Stroke and Dementia: What Lessons for Us

Regional Geriatric Rounds
March 16, 2012

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CEO & Scientific Director
Canadian Stroke Network

canadianstrokenetwork.ca accidentscerebrovasculaires.ca
What You Will Learn

- Strokes can be evident or covert
- Consequences of stroke including cognitive impairment
- The demographic changes that are driving the increase in vascular risk factors
- Life style changes and other measures that may reduce exposure to stroke and its consequences
The Traditional Definition of STROKE

• A stroke is the most likely explanation when there is sudden loss of neurological (motor, speech) function, sudden onset of dizziness or visual difficulty, or sudden appearance of abnormal sensation

• Stroke occurs when a blood vessel supplying a brain region is occluded

• Stroke damage is immediate and irreversible

…but the definition of Stroke is expanding
Traditional “Current State of Affairs” in STROKE in Canada

- An evident stroke occurs every ten minutes in Canada (6 per day in Ottawa)
- Third leading cause of death
- 15,000 deaths per year
- First cause of neurological disability
- 50,000 strokes per year in Canada
- 300,000 stroke survivors

…but these statistics are changing
EVIDENT STROKE
Consequences of Evident STROKE

1. On the patient’s physical health
2. On the patient’s mental health
3. On the primary family care giver
4. On the community
5. On the health care budget
Large STROKES Make Dementia More Likely

Pooled cumulative incidence of post-stroke dementia excluding pre-stroke dementia in hospital-based cohorts

Thrombus Origin

- Atherothrombotic (30%)
- Cardioembolic (25%)
- Arteriolar or lacunar (20%)
- Idiopathic (20%)
- Other (5%) Prothrombotic, cryptogenic, vasculitis, etc.
Studies with rt-PA

Acute STROKE Care – A Shift in the Treatment Paradigm

- STROKE is treatable
- Short window of opportunity
- Treatment requires stroke expertise and carries a risk
- Stroke care must be organized to improve outcome

Time Is Brain
Canadians Are Not Ready to Respond to the Renewed STROKE Threat

• In 2003, 8 years after results of t-PA trial, 33% of Canadians at risk of stroke knew that paralysis or weakness is a sign of stroke.

The Health Care System in Canada is not Organized to give t-PA

• In 2002, less than 10% of stroke patients arriving in the emergency room within 2.5 hours received t-PA.
Place Canada at the forefront of stroke research through multi-disciplinary research, high-quality training, and partnerships.

Translate the research into health and economic benefits.
Knowledge Translation: What Needs to Happen on the Ground

- Large scale ***public awareness campaign*** of the signs and symptoms of stroke and call to action
- Comprehensive ***surveillance*** system
- Developing ***best practices and standards*** of care in stroke and making them accessible, reinforced by stroke centre accreditation
- Novel stroke ***training programs*** for health professionals, including team-based approaches for stroke care
- ***Enhanced research*** in stroke, including clinical trials
RECOGNIZE and REACT CAMPAIGN
The Grand Challenges: Changing Health Care Systems

- Stroke treated as a medical emergency
- Designated centres
- Redirect/bypass protocols
- Stroke teams
- Stroke inpatient units (acute and rehabilitation)
- Stroke community care and support services
- Organized secondary prevention clinics
Regional Stroke Network

- **Regional Stroke Centre**
  - Neurosurgeon
  - MRI
  - Angiography
  - Leadership for regional plans

- **District Stroke Centre**
  - Neurologist/ Stroke Expert
  - 24/7 CT Scanner
  - Leadership for district plans

- **Community Network**
  - Local Hospital
  - CCAC
  - Primary Care Practitioner
  - LTC/Rehab/CCC
  - PHU
  - Support groups
Optimal STROKE Management With t-PA: t-PA Target Times

- Rapid coordinated emergency response facilitates early diagnosis and treatment

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<td>Admission to Monitored Bed</td>
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Ontario t-PA Rates for Patients Arriving within 2.5 Hours to Regional STROKE Centres
Challenges Remain: Canadians Are Not Ready to Respond to the STROKE Threat (2009) ...

- 57% of Canadians are able to identify at least 2 warning signs; 22% are unable to identify any of the warning signs (39% in 2003)
- 67% of Canadians would call 911 or an ambulance if they thought someone was having a stroke
- 26% of Canadians are able to identify high blood pressure as a risk factor for stroke; 23% of Canadians are unable to identify any of the principle risk factors for stroke
Major Strokes are Now Treatable, but the Profile of Stroke is Changing…..and we must respond

- Strokes can be clinically evident due to vessel occlusion or covert due to small vessel disease
- Strokes lead to mental illness
- Our population is getting older, fatter, and more hypertensive, suggesting stroke incidence will rise
- Small vessel disease may affect multiple organs leading to small strokes and dementia, but also kidney, heart and retina failures
- We are still very challenged with prevention of stroke
Figure 2 – MRI scans of 2 MCI-patients (fluid-attenuation inversion recovery axial sequences). A, PVH=1, WMH=3; B, PVH=2, WMH=8

PVH: Periventricular Hyperintensities; WMH: White Matter Hyperintensities

Stroke. 2007; 38: 2595-2597.


Most STROKES are Not Symptomatic
Most STROKES are Covert

• WMH are the result of arteriolar occlusion
• WMH may produce no symptoms, unrecognized or mild ones, but eventually are associated with cognitive dysfunction, dementia, psychosis, depression.
• The extent of WMH on initial MRI, if untreated, predicts progression of lesions.

Prevalence (%) of covert and symptomatic infarcts visible on MRI per 5-year age category

Stroke. 2002 May; 33(5): 1179-80
Covert STROKES Occur at 5-10 Times the Frequency of Evident STROKES

A Canadian has a stroke every 10 minutes. 50,000 symptomatic strokes per year and 300,000 living with its effects. 20% chance of second stroke within 2 years. For every symptomatic stroke there are 9 ‘silent’ strokes resulting in cognitive impairment. 16,000 Canadians die from Stroke each year. Price Tag: $3.6 Billion annually.
STROKE, Dementia and Other Vascular Diseases
Risk of Dementia with Brain Small Vessel Disease (SVD)

- In population-based studies (not including imaging), cerebrovascular risk factors alone (Age, gender, BP, DM, smoking, heart disease) are associated with worse cognitive function
  
  BMC Neurol 2008; 8:12

- Presence of WMH increases risk of dementia 4-fold
  

- WMH affects executive cognitive (frontal lobe) functions, produce more perseverative errors, and have less effect on attention and working memory
Incident dementia cases according to the DSM-IIIR criteria and after reclassification – based on presence of vascular risk factors

*26% of these developed vascular disease in subsequent three years

Dement Geriatr Cogn Disord 2006; 22:244-249
SVD Isn’t a Problem Just for the Brain. Several Conditions are Associated with Brain SVD

- Frequency of blindness due to “age-related macular degeneration” (ARMD) equals that of evident strokes
- Patients with ARMD are more likely to be demented and more likely to get strokes
- Up to 50% of chronic heart failure patients experience cognitive impairment – Pressler SJ, 2008
- 51% of patients in renal failure have small strokes - Vermeer S, et al. Lancet Neurology. 2007; 6:611-19
# General Risk Factors For VASCULAR DISEASE

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**General Risk Factors For VASCULAR DISEASE**

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- Smoking
- Diabetes
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- Sedentary lifestyle
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# Blood Pressure in Canadian Adults

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Wilkins K., Campbell NRC, et al. Statistics Canada, March 2010
Elevated Blood Pressure in Midlife Results in Poor Cognitive function in Later Life

Each 1 mmHg Increase in BP, Over Time, Increases the Risk of Poor Late-Life Cognitive Function by Approximately 1%.

*population attributable risk (PAR) estimates the proportion of a disease that theoretically can be attributed to a specific risk factor; estimates from the **INTERHEART** & the **INTERSTROKE** study
Prevalence of Hypertension in Canada is Increasing Despite Best Medical Efforts at Treatment
Community Cardiovascular Health Awareness Program (C-CHAP)

Blood Pressure Status (n=15064)

- **28%** Treated & Controlled
- **32%** Normotensive
- **12%** Elevated & unaware
- **3%** Diagnosed, not treated, normal
- **3%** Elevated, diagnosed, not treated
Risk Factor Management: Control of BP in Canada

- Hypertensive: 100%
  - Aware: 58%
    - Treated: 39%
      - Controlled: 16%
    - Not treated: 19%
      - Not controlled: 23%
  - Unaware: 42%

Clin InvesMed 2003;26-78
Changes in Antihypertensive Prescriptions in Ontario, Canada (IMS)

Total antihypertensive prescription

YEAR

RATE / 10,000

Hypertension 2006;47:22-28

The Hypertension Paradox – More Uncontrolled Disease Despite Improved Therapy

### 1994-2005 Canadian Trends in HYPERTENSION Stratified by Age & Sex

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Wilkins K., Campbell NRC, et al. Statistics Canada, March 2010
ABSTRACT

Objective:
To qualitatively and quantitatively assess the association of prehypertension with incident stroke through a meta-analysis of prospective cohort studies.

Methods:
We searched Medline, Embase, the Cochrane Library, and bibliographies of retrieved articles. Prospective cohort studies were included if they reported multivariate-adjusted relative risks (RRs) and corresponding 95% confidence intervals (CI) of stroke with respect to baseline prehypertension.

ABSTRACT

Results:
Twelve studies with 518,520 participants were included. Prehypertension was associated with risk of stroke (RR 1.55, 95% CI 1.35-1.79; p < 0.001). Seven studies further distinguished a low prehypertensive population (systolic blood pressure [SBP] 120-129 mm Hg or diastolic blood pressure [DBP] 80-84 mm Hg) and a high prehypertensive population (SBP 130-139 mm Hg or DBP 85-89 mm Hg). Among persons with lower-range prehypertension, stroke risk was not significantly increased (RR 1.22, 0.95-1.57). However, for persons with higher values within the pre-hypertensive range, stroke risk was substantially increased (RR 1.79, 95% CI 1.49-2.16).

Conclusions:
Prehypertension is associated with a higher risk of incident stroke. This risk is largely driven by higher values within the prehypertensive range and is especially relevant in nonelderly persons. Randomized trials to evaluate the efficacy of blood pressure reduction in persons with this designation are warranted.

Increased prevalence of risk factors

Poor compliance with treatment

HYPERTENSION

DRIVERS

Salt

Poor nutrition

Stress

Obesity

Poverty

Perverse subsidies (corn)

Taxation Laws

Design of cities

Public transportation systems

OUTCOMES

The brain is more sensitive to HBP (INTERHEART vs INTERSTROKE)

Cognition: Major driver of dementia

Interferes with vascular repair

Slows post stroke recovery

Many organs damaged
### 1994-2005 Canadian Trends in OBESITY Stratified by Age & Sex

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<td>26</td>
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</table>
Sustainable Urban Transport and Obesity Rates

Transit  Bike  Walk  Obesity

Switzerland: 10%  18%  62%  11%
Netherlands: 8%  30%  52%  6%
Spain: 9%  12%  45%  11%
Sweden: 10%  20%  42%  8%
Germany: 5%  18%  40%  10%
Finland: 10%  23%  39%  8%
Denmark: 8%  23%  39%  8%
Norway: 10%  12%  35%  8%
UK: 15%  10%  34%  8%
France: 10%  25%  25%  7%
Ireland: 11%  10%  16%  10%
CANADA: 20%  13%  19%  9%
Australia: 18%  14%  14%  8%
USA: 30%  11%  30%  4%

Globe & Mail February 2012
Sodium Abuse

AI = Adequate Intake
UL = Upper Limit

Sodium usual intake distribution
Males 19+
CCHS 2004 Data

Canadian Stroke Network
Réseau canadien contre les accidents cérébrovasculaires
Treatment Study: DASH Sodium

Randomized 412 adults (mixed B.P. status, racial groups, sexes) to:
- Control diet - low in fruit, veg and dairy, fat content typical of US
- DASH diet - high in fruit, veg and low-fat dairy, reduced fat content
- Consume diet for consecutive 30 day periods in random order at each of 3 levels of salt

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Change in mean B.P. vs. control (systolic)</th>
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<td>Control diet</td>
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<tr>
<td>9g/d salt</td>
<td>Control level</td>
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<tr>
<td>6g/d salt</td>
<td>- 2 mmHg</td>
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<tr>
<td>3g/d salt</td>
<td>- 7 mmHg</td>
</tr>
<tr>
<td>DASH diet</td>
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</tr>
<tr>
<td>9g/d salt</td>
<td>- 6 mmHg</td>
</tr>
<tr>
<td>6g/d salt</td>
<td>- 7 mmHg</td>
</tr>
<tr>
<td>3g/d salt</td>
<td>- 9 mmHg</td>
</tr>
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</table>

NEJM 2001; 344:3-10
Recognized Benefits of Blood Pressure Lowering

- 35-40% reduction in stroke
- 20-25% reduction in myocardial infarction
- 50% reduction in heart failure
- Evidence for ACE inhibitors, beta blockers, diuretics, calcium channel blockers… (and now, angiotensin II receptor antagonists)

Improving cardiovascular health at the population level: a 39 community cluster-randomized trial of the Cardiovascular Health Awareness Program (C-CHAP)

Background:
Community-level interventions that target high blood pressure and other modifiable risk factors aim to improve cardiovascular health at the population level. We conducted a community cluster-randomized trial to evaluate the effectiveness of a Cardiovascular Health Awareness Program (CHAP).

Methods:
Thirty-nine mid-sized communities in Ontario, Canada were stratified by location and population size and were randomized to receive CHAP (n = 20, mean population aged 65 years 3,394) or no intervention (n = 19, mean 65 years 3,830). In CHAP communities, residents aged ≥ 65 years were invited to attend cardiovascular risk assessment sessions held at pharmacies and delivered by trained peer-volunteers. Risk profiles were provided to participants, their family physicians and pharmacists. The primary endpoint was a composite of hospital admissions for stroke, acute myocardial infarction and congestive heart failure among residents aged ≥ 65 years according to hospital discharge data. Analysis was by intention to treat.

Findings:
Adjusting for hospital admission rates in the year prior to intervention, CHAP was associated with a 9% relative reduction in our composite endpoint (rate ratio 0.91 [95% CI 0.86–0.97], p = 0.002).

Interpretation:
A collaborative, multipronged community-based health promotion program, targeted at older adults can lead to an important reduction in cardiovascular morbidity.

Healthy Living Is the Best Revenge

Findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam study

• 23,153 German adults aged 35-65 yrs
• Healthy factors: Never smoking, BMI <30 kg/m2, >/=3.5 hrs physical activity per week, healthy diet (high intake fruits, veggies, & whole-grain bread & low meat consumption); 9% had all 4 healthy factors
• Reduction in risk of developing target chronic diseases if all factors*:
  – Chronic disease overall: 78% (95% CI: 72%, 83%)
  – Diabetes: 93% (95% CI: 88%, 95%)
  – Myocardial infarction: 81% (95% CI: 47%, 90+%
  – Stroke: 50% (95% CI: -18%, 79%)
  – Cancer: 36% (95% CI: 5%, 57%)
  – *After adjustment for age, sex, education, and occupational status
EMOTIONS, STROKE AND THE IMMUNE SYSTEM
# Conditions Associated with Small Vessel Disease

## Prevalence of MRI-defined silent brain infarcts (SBIs) among selected population

<table>
<thead>
<tr>
<th>Type of Patient</th>
<th>N</th>
<th>Mean age (range), years</th>
<th>SBI (range), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke patients (including cardioembolic stroke)</td>
<td>171</td>
<td>69 (26-93)</td>
<td>57 (NA)</td>
</tr>
<tr>
<td>Patients with coronary artery disease 35-37</td>
<td>493</td>
<td>60 (34-84)</td>
<td>32 (17-60)</td>
</tr>
<tr>
<td>Patients with cardiovascular risk factors 33-43</td>
<td>788</td>
<td>67 (40-93)</td>
<td>39 (21-51)</td>
</tr>
<tr>
<td>Patients with asymptomatic carotid stenosis 44</td>
<td>189</td>
<td>68 (45-82)</td>
<td>23 (NA)</td>
</tr>
<tr>
<td>Patients with hypertension 45-58</td>
<td>1003</td>
<td>69 (40-88)</td>
<td>43 (20-86)</td>
</tr>
<tr>
<td>Patients with diabetes mellitus 59-63</td>
<td>685</td>
<td>62 (41-88)</td>
<td>38 (13-82)</td>
</tr>
<tr>
<td>Patients with chronic renal failure 55, 61, 64, 65</td>
<td>296</td>
<td>58 (48-74)</td>
<td>51 (25-85)</td>
</tr>
<tr>
<td>Patients with dementia 66</td>
<td>143</td>
<td>73 (?)</td>
<td>33 (NA)</td>
</tr>
<tr>
<td>Patients with depression 67-69</td>
<td>131</td>
<td>63 (50-76)</td>
<td>46 (39-49)</td>
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<tr>
<td>Patients with migraine 70</td>
<td>295</td>
<td>48 (30-60)</td>
<td>8 (NA)</td>
</tr>
<tr>
<td>Patients with sickle cell disease 71-72</td>
<td>94</td>
<td>24 (16-44)</td>
<td>30 (20-36)</td>
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</table>


SBI = Silent Brain Infarcts
The pathway from depression to dementia and the mechanisms that play a role. Small Vessel disease (SVD) and stroke may or may not be the exclusive pathway from depression to dementia, as the upper line suggests.

ABSTRACT:

• The literature emphasizes the risk of depression after a stroke. Less well known is the fact that depression may be as big a risk factor for strokes as hypertension, particularly in the older age group. This article reviews the risk for stroke and cognitive impairment consequent to depression, and describes the cardiovascular and immunological mechanisms that would appear to link depression to its cerebrovascular consequences. As well, the article refers to the brain imaging signatures that may allow prediction of impending brain injury. Finally, some questions that might be explored by future research are suggested, and some practical means to identify and help those at risk for the development of depression-associated vascular disease of the brain are suggested.
SUMMARY: Vascular Disease Prevention and You the Citizen – SOME EASY WINS

1. Management of Hypertension
   - Measure your & family’s BP regularly
   - Salt management
   - Medical therapy for HBP

2. Healthy Lifestyles
   - Legislation, taxation, and pervasive rewards

3. Atrial fibrillation
   - Anticoagulation
   - Longer period for detection
   - Pradax

4. Immediate attention to TIA
“Knowing is not enough; we must apply.
Willing is not enough; we must do.”

Johann Wolfgang von Goethe
3rd Canadian Stroke Congress • 3e Congrès canadien de l’AVC
September 29 - October 2, 2012 • 29 septembre - 2 octobre 2012