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Stroke in young adults: causes, consequences and long-term outcomes.

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Heart & Stroke™ HEART & STROKE FOUNDATION Canadian Partnership for Stroke Recovery Sunnybrook HEALTH SCIENCES CENTRE U of T NEUROLOGY

EVALUATION

For the **Provincial Stroke Rounds Planning Committee**:

- To plan future programs
- For quality assurance and improvement

For **You**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

For **Speakers**: The responses help understand participant learning needs, teaching outcomes and opportunities for improvement.

https://www.surveymonkey.com/r/ZR7L9SX

Please take 2 minutes to fill out the evaluation

Thank you!

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DISCLOSURES

Personal support:

- Heart & Stroke Foundation of Canada: Ontario Clinician-Scientist Phase II
- UofT and Sunnybrook Departments of Medicine

Grants/Research support:

- CIHR, HSFC, Brain Canada, Ontario Brain Institute

Mitigating Potential Bias: I have mitigated bias by having no commercial conflicts of interest and by ensuring there was no industry involvement in creating this talk. I will not be discussing off-label medication or device usage.

MITIGATING POTENTIAL BIAS (PROVINCIAL STROKE ROUNDS COMMITTEE)

The Provincial Stroke Rounds Committee mitigated bias by ensuring there was no Industry involvement in planning or education content.

LEARNING OUTCOMES

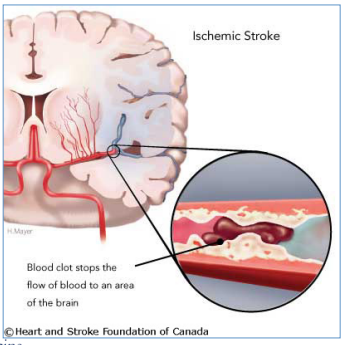
Through this talk, participants will understand:

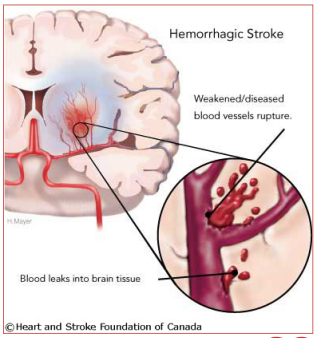
1) that stroke is not just a geriatric disease,
2) the varied causes and the wide range of outcomes for young adults with stroke,
3) the importance of early assessment and treatment, and aggressive long-term risk reduction.

STROKE is a "Brain Attack"

- Stroke = Sudden neuronal damage causing loss of specific brain functions due to:

Ischemic Stroke	Hemorrhagic Stroke
Interruption of blood flow (heart; large & small vessels)	**Bleeding through BBB into the brain** (SAH, ICH)
80-85%	**15-20%**





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Images courtesy of: Heart & Stroke

Stroke by the #'s

IN CANADA
SOMEONE HAS A
STROKE
EVERY 9 MINUTES

- 62,000 annually
- 15% fatal, 60-75% disability.
- #1 leading cause of adult neurological disability
- 4th leading cause of death worldwide
- >450,000 Canadians living with the effects

STROKE IN YOUNG ADULTS

- What is young?

  "It's never too late to have a happy childhood." Tom Robbins
  "Youth is wasted on the young." Oscar Wilde
  "It takes a very long time to become young." Pablo Picasso

- Scientific literature equally variable
- Most common 15-18 to 44-55
- Risk factors and causes vary by which groups are considered "young".

Stroke in young adults

- 3-19% of all strokes
- Lower ranges 18-44; higher if to 54 or 64
- Prevalence (18-64) > MS!
  (Ng et al., *Brain disorders in Ontario: prevalence, incidence and costs from Health Administrative Data*,, July 2015)
- Overall, 10-20 / 100,000 (Kittner et al., *Stroke* 1993; Harmsen et al., *Stroke* 2009; Putaala *Stroke*, 2009))
- ~50% ischemic; 20% ICH; 30% SAH (Jacobs et al., *Stroke* 2002)
- Rates increase with age even in young

Epidemiology in young adults

- Stroke rates in younger adults seem to be increasing, along with increasing risk factors. (George et al., JAMA Neurol; Apr 2017; *Ann Neurol*, 2011;70:713-721)
- Average age at stroke dropping (Kissela et al., *Neurology* 2012;79(17):1781-7)
- Data may be influenced by more people in the age group, better diagnosis, coding incentives etc. (Burke and Skolarus, JAMA Neurol Apr 2017)

Stroke in young adults - Canadian Data

- Younger adults (<45) are less likely to arrive by ambulance (62% versus 66%)
- Ambulance use has *not* increased in younger women between 2003-2016 (though it has for younger men and older adults)
- Younger patients arrive to hospital later after stroke onset (median 8.3 versus 6.8 hours)
- Again, younger females show the largest delay (median 9.2 hours)

Kapoor et al., Can. J Neurol Sci, 2020;47(6) PMID: 32507117

Stroke in young adults - Canadian Data

- Younger adults 3.9% of stroke in Canada
- More bleeds (37% vs. 15%)
- Less likely to use ambulance (62% vs. 66%); young women least likely (61%).
- Ambulance use has *not* increased in younger women 2003-2016 (but has for all other groups)
- Younger patients arrive to hospital later (8.3 vs 6.8 hrs)
  - younger females show the largest delay (9.2 hours)

Kapoor et al., Can. J Neurol Sci, 2020;47(6) PMID: 32507117

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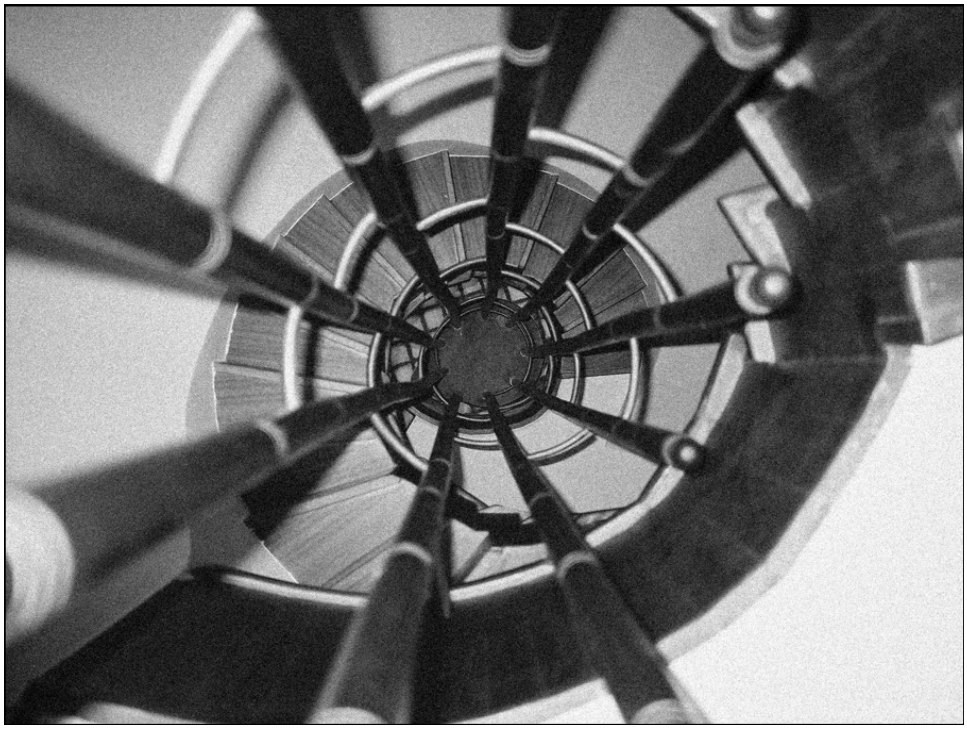
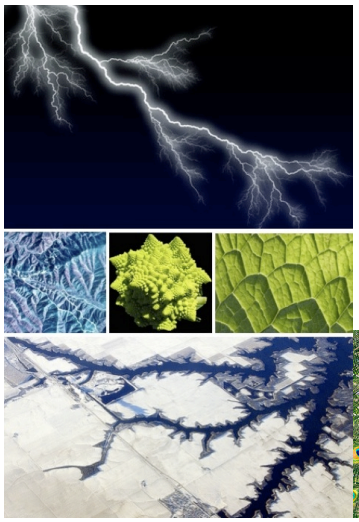
Stroke in young adults – a missed emergency

- Even if they do come to an emergency room, the diagnosis may be delayed or missed for many reasons:
  - there may not be any vascular risk factors;
  - many more common presentations can mimic symptoms (e.g. seizures, migraine, toxicity);
  - there may be rare/less apparent causes
  - even physicians think of stroke as a disease of the elderly.

(Kuruvilla et al., J Stroke Cerebrovasc Dis, 2011:20:523-527)

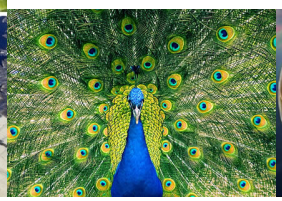


ETIOLOGY OF STROKE IN YOUNG ADULTS



There are more things in heaven and earth, Horatio, than are dreamt of in your philosophy…

Hamlet Act 1, scene V, 159–167



ETIOLOGY OF STROKE IN YOUNG ADULTS

- Largest study: Helsinki young stroke registry. 1008 age 15-49. Modified TOAST criteria:
  - Large artery atherosclerosis (8%)
  - Cardioembolism (20%)
  - Small vessel or lacunar (14%)
  - Unknown causes (idiopathic) (33%)
  - Other
    - Dissection (15%)
    - Miscellaneous (migraine, vasculitis, venous thrombosis, coagulopathies)

Putaala *Stroke*, 2009;40:1195-1203

Study	Putaala (Stroke 2009)	Cerrata (Cerebrovasc Dis 2004)	Kittner (Neurology 1998) * allowed >1 possible cause	Michael (CJNS 2000)
Age range	15-49	16-49	15-44	15-45
#	1008	273	428	356
Cardioembolic	20%	24%	31%	14%
Large vessel	8%	16%	4%	6%
Small vessel	14%	17%	20%	8%
Dissection	15%	13%	11% (** Nonathero vasculopathy)	13%
Other miscellaneous	10%	10%	31%	15%
Unidentified / Cryptogenic	33%	24%	32%	44%

ETIOLOGY OF STROKE IN YOUNG ADULTS

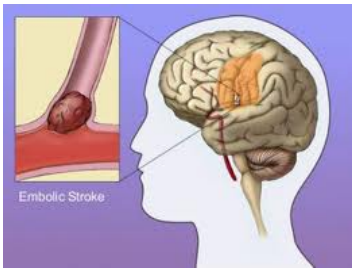
- Etiologies change with age even in this group
- At least 1/3 have undetermined causes
  - Fewer undetermined with increasing age
  - More large artery atherosclerosis and small-vessel disease after age 35, consistent with increasing risk factors with age

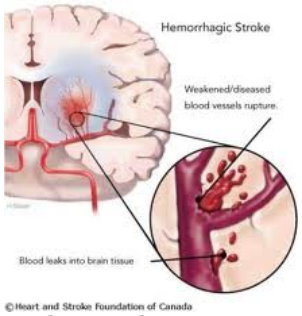
Putaala *Stroke*, 2009;40:1195-1203

ETIOLOGY: OTHER MISCELLANEOUS

- Migraine, vasculitis, venous thrombosis, coagulopathies, hematological disorders, antiphospholipid antibody syndrome, SLE, post-radiation arteriopathy, eclampsia, systemic diseases, cancer, procedures, prescriptions, infections, illicit drug use, reversible cerebral vasoconstriction syndrome, moya-moya vasculopathy, CADASIL, MELAS, Fabry's, Ehler's-Danlos Type IV, sickle cell disease, osteogenesis imperfecta, pseudoxanthoma elasticum, pregnancy-specific causes (eclampsia, HELLP, CVST, peripartum cardiomyopathy)…

STROKE IN PREGNANCY





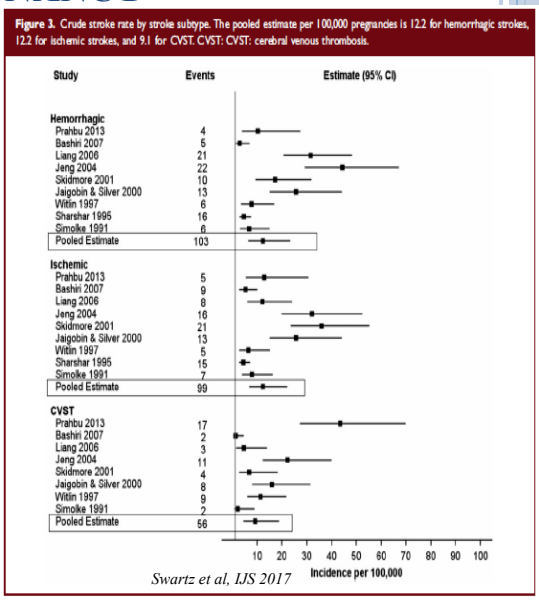
- ~1/3 ischemic, 1/3 venous sinus thrombosis, 1/3 intracranial hemorrhage (note: overlaps)
- Risk is much higher immediately peri-partum and 6 weeks post-partum (days -2 to +1 have 34x RR)

Ros et al., Epidemiology 2001, 12(4):456-460

STROKE IN PREGNANCY

- Low *absolute* risk, high *relative* risk
- Crude rates from meta-analysis: 30/100,000 deliveries.
- 12.2 ischemic, 12.2 Hemorrhagic; 9.1 CVST

Swartz et al., IJS 2017, 12(7): 687-697.



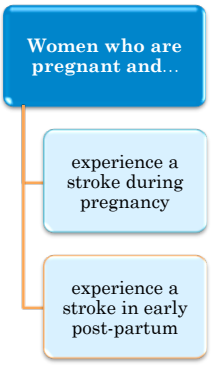
Swartz et al, IJS 2017

STROKE IN PREGNANCY

Guidelines

Canadian Stroke Best Practice Consensus Statement: *Acute Stroke Management during pregnancy*

Ladhani, Swartz et al., Int J **Stroke**. 2018 Oct;13(7)
doi: 10.1177/1747493018786617.
PMID: 30021491



Guidelines

International Journal of Stroke WSO

Canadian stroke best practice consensus statement: Secondary stroke prevention during pregnancy

International Journal of Stroke
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DOI: 10.1177/1747493017743801
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Swartz, Ladhani et al., Int J **Stroke**. 2018 Jun;13(4)
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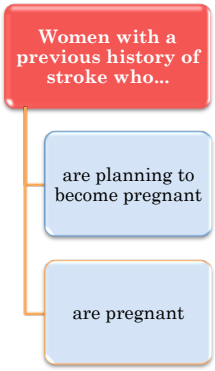
PMID: 29171360



ACUTE STROKE TREATMENT IN THE YOUNG

- Same in younger as in older – rule out bleeding - tPA, EVT for ischemic; BP control, reverse coagulopathies for hemorrhages (see www.strokebestpractices.ca – Hyperacute chapter).
- Young patients have at least as much benefit as older patients from both IV tPA and endovascular interventions and stroke unit care.
- Early decompressive hemicraniectomy can be considered for severe large MCA infarction to improve mortality and long-term functional outcomes. (Vahedi et al., *Lancet Neurol*, 2007)

SECONDARY PREVENTION

- Lifestyle change, aggressive vascular risk reduction, treat underlying conditions if found, smoking cessation, avoid recreational drug use (including marijuana –Wolff et al., *Stroke* 2011; Westover et al., *Arch Gen Psychiatry* 2007)
- May get even more benefit from BP reduction.
- Ubiquitous statins controversial, but young patients were in SPARCL trial.
- Current trials of DOAC's for "ESUS" (Embolic Stroke of Uncertain Source) – RESPECT including young adults.

OUTCOMES

Large Austrian study of 2223 patients <55

- 88% good outcome. Declines with age by 3-4% per decade from 18-55 (Knoflach, *Neurology*, 2012;78:279-285)

Helsinki data suggests mortality of <3% at 1 month, but 4.7% at 1 year and 10.7% at 5 years.

Higher mortality with age, malignancy, heart failure, heavy alcohol use, diabetes, stroke severity and large artery stroke (Putaala Stroke 2009, Spengos Eur J Neurol, 2010)

GOAL (Global Outcome Assessment Life-long after stroke in young adults) multicentre retrospective individual patient data meta-analysis (Ekker et al., BMJ Open, 2019, Nov 14;9(11))

STROKE IN YOUNG ADULTS: OUTCOMES

- Vary by patient factors (age, baseline function, gender), stroke factors (severity, cause, treatment) and risk factors
- Dissection: <5% death rate; recurrence ~2% in first year then 1% per year
- CVST: 75-80% complete recovery but 15% die or dependent
- Acute ischemic stroke: do better with tPA vs older (Toni, Neurology, 2012)

RECURRENCE RISKS

- Those without risk factors have fewer recurrent strokes (4.7% vs. 13.6%), fewer other arterial events (0 vs 6%) and lower mortality (3.4% vs 14.3%). (Putaala, Stroke 2012)
- The presence of silent brain infarcts increases the risk of recurrent stroke ~2.5 times (Putaala, Neurology 2011)
- history of prior TIA also increases recurrence risk (Nedeltchev, JNNP 2005)

the risk after stroke does not stop at 90 days…

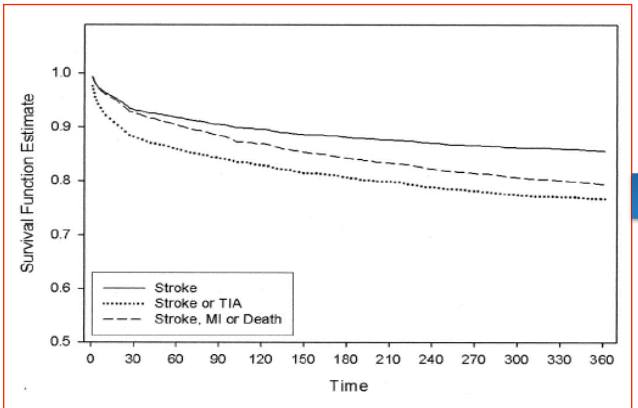


Figure 1. Stroke-free survival. Survival function estimate = estimated proportion of the patients who are outcome free.

?

Hill et al., Neurology 2004

Long-term Outcomes of the "Stable" People?

- 38,241 discharged after stroke/TIA 2003-2013.
- Excluded any hospitalization; stroke/MI/death/ institutionalization (30%)
- Remaining 70% (n=26,366) **stable for 90-days**
  - 53% male
  - Median age 72 (IQR = 60-80)
  - 61% ischemic stroke; 39% TIA
  - 86% mild, 10% moderate, 4% severe
  - Matched to 263,660 (10:1) controls by age, sex, geography and income quintile.

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J. Edwards et al., CMAJ, 2017

LONG-TERM OUTCOMES OF THE PEOPLE WE DISCHARGE?

- Combined outcome: 9.5% in the year AFTER the highest risk period ended and 34% by 5 years

Outcomes	Stroke/TIA Patients N (%)	Matched Controls N (%)	Hazard Ratio (95% CI)
Composite Measure			
1 year	2496 (9.5)	14212 (5.4)	2.4 (2.3-2.5)
3 year	5036 (23.6)	29229 (13.6)	2.2 (2.1-2.3)
5 year	5328 (34.0)	32797 (21.1)	2.1 (2.1-2.2)

J. Edwards et al., CMAJ, 2017

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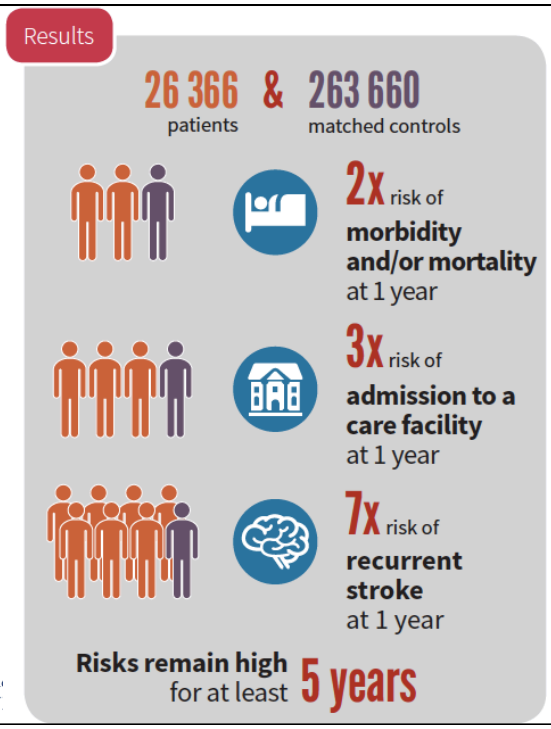

Edwards et al., CMAJ 2017

LONG-TERM OUTCOMES OF YOUNG STROKE

- Combined outcome in 2.2% @ 1 year (AFTER the highest risk period ended) and at 1.2% per year for 5 years (7% total by 5 years).
- Compared to matched controls, the 1-year risk is >7 fold and remains >5 by 5 years.
- Risk remains elevated even after accounting for vascular risk factors.

Outcomes	Stroke/TIA Patients N (%)	Adjusted Hazard Ratio for young vs young controls (95% CI)	Adjusted Hazard Ratio for older vs. older controls (95% CI)
Composite Measure			
1 year	29 (2.2)	**7.3 (4.0-13.6)**	1.3 (1.2-1.3)
3 year	51 (4.7)	**4.3 (2.6-7.3)**	1.4 (1.3-1.4)
5 year	56 (7.1)	**5.2 (2.8-9.4)**	1.3 (1.3-1.4)

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J. Edwards et al., JAHA, 2019(8)
https://doi.org/10.1161/JAHA.118.010370

Is "GOOD" GOOD ENOUGH?

> 2.4 years post-stroke, 68% had "excellent outcome" (mRS 0-1). BUT:

- **54%** cognitive impairment (MoCA <26)
- **52%** some restrictions in reintegration to society (RNLI > 0).
- **30%** were both, cognitively impaired and had restrictions
- **32%** endorsed symptoms of depression (PHQ-2 >0)
- **19%** reported a change in work status

A. Kapoor et al., Stroke, 2017

Is "GOOD" GOOD ENOUGH?

Younger patients (<65 vs. >=65)

- Less often have symptoms of cognitive impairment (MoCA <26: 46% vs. 68%)
- Express more symptoms of depression (24% vs. 15%)
- Less often impaired on ADL's (mRS 2 or higher: 25% vs. 51%)
- Show no difference in restrictions of return to normal living (62% vs. 64%).

A. Kapoor et al., Stroke, 2017

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Return to Work? Systematic review

- Younger patients (<65) return to work gradually: ~40% at 6 months, 66% by 2-4 years
- Predictors: Greater independence in ADL, fewer neurological deficits, better cognitive ability.
- Interventions that improve function (tPA; likely EVT and stroke unit care) increase return.
- Younger men > younger women.
- Office / "white collar" workers > "blue collar"
- Individualized workplace intervention (vocational training) may increase rates of return (60% with intervention vs. 20% control).

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Edwards, Kapoor et al., Int J Stroke, 2017

COMPLICATIONS POST-STROKE

Many common comorbidities (examples):

- **D**epression, Anxiety
- **O**bstructive Sleep Apnea
- **C**ognitive impairment
- Communication limitations
- Gait, mobility and falls
- Continence challenges
- Seizure risk

SPECIAL CONSIDERATIONS

- Occupational issues – return to work; modifications; loss of career trajectory
- Driving (*)
- Financial issues
- Relationship issues; sexuality; birth control
- Conceiving, parenting and child rearing
- Metaphysical struggles (invincibility; "why me?")

  (see Lawrence, Br. J. Nursing 2010)

E-book Free to download.

Search for:

"Stroke in the young guidebook"

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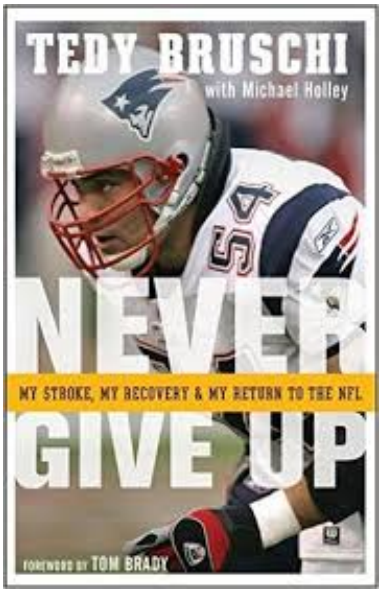
"by making my condition public at this time, I can help other people by encouraging them to seek medical help if they experience some of the symptoms associated with a stroke – regardless of their age or general health"

– Kris Letang, Pittsburgh Penguins, stroke at age 26.



– Tedy Bruschi, New England Patriots Linebacker, stroke at age 31. Returned to pro football.

In 2012, 7 years post-stroke, he successfully ran the Boston Marathon.

Summary – stroke in the young

- Stroke is not a geriatric disease – impacts across the lifespan from infants to elderly. Young adults constitute a sizable minority of stroke patients
- Causes of stroke in young adults are varied, and in 1/3 of cases no cause can be found
- Not just an acute event – long-term risks
- Large societal impact – life, function, productivity, recurrence risks
- Large personal impact – medical, psychological, social

SUMMARY

- An organized approach to etiologies, investigations, treatment and prevention is needed for stroke in young adults and in pregnancy.
- A holistic approach to the person and impact of the event are key to helping patients and families live well after stroke.
- Ongoing, aggressive vascular risk reduction approaches are important to minimize long-term recurrence risks.

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HEART & STROKE FOUNDATION Canadian Partnership for Stroke Recovery

Research, Education, Implementation Networks:

ONDRI
CCNA Canadian Consortium on Neurodegeneration in Aging
CCNV Consortium canadien en neurodégénérescence associée au vieillissement
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ontario stroke network Advancing the Ontario Stroke System
ICES
CSC CNC Canadian Stroke Consortium / Consortium Neurovasculaire Canadien

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For **You**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

For **Speakers**: The responses help understand participant learning needs, teaching outcomes and opportunities for improvement.

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Thank you!

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