

Effect of a 60-Minute Door-to-Needle Tissue Plasminogen Activator on Stroke Disability: A Rapid Review

Health Quality Ontario

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (<http://www.gradeworkinggroup.org/index.htm>), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit <http://www.hqontario.ca> for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: <http://www.hqontario.ca/evidence/publications-and-ohnac-recommendations>.

Table of Contents

List of Abbreviations	5
Background	6
Objective of Analysis	6
Clinical Need and Target Population.....	6
<i>Description of Disease/Condition and Study Rationale</i>	6
Technology/Technique	6
<i>Regulatory Status</i>	6
Rapid Review	7
Research Question	7
Research Methods.....	7
Expert Panel.....	7
Results of Rapid Review	8
Conclusion	9
Acknowledgements	10
Appendices	12
Appendix 1: Literature Search Strategies	12
<i>Search Results</i>	12
References	13

List of Abbreviations

CBPR	Canadian Best Practice Recommendations for Stroke Care
ECASS	European Cooperative Acute Stroke Study
QBP	Quality-based procedures
tPA	Tissue plasminogen activator

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this rapid review is to determine whether the administration of tissue plasminogen activator (tPA) in eligible ischemic stroke patients within 60 minutes of their arrival to a health facility reduces stroke-related disability and prolongs survival.

Clinical Need and Target Population

Description of Disease/Condition and Study Rationale

Following the results of the European Cooperative Acute Stroke Study (ECASS) 3 trial in 2008, (1) the Canadian Best Practice Recommendations for Stroke Care (CBPR) (2) endorsed the use of tPA treatment for eligible ischemic stroke patients within 4.5 hours of the onset of stroke symptoms. CBPR further recommended that for patients meeting the criterion of 4.5 hours, tPA treatment should begin as soon as possible, ideally within 60 minutes of arrival at a health facility. Ontario's current practice is to abide by this recommendation; however, we are unaware of any study that has examined the effectiveness of this practice (≤ 60 minutes vs > 60 minutes) on clinical outcomes.

Technology/Technique

Tissue plasminogen activator is a medication used to break down blood clots in patients who have had an ischemic stroke. It works by catalyzing the conversion of plasminogen to plasmin, the principal enzyme for clot breakdown.

Regulatory Status

Tissue plasminogen activator was approved by Health Canada in 1999 to be used within 3 hours of the onset of stroke symptoms. Following the evidence that it could be effective up to 4.5 hours from the start of the symptoms, in 2009 the Heart and Stroke Foundation issued Canadian Stroke Best Practices Recommendations (2) to extend this treatment time.

Rapid Review

Research Question

Does the 60-minute door-to-needle tPA treatment reduce stroke-related disability and mortality?

Research Methods

Literature Search

Search Strategy

A literature search was performed on July 16, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing and Allied Health Literature (CINAHL), and EBM Reviews, for studies published from January 1, 2012, to July 16, 2014. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

See Appendix 1 for a detailed description of the search strategy, including terms and results.

Inclusion Criteria

- English-language full-text publications
- articles published between January 1, 2012, and July 16, 2014
- health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, observational studies
- studies involving patients who have had an ischemic stroke
- studies involving the administration of tPA within 60 minutes of patient arrival at a health facility

Exclusion Criteria

- studies involving patients who have had a hemorrhagic stroke
- studies involving patients who have had an ischemic stroke who are at risk of hemorrhage

Outcomes of Interest

- score on modified Rankin Scale
- death

Expert Panel

On July 24, 2014, an Expert Advisory Panel on Acute Care for Stroke Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from the community laboratories.

The role of the Expert Advisory Panel was to contextualize the evidence produced by Health Quality Ontario and provide advice on quality-based procedures for stroke in the hospital setting in Ontario. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Results of Rapid Review

The database search yielded 1,908 citations published between January 1, 2012, and July 16, 2014 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

No study met the inclusion criteria.

Conclusion

We identified no study from the period January 1, 2012, through July 16, 2014, that has examined the effectiveness of tPA administered to eligible ischemic patients within 60 minutes of their arrival at a health facility.

Acknowledgements

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Expert Advisory Panel on Post-Acute, Community-Based Care for Stroke Patients

Panel Members	Affiliation(s)	Appointment(s)
Co-Chairs		
Dr Mark Bayley	Toronto Rehabilitation Institute University of Toronto	Medical Director of the Neuro-rehabilitation Program Associate Professor
Karyn Lumsden	Central West Community Care Access Centre (CCAC)	Vice-President of Client Services
Neurology		
Dr Leanne Casaubon	Toronto Western Hospital; University of Toronto	Assistant Professor, Division of Neurology, Stroke Program
Physical Medicine and Rehabilitation		
Dr Robert Teasell	Stroke Rehabilitation Program at Parkwood Hospital Western University	Medical Director Professor
Family Medicine		
Dr Adam Stacy	Ontario Medical Association	Board Member
Nursing		
Connie McCallum	Niagara Health System	Nurse Practitioner, TIA/Stroke Prevention Clinic
Trixie Williams	Central East LHIN	Lead, Vascular Health
Arms Armesto	Sunnybrook Health Sciences Centre	Clinical Nurse Specialist
Karen Sutherland	St. Joseph's Health Care London Parkwood Hospital	Service Lead, Specialized Community Stroke Rehabilitation Team
Occupational Therapy		
David Ure	Parkwood Hospital	Coordinator, Community Stroke Rehabilitation Team
Rebecca Fleck	Hamilton Health Sciences Centre	Regional Stroke Educator and Research Coordinator

Panel Members	Affiliation(s)	Appointment(s)
Physiotherapy		
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Stefan Pagliuso	Hamilton Health Sciences Centre	Regional Stroke Rehabilitation, Community and LTC Coordinator
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Holly Sloan	Trillium Health Centre	
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Joanne Avery	Providence Healthcare, Outpatient Stroke Clinic	Social Worker
Administration		
Christina O'Callaghan	Ontario Stroke Network	Executive Director
Jim Lumsden	The Ottawa Hospital, LHIN—Champlain Regional Stroke Program	Director
Paula Gilmore	London Health Sciences Centre, Southwestern Ontario Stroke Strategy	Community and Long-Term Care Coordinator
Mathew Meyer	Ontario Stroke Network	
Joan Southam	CBI-LHIN	Home Health Senior Manager and Project Specialist
Patient Representation		
Daniel Brouillard	Kingston Heart Clinic	Internist, Stroke Survivor
Nicole Martyn-Capobianco	University of Guelph-Humber	Program Head of Human Services

Abbreviations: LHIN, local health integration network; TIA, transient ischemic attack.

Appendices

Appendix 1: Literature Search Strategies

Search Results

Search date: July 16, 2014

Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, All EBM databases (see below), Embase

Medical librarians: Corinne Holubowich and Caroline Higgins

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 2014>, EBM Reviews - ACP Journal Club <1991 to June 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <June 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <2nd Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <2nd Quarter 2014>, Embase <1980 to 2014 Week 28>, Ovid MEDLINE(R) <1946 to July Week 1 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 15, 2014>

Search Strategy:

#	Searches	Results
1	exp Stroke/ or exp brain ischemia/	301064
2	exp intracranial hemorrhages/ use mesz	55540
3	exp brain hemorrhage/ use emez	85475
4	exp stroke patient/ use emez	11099
5	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*).ti,ab.	453631
6	or/1-5	653023
7	Tissue Plasminogen Activator/	37935
8	((activator* adj (tissue or plasminogen)) or alteplase or activase or tisokinase or ttpa or lysatec or tpa or actilyse).mp.	56887
9	or/7-8	83455
10	6 and 9	17836
11	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congressess.pt.	4160571
12	Case Report/ or Comment/ or Editorial/ or Letter/ or conference abstract.pt.	7362410
13	or/11-12	7382375
14	10 not 13	12958
15	limit 14 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR; records were retained]	11770
16	limit 15 to yr="2012 -Current" [Limit not valid in DARE; records were retained]	2810
17	remove duplicates from 16	1979

References

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- (2) Lindsay MP GG, Bayley M, Phillips S (Editors), on behalf of the Canadian Stroke Best Practices and Standards Working Group. Canadian best practice recommendations for stroke care. Ottawa, Ontario, Canada: 2013.

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