26,293 people sampled from health insurance registries in 9 provinces, from 1996 to 1990. They found that 16% percent of men and 13% of women had diastolic blood pressure $\geq$ 90 mm Hg or were receiving treatment (or both). Approximately 26% of these subjects were unaware of their hypertension, 42% were being treated and their condition controlled, 16% were treated and not controlled, and 16% were neither treated nor controlled.

More optimistic figures came from a survey based on self-reporting by persons who volunteered for a survey published in 2011[4]: supposedly, 64.6% of hypertensive individuals were controlled in 2009, vs 13.2% in 1992. This occasioned much back-patting among the leaders of the Canadian Hypertension Education Program.

However, in 2007 Petrella et al.[5] reported from a large family medicine database in Southwestern Ontario (> 45,000 patients seen in 2000-2003) that 17.3% of patients were hypertensive; of those 68% were untreated and only 15.8% were receiving treatment and controlled to levels recommended in the then prevalent consensus guidelines.

In this issue of the *Canadian Journal of Cardiology*, Gupta et al.[6] report on a survey of 3015 healthy, middle-aged Canadians, free of cardiovascular disease or diabetes. They found that 34.3% were hypertensive, and of those 57% were controlled, implying that almost half (43%) were not controlled. This estimate of control rates might be somewhat optimistic, because the participants were volunteers.

The view from my stroke prevention clinic looks similar. From the database of a study of secular trends in stroke subtypes[7] in 3445 patients referred to my urgent transient ischemic attack clinic at University Hospital in London, Ontario, I was able to determine the distribution of blood pressure at the time of referral, and control rates year by year, between 2000 and 2012 (approximately 300 patients per year). The blood pressures analyzed were those at the first visit, which reflected community control of blood pressure, and the patients were not selected for hypertensive status, because referrals were assigned by a receptionist to the first clinic available, regardless of which neurologist was conducting clinic that day. Figure 1 shows the distribution of systolic and diastolic blood pressures at the time of referral; as might be expected in a secondary stroke prevention clinic, some patients had quite high pressures, even though virtually all were being followed by a family physician. Figure 2 shows that the control rate for systolic hypertension was approximately 50%; control of diastolic hypertension was better, approximately 80%, but neither changed appreciably over the

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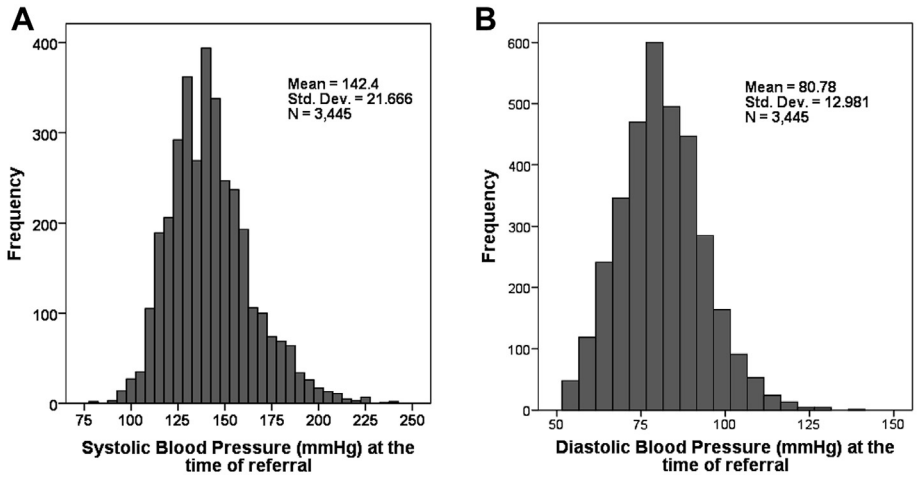

Figure 1. Distribution of blood pressure at the time of referral to an urgent transient ischemic attack clinic. As might be expected in a secondary stroke prevention clinic, some patients had very high blood pressure. (**A**) Systolic pressure. (**B**) Diastolic pressure.

11 years. In contrast, levels of low-density lipoprotein cholesterol at the time of the referral decreased dramatically over that time, as shown in Figure 3.

Why can low-density lipoprotein cholesterol be treated so much better than blood pressure? Patient reasons for resistant hypertension include: (1) noncompliance; (2) consumption of substances that aggravate hypertension, such as excess sodium, ethanol, licorice, decongestants, or nonsteroidal anti-inflammatory drugs (with the exception of sulindac[8]); (3) secondary hypertension; and (4) reluctance to take drugs.

As or more important is the failure of physicians to adequately treat hypertension, and adequately assess the cause of blood pressure that is resistant. Therapeutic inertia—the tendency to not prescribe medication, or increase the intensity of medication when blood pressure remains high—can be overcome. We showed this in the North American Carotid Endarterectomy Trial. If blood pressure therapy was not increased in intensity at any patient visit at which the blood pressure was above target levels, the site principal investigator received from Brian Haynes a letter pointing this out, and insisting that the protocol be followed. Even though the study was carried out between 1988 and 1998, we virtually eliminated intracerebral hemorrhages: they accounted for only 0.4% of strokes in the study population.[9]

What seems more difficult to overcome is diagnostic inertia. Even though Laragh described the benefit of measuring plasma renin for selection of antihypertensive therapy in the 1970s,[10] and I have been trying to explain since 1999,[11] that measurement of plasma renin and aldosterone is vital to control of resistant hypertension, this simple manoeuvre is seldom performed. Even though the guidelines recommend this (in the fine print) for patients with resistant hypertension, most doctors seem to persist in prescribing cookie-cutter therapy to all patients, as if they were all the same.

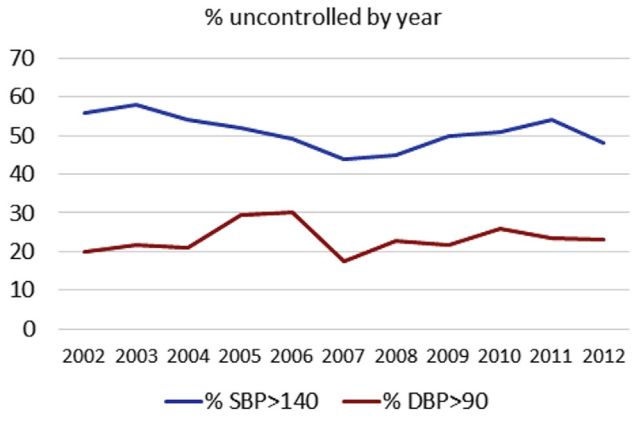

Figure 2. Percentage of patients with uncontrolled blood pressure at the time of referral to an urgent transient ischemic attack clinic, from 2002 to 2012. Approximately half of the patients had systolic pressure > 140 mm Hg, and approximately 20% had diastolic pressure > 90 mm Hg. This did not change substantially between 2002 and 2012.

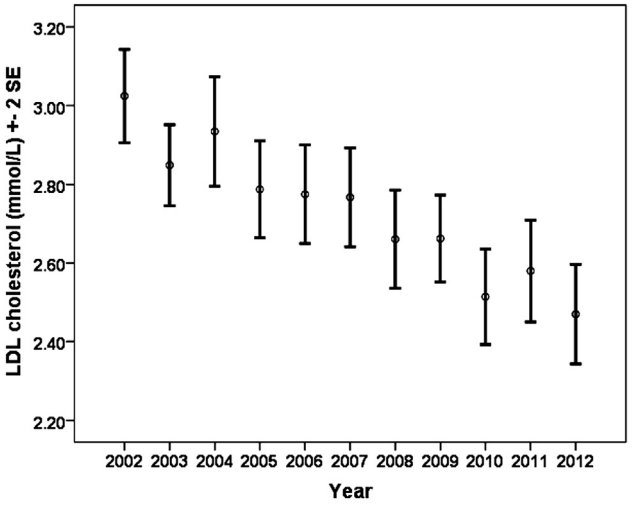

Figure 3. Plasma low-density lipoprotein (LDL) cholesterol levels at the time of referral to an urgent transient ischemic attack clinic from 2002 to 2012. LDL levels decreased dramatically, undoubtedly because of increasing use of statins over that time. Reproduced from Bogiatzi et al.[7] with permission from Wolters Kluwer Health.

In 20 years of running the hypertension clinic of last resort for Southwestern Ontario and beyond, I only saw 52 patients with pheochromocytoma, 3 with adult aortic coarctation, 9 with hypernephroma, and 9 from licorice. After excluding such rare causes, the remaining 10,000 or so cases had their problem in the renin/angiotensin/aldosterone axis. Approximately 20% of patients with resistant hypertension have primary hyperaldosteronism, for which the primary treatment is aldosterone antagonists (spironolactone or eplerenone—the latter better for men because of the high frequency of gynecomastia with spironolactone). Surgery is rarely appropriate for most patients with primary aldosteronism, because as is being increasingly recognized, many (or perhaps most, or maybe even all) cases are due to bilateral adrenocortical hyperplasia. Only approximately 5% of my patients with primary aldosteronism have required surgery, and in most cases it was bilateral adrenalectomy (or partial adrenalectomy) that was required. Among my patients with carotid stenosis and resistant hypertension being followed closely in carotid endarterectomy trials, 25% had renovascular hypertension,[12] and some of those patients required revascularization to achieve blood pressure control. Randomized trials that failed to show benefit of renal revascularization were flawed by inclusion of patients with incidental mild renal artery stenosis, high crossover rates, and waiting too long to vascularize the kidney.[13] Approximately 6% of patients attending hypertension clinics will have variants of Liddle syndrome, a mutation of the renal tubular sodium channel that causes retention of salt and water, and for which the specific treatment is amiloride.[14]

All of these conditions are detected and treated and controlled by measuring plasma renin and aldosterone, thoughtful interpretation of the results, and tailoring of therapy to the disordered physiology. An algorithm for doing so, and reasons for particularly doing so in patients of African origin, were described in this journal in 2012.[15] It is best to measure them in a stimulated condition (eg, after a dose of short-acting diuretic, during diuretic therapy[16]). Patients with primary aldosteronism have a low renin and high aldosterone level, patients with renal/renovascular hypertension have a high renin level with secondary hyperaldosteronism, and patients with a Liddle phenotype (and some other causes of salt and water retention) have low renin and low aldosterone levels.

What needs to be done to improve blood pressure control? An important step would be a randomized trial of usual therapy for hypertension, vs individualized treatment based on renin-aldosterone profiling. Ideally this should be done as a cluster randomization trial, in patients whose blood pressures are not controlled despite use of 3 medications, including a diuretic. This would be particularly important in patients of African origin. That might be what it would take for physicians to widely adopt this approach. In the meantime, I see no good reason for not doing so now.

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