The Quality of Hyperacute Ischemic Stroke Treatment in Canada

Ganesh A, Camden M, Lindsay P, Kapral MK, Cote R, Fang J, Zagorski B, Hill MD for the Canadian Stroke Audit Group

From the Calgary Stroke Program, Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada

Correspondence to:

Michael D. Hill, Professor, Calgary Stroke Program, Department of Clinical Neurosciences, University of Calgary, Foothills Hospital, Rm 1242A, 1403 29th Streeet NW, Calgary, Alberta, T2N 2T9, Canada
FAX 403 283 2270; EMAIL michael.hill@ucalgary.ca

Acknowledgements and Funding:

The study was funded by the Canadian Stroke Network and the Heart & Stroke Foundation of Canada

Conflicts of interest:

None.

Statement of Authorship:

AG and MDH wrote the first draft.
PL operationally organized and administered the study.
All authors contributed to analysis, discussion and critical revision of the final manuscript.

Full title: The Quality of Hyperacute Ischemic Stroke Treatment in Canada

Cover title: The Quality of Hyperacute Ischemic Stroke Treatment in Canada

Keywords: stroke, thrombolysis, quality care, stroke centre

Word Count: 250 (abstract); 1737 (text)

Figures: 0

Tables: 4

Abstract

Background – The use of thrombolysis in acute stroke is an important indicator of the quality of stroke care, as it requires healthcare providers to work collaboratively, rapidly, and accurately to optimize patient outcome. We conducted a national chart audit to assess the quality of acute stroke care in Canada, using the rate of thrombolysis as the key indicator.

Methods – National administrative data were used to identify discharge diagnoses of stroke in the 10 provinces between 2008 and 2009, and a weighted random sample was drawn for detailed chart review, focused on identifying indicators of acute stroke care. The proportion of thrombolysis use, complications, and outcomes were determined, with rates adjusted for age and sex, and stratified by hospital type.

Results – The final audit sample included 9,588 patient charts representing 88% of the 43,651 admitted stroke cases in Canada. A total of 5.4% (95% confidence interval [CI] 5.1-5.6) of all stroke and 6.1% (95% CI 5.8-6.4) of ischemic stroke patients received thrombolysis, with comprehensive stroke centres treating roughly one-third of their ischemic cases – double that of primary stroke centres. Most often, 35-49% of the time, thrombolysis was not given due to stroke onset-to-arrival time beyond 4.5 hours.

Interpretation – Thrombolysis rates for acute stroke in Canada remain low, limited by delays in both the arrival of patients to hospital, and in the in-hospital processes of neuroimaging and thrombolysis administration. Our data demonstrates the critical need for concerted national efforts to improve education regarding acute stroke treatment and speed up in-hospital stroke management.

Introduction

The evidence-to-practice gap in acute stroke treatment is thought to be large on a population basis. While treatments have evolved rapidly, uptake and application of these treatments has been slow and inconsistent [1]. The use of thrombolysis for acute ischemic stroke is an important quality indicator. The rates of acute thrombolysis use in the United States [2], Ireland [3], the United Kingdom [4], and Sweden [5] represent only a small fraction of the total ischemic stroke population.

The demonstration that thrombolysis for stroke is an effective treatment has wrought much system change. Although there is unequivocal evidence for the benefit of timely thrombolysis [6], it is a difficult therapy to administer appropriately, in large part because of the tremendous need for speed in application and careful clinical judgement [7]. Teams of health care providers must work in concert, very rapidly, making the correct decisions to achieve good outcomes. Results from Helsinki have shown that very fast treatment times are possible, but these are dependent on a well-functioning global system pushing data collection into the pre-hospital phase, and direct linkage of the pre-hospital and in-hospital response teams [8]. Prior Canadian data showed a low rate of thrombolysis and slow treatment times [9].

We sought to assess the quality of acute stroke care in Canada by conducting a national chart audit. The key indicator was the rate of stroke thrombolysis.

Methods

Subjects were identified using national administrative data sources. All patients with a discharge diagnosis of stroke admitted in the fiscal year, April 1, 2008 to March 31, 2009 were eligible for inclusion in the study. The diagnosis of stroke was considered using the following codes from the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10): I60, I61, I63, I64, G45 [10]. Only the most responsible or first position diagnosis was considered.

We only included the 10 Canadian provinces in this sample, excluding the 3 territories due to their small populations. Privacy assessments and ethical board reviews were conducted in each province. We drew a weighted random sample for detailed chart review for all the provinces, with the exception of Manitoba, where the sample was non-random and obtained from two regions, including seven hospitals, at the discretion of the provincial health authority. Sampling was over-weighted for smaller provinces and under-represented populations. Each hospital was classified as a "Comprehensive Stroke Centre" or a "Primary Stroke Centre", if they contained the specific elements for such designations published in the literature, or as "Other" if they did not satisfy the criteria for either special designation [11 12]. Hospitals with fewer than 20 stroke admissions per year were excluded.

Charts were audited through on-site review by 51 trained chart abstractors. Each chart was reviewed to obtain details of patient demographics, pre-stroke independence, cardiovascular comorbidities, severity of neurological deficits, as well as indicators of acute stroke care. These indicators included whether or not the patient received thrombolysis, arrival by ambulance, as

well as the time from onset of symptoms and presentation to hospital, to receiving a Computed Tomography (CT) scan or thrombolytic treatment. Outcome indicators were in-hospital death at 7 and 30 days, hemorrhagic transformation, and length of stay in hospital. If a patient with acute stroke did not receive thrombolysis, the reasons for non-treatment were recorded whenever available.

Data were recorded on-line, stored in a secure central database, de-identified, and pooled anonymously. In Ontario, results were combined with an internal chart review. Data cleaning was performed with removal of duplicate charts, cases where more than 30% of the audit data were missing, and where a most responsible diagnosis was not documented. Analyses were performed using standard descriptive statistics. A statistical weighted adjustment was applied to the audit results, based on hospital stroke volumes and the number of charts sampled, to avoid potential bias resulting from unequal sampling and to ensure that the results were representative of stroke care across Canadian hospitals. Rates were adjusted for age and sex using the direct method to the 2001 Canadian census [13]. Adjustment for co-morbidities used the Charlson index, stratified into 3 categories (0, 1, 2 or more comorbid diagnoses) [14]. We report the proportion of thrombolysis use, complications, and outcomes stratified by hospital type.

Results

We reviewed 10,130 charts from the ten Canadian provinces. Of all the hospitals identified in each province that admitted stroke patients in 2008-2009 (623 hospitals in total), 295 hospitals were included in the audit (Table 1a). Amongst the 623 identified hospitals there were 43,651 admitted cases of stroke in Canada in 2008-2009. 9,588 patient charts from 295 hospitals were

included in the audit sample, which represented 22% of the total stroke cases, and these remained in the final data-set following data cleaning. After applying the weighting adjustment, the total audit sample represented 38,206 cases, or 88% of the total stroke cases.

A total of 5.4% (95% confidence interval [CI] 5.1-5.6) of all stroke and 6.1% (95% CI 5.8-6.4) of ischemic stroke patients received thrombolysis in Canada (Table 1b). The patient characteristics for this thrombolysed group are recorded in Table 2. Comprehensive stroke centres treated approximately one third of the ischemic stroke patients and provided a thrombolysis rate double that of primary stroke centres. Most patients who were thrombolysed arrived by ambulance. Interval times were slow and are shown in Table 2. Outcomes for thrombolysed patients are shown in Table 3. Overall, 13.6% of thrombolysis recipients were deceased at 30 days. 7.3% developed hemorrhagic transformation and the average length of stay was 16 days. The most common reason for not giving thrombolysis was stroke onset-to-arrival time beyond 4.5 hours – this accounted for 42.3% of non-thrombolysed cases nationally (Table 4).

Interpretation

In this national chart audit, we used a comprehensive estimate of the total stroke volume in Canada and then carefully reviewed charts to estimate the rate of thrombolysis for acute stroke. Stroke thrombolysis rates were low overall, higher at comprehensive stroke centres, and most often limited by a delayed presentation to hospital.

Calculation of thrombolysis rates has been widely varied by jurisdiction and therefore difficult to compare across centres and internationally, most often because the denominator of total stroke cases is variably estimated [2-5]. Approximately a quarter of patients not thrombolysed, were noted to be too mild to offer treatment. This is similar to data from a decade ago [15]. Yet, approximately a third of these patients will end up dead or disabled [15 16], indicating that some of these patients could also have been treated.

Our results demonstrate that the major barrier to thrombolysis remains getting patients to the hospital rapidly. Even at comprehensive stroke centres where most patients arrive by ambulance, and thus present with a presumed stroke diagnosis allowing for activation of "stroke code" or "brain attack" pathways, the mean onset-to-arrival time is slightly more than 3 hours. Improving access at this level is challenging for a number of reasons. First, the disease itself renders patients incapable of seeking help, and stroke typically does not hurt and does not uniformly engender a sense of urgency for treatment [17]. In addition, the public often does not know how to recognize stroke in another person and seek help [18]. Furthermore, the vast geography of Canada limits the speed of access for those in rural areas.

A more easily remedial barrier to timely thrombolysis is the marked delay in in-hospital processes. Mean times from door-to-imaging and imaging-to-treatment are very long. Current guidelines recommend that all patients be treated within 60 minutes of arrival [19]. It is estimated that for every minute the middle cerebral artery remains blocked, 1.9 million neurons and 12km of axons are destroyed [20]. In Helsinki, median door-to-needle times of 20 minutes have been demonstrated [8]. Compared to average Canadian times which are 100 minutes longer,

we can expect that Canadian thrombolysis patients will fare substantially worse than Finnish patients. Fortunately, improving in-hospital processes – door-to-treatment time – is much more feasible since they are in the control of a relatively small number of individuals. Canada has made progress in this regard in the last decade. Following the publication of the CASES study [9], which provided a framework for the development of acute stroke protocols across Canada, and the first Canadian Best Practice Recommendations for Stroke Care [21], which highlighted the need for emergent treatment in cases presenting within 4.5 hours, selected Canadian centres have achieved substantial improvements in their door-to-treatment times [22-24].

An important limitation of our study is that we relied on hospital administrative data to estimate the total number of stroke cases in Canada. However, we believe that such data do not capture all strokes that occur in Canada; patients that do not encounter the hospital system would not be included in this number. Thus, our denominator for estimating the proportion of thrombolysed cases, was likely underestimated. In assessing time to treatment, we did not distinguish intravenous from endovascular thrombolysis; at selected comprehensive stroke centres, endovascular treatment may have been offered at later time windows, increasing mean treatment times.

The chief strength of our study was the comprehensive sampling strategy used to examine a national and population-based estimate of stroke thrombolysis in Canada. Since all thrombolysis patients in Canada are admitted to hospital, we believe that we have captured a comprehensive numerator of all thrombolysed stroke patients in determining the national thrombolysis rate.

It is not known what an expected maximal thrombolysis rate should be, but it is estimated that up to 24% of stroke patients are eligible for thrombolytic treatment if delays between onset and admission to hospital are avoided [25]. Stroke thrombolysis decision-making requires careful judgement of the degree of disability and estimate of treatment risk; this expertise is not readily available at all Canadian hospitals. Whereas comprehensive stroke centres demonstrated higher thrombolysis rates in our study, they only serve approximately one third of the stroke population. Therefore, in addition to training stroke neurologists, an emphasis on the education of primary urgent and/or emergency care physicians regarding acute stroke treatment is critical to optimize both the thrombolysis rate and speed of treatment. The centralization of stroke systems of care, known to be of benefit [26 27], is happening in Canada, with a number of centers achieving Stroke Distinction with Accreditation Canada [28],but this has not yet translated into an improvement in the speed of treatment. Ultimately, current interval times represent a persistent and unacceptable evidence-to-practice gap and clearly indicate that our stroke systems of care require a concerted effort to improve.

Table 1a – Number of hospitals and stroke patients captured in the national chart audit for the 10 Canadian provinces (2008-2009)

	Total Hospitals	*Stroke Admissions 2008-09*	*Eligible Audit Hospitals*	*Stroke Admissions (Eligible Hospitals)*	*Final Audit Sample*
British Columbia	81	5690	46	5446	1198
Alberta	88	3668	22	3194	880
Saskatchewan	61	1787	13	1385	271
Manitoba	57	1633	7	1030	231
Ontario	145	16589	103	15076	2567
Quebec	101	10633	66	8769	1621
New Brunswick	22	1419	12	1293	1007
Nova Scotia	31	1191	12	1108	998
Prince Edward Island	7	231	4	239	212
Newfoundland	30	810	10	666	603
Totals	623	43651	295	38206	9588

Table 1b – Proportion of stroke patients presenting to Canadian hospitals who received thrombolysis, stratified by hospital type (2008-2009)

	*n/N**	*Thrombolysed% (CI_{95})*
All stroke	2049/38206	5.4 (5.1-5.6)
Ischemic stroke type only[§]	2049/33561	6.1 (5.8-6.4)
Comprehensive Stroke Centre	1364/12400	11.0 (10.4-11.6)
Primary Stroke Centre	569/10008	5.7 (5.2-6.2)
Other	116/11153	1.0 (0.8-1.2)

*N = weighted sample
[§]ischemic stroke type = all stroke less hemorrhagic stroke types

Table 2 – Clinical and treatment characteristics of Canadian patients presenting with acute stroke who received thrombolysis (2008-2009)

	Comprehensive Stroke Centre N=297 N, weighted = 1363.8 (66.5%)	***Primary Stroke Centre N=162 N, weighted = 569.4 (27.8%)***	***Other N=21 N, weighted = 116.3 (5.7%)***	***All hospitals N=480 N, weighted = 2049.5***
Age ≥ 70 years (%)	60.2	55.1	73.9	59.5
Female Sex (%)	45.4	45.2	48.7	45.5
Hypertension (%)	67.0	65.2	77.3	67.1
Atrial fibrillation (%)	21.4	16.7	14.1	19.7
Diabetes mellitus (%)	22.0	14.3	15.1	19.4
Past stroke (%)	16.1	23.2	11.5	17.8
CAD (%)	31.5	15.5	67.2	29.1
Current smoker (%)	15.5	10.0	36.4	16.1
Peripheral Vascular Disease (%)	2.4	1.3	18.1	3.0
Pre-stroke Independence (%)	73.8	71.5	55.7	72.1
CNS score ≤ 8 (%)	70.9	70.9	55.7	70.0
Arrived by Ambulance (%)	96.2	83.4	69.7	91.2
Onset to Door Time (hours, mean, SE)	3.3 (1.1)*	5.1 (0.8)	32.2 (5.7)	5.4 (0.8)
Door-to-CT time (hours, mean, SE)	0.7 (0.1)	3.4 (2.7)	4.4 (---)	1.5 (0.7)
CT-to-treatment time (minutes, mean, SE)	79.0 (8.6)	71.9 (4.9)	84.4 (---)	77.2 (6.3)
Door to Treatment time (minutes, mean, SE)	138.1 (17.7)	100.9 (15.3)	112.7 (1.9)	121.1 (11.4)
Onset to Treatment time (hours, mean, SE)	4.6 (1.1)	3.4 (0.3)	2.9 (0.1)	4.2 (0.7)

CAD = coronary artery disease, CNS = Canadian Neurological scale, CT = computed tomography, SE = Standard Error

*Onset-to-door time statistically different among 3 groups ($p<0.001$). Primary centre compared to comprehensive centre ($P=0.05$). Other interval times not statistically different.

Table 3 – Outcomes in Canadian patients presenting with acute stroke who received thrombolysis (2008-2009)

	Comprehensive Stroke Centre N=297 N, weighted = 1363.8 (66.5%)	***Primary Stroke Centre N=162 N, weighted = 569.4 (27.8%)***	***Other N=21 N, weighted = 116.3 (5.7%)***	***All hospitals N=480 N, weighted = 2049.5***	***P****
In hospital death at 7 days (%)	7.2	8.3	5.2	7.4	0.45
In hospital death at 30 days (%)	13.3	15.1	10.8	13.6	0.36
Hemorrhagic transformation (%)	8.0	7.2	---	7.3	0.006
Length of stay in days: mean (SE)	15.7 (1.3)	16.7 (4.7)	15.7 (2.5)	16 (1.6)	0.96

*P values represent a test of proportions among 3 groups; length of stay was assessed by ANOVA. The only difference among groups was seen on hemorrhagic transformation because no hemorrhages were observed in one group with a very small sample size.

Table 4 – Reasons documented for not giving thrombolysis to patients with ischemic stroke presenting to Canadian hospitals, classified by hospital type and expressed as percentages (2008-2009)

	Comprehensive Stroke Centre N=2878 ***N, weighted = 11036.8***	***Primary Stroke Centre N = 2707*** ***N, weighted = 9439.1***	***Other N = 2399*** ***N, weighted = 11036.6***	***All Hospitals N = 7984*** ***N, weighted = 31512.5***
Symptom onset over 4.5 hours	48.8	35.3	41.6	42.3
Neurological deficit judged too mild	26.6	22.0	24.3	24.4
Neurological deficit judged too severe	3.4	2.7	3.5	3.2
Clear medical contraindication	6.6	4.3	3.4	4.8
Delayed decision	0.2	0.3	0.3	0.3
Documented physician decision	6.4	8.0	5.3	6.5
Not documented	20.0	29.7	26.9	25.3

References

1. Demaerschalk BM. Evidence-based clinical practice education in cerebrovascular disease. Stroke 2004;**35**(2):392-6
2. Adeoye O, Hornung R, Khatri P, Kleindorfer D. Recombinant tissue-type plasminogen activator use for ischemic stroke in the United States: a doubling of treatment rates over the course of 5 years. Stroke 2011;**42**(7):1952-5
3. Collins D, O'Neill D, McCormack P. Potential for treatment with thrombolysis in an Irish stroke unit. Irish Medical Journal 1999;**92**(1):236-8
4. Rudd A, Hoffman A, Grant R, Campbell J, Lowe D, Stroke IWPf. Stroke thrombolysis in England, Wales and Northern Ireland: how much do we do and how much do we need? J Neurol Neurosurg Psychiatry 2011;**82**(1):14-19
5. Asplund K, Glader E, Norrving B, Eriksson M, Collaboration R-S. Effects of extending the time window of thrombolysis to 4.5 hours: observations in the Swedish stroke register (riks-stroke). Stroke 2011;**42**(9):2492-7
6. Wardlaw J, Murray V, Berge E, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. Lancet 2012;**379**(9834):2364-72
7. Eissa A, Krass I, Bajorek B. Barriers to the utilization of thrombolysis for acute ischaemic stroke. Journal of Clinical Pharmacy and Therapeutics 2012;**37**(4):399-409
8. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. Neurology 2012 doi: 10.1212/WNL.0b013e31825d6011[published Online First: Epub Date]|.
9. Hill M, Buchan A, Investigators CAfSESC. Thrombolysis for acute ischemic stroke: results of the Canadian Alterplase for Stroek Effectiveness Study. CMAJ 2005;**172**(10):1307-10
10. International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Secondary International Statistical Classification of Diseases and Related Health Problems, 10th Revision 2004. http://apps.who.int/classifications/icd10/browse/2010/en.
11. Alberts M, Latchaw R, Jagoda A, et al. Revised and updated recommendations for the establishment of primary stroke centers: a summary statement from the brain attack coalition. Stroke 2011;**42**(9):2651-65
12. Alberts M, Latchaw R, Selman W, et al. Recommendations for Comprehensive Stroke Centers - A Consensus Statement from the Brain Attack Coalition. Stroke 2005;**36**(7):1597-616
13. Age, Sex, Marital Status and Common-law Status, 2001 Census Technical Report Ottawa, Ontario: Statistics Canada, 2003.
14. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. Journal of Clinical Epidemiology 2004;**57**(12):1288-94
15. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. Neurology 2001;**56**(8):1015-20
16. Smith EE, Abdullah AR, Petkovska I, Rosenthal E, Koroshetz WJ, Schwamm LH. Poor outcomes in patients who do not receive intravenous tissue plasminogen activator because of mild or improving ischemic stroke. Stroke 2005;**36**(11):2497-9 doi: 10.1161/01.STR.0000185798.78817.f3[published Online First: Epub Date]|.
17. Langdorf M, Bearie B, Kazzi A, Blasko B, Kohl A. Patients' vs. physicians' assessments of emergencies: the prudent layperson standard. The California Journal of Emergency Medicine 2003;**4**(4):75-81
18. Greenlund K, Neff L, Zheng Z, et al. Low public recognition of major stroke symptoms. American Journal of Preventive Medicine 2003;**25**(4):315-9
19. Lindsay P, Bayley M, Hellings C, Hill MD, Woodbury E, Phillips S. Canadian Best Practice Reccomendations for Stroke Care (updated 2008). Cmaj 2008;**179**(12):S1-S125
20. Saver JL. Time is brain--quantified. Stroke 2006;**37**(1):263-6 doi: 10.1161/01.STR.0000196957.55928.ab[published Online First: Epub Date]|.
21. Lindsay P, Bayley M, McDonald A, Graham I, Warner G, Phillips S. Toward a more effective approach to stroke: Canadian Best Practice Recommendations for Stroke Care. CMAJ 2008;**178**(11):1418-25
22. Hill M, Barber P, Demchuk A, et al. Building a "brain attack" team to administer thrombolytic therapy for acute ischemic stroke. CMAJ 2000;**162**(11):1589-93
23. Ghrooda E, Alcock S, Jackson A. Improvement in thrombolytic therapy administration in acute stroke with feedback. Can J Neurol Sci 2012;**39**(6):789-92

24. Mehdiratta M, Woolfenden A, Chapman K, et al. Reduction in IV t-PA door to needle times using an Acute Stroke Triage Pathway. Can J Neurol Sci 2006;**33**(2):214-6
25. Boode B, Welzen V, Franke C, van Oostenbrugge R. Estimating the number of stroke patients eligible for thrombolytic treatment if delay could be avoided. Cerebrovasc Dis 2007;**23**(4):294-8
26. Meretoja A, Roine R, Kaste M, et al. Effectiveness of primary and comprehensive stroke centers. PERFECT Stroke: a nationwide observational study from Finland. Stroke 2010;**41**(6):1102-7
27. Foley N, Salter K, Teasell R. Specialized stroke services: a meta-analysis comparing three models of care. Cerebrovasc Dis 2007;**23**(2-3):194-202
28. Stroke Distinction. Secondary Stroke Distinction 31 December 2013 2013. http://www.accreditation.ca/stroke-distinction.