

# Thrombolysis in the air

## *Air-ambulance paramedics flying to remote communities treat patients before hospitalization*

Hassanali Kapasi, CIA   Len Kelly, MD, CCFP   Jonathon Morgan, MD, CCFP, FCFP

### abstract

**PROBLEM ADDRESSED** First Nations\* communities in the North have a high prevalence of coronary artery disease and type 2 diabetes and face an increasing incidence of myocardial infarction (MI). Many conditions delay timely administration of thrombolysis, including long times between when patients first experience symptoms and when they present to community nursing stations, delays in air transfers to treating hospitals, uncertainty about when planes are available, and poor flying conditions.

**OBJECTIVE OF PROGRAM** To develop a program for administration of thrombolysis on the way to hospital by air ambulance paramedics flying to remote communities to provide more rapid thrombolytic therapy to northern patients experiencing acute MIs.

**COMPONENTS OF PROGRAM** Critical care flight paramedics fly to northern communities from Sioux Lookout, Ont; assess patients; communicate with base hospital physicians; review an exclusion criteria checklist; and administer thrombolytics according to the *Sioux Lookout District Health Centre/Base Hospital Policy and Procedure Manual*. Patients are then flown to hospitals in Sioux Lookout; Winnipeg, Man; or Thunder Bay, Ont.

**CONCLUSION** This thrombolysis program is being pilot tested, and further evaluation and development is anticipated.

### résumé

**PROBLÈME EXAMINÉ** La prévalence des coronaropathies et du diabète de type II chez les collectivités des Premières Nations\* dans le Nord se révèle élevée et ces dernières sont aux prises avec une incidence grandissante des infarctus du myocarde. Plusieurs circonstances retardent l'administration opportune d'un traitement thrombolytique, notamment les longs délais entre l'expérience des premiers symptômes et la consultation auprès d'un poste communautaire de soins infirmiers, les retards dans les transferts par avion vers les hôpitaux traitants, l'incertitude entourant la disponibilité des avions et les mauvaises conditions de vol.

**OBJECTIF DU PROGRAMME** Élaborer un programme visant l'administration d'un traitement thrombolytique par le personnel paramédical en route vers l'hôpital, par avion ambulance, à partir de collectivités éloignées, en vue de dispenser plus rapidement une telle thérapie aux patients du Nord souffrant d'un infarctus aigu du myocarde.

**COMPOSANTES DU PROGRAMME** Les paramédicaux de soins intensifs se rendent en avion dans les collectivités nordiques à partir de Sioux Lookout, en Ontario; ils évaluent les patients; ils communiquent avec les médecins de la base hospitalière; ils passent en revue un aide-mémoire de critères d'exclusion et administrent une thérapie thrombolytique selon les directives du manuel de politiques et de procédures du Centre de santé et de la base hospitalière de Sioux Lookout. Les patients sont ensuite transportés vers un hôpital de Sioux Lookout, de Winnipeg (Manitoba) ou de Thunder Bay (Ontario).

**CONCLUSION** Ce programme de traitement thrombolytique fait l'objet d'un projet expérimental et on prévoit l'évaluer plus en profondeur et le développer davantage.

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*Cet article a fait l'objet d'une évaluation externe.*

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\*First Nations is used throughout this article to refer to the original inhabitants of Canada and their descendants.

\*Les Premières Nations désignent dans cet article les personnes qui habitaient le Canada à l'origine ainsi que leurs descendants.

**T**he advent of thrombolytics has revolutionized care of acute myocardial infarction (AMI). We have learned that "time is muscle." Numerous large randomized controlled trials have demonstrated that early administration of thrombolytic therapy significantly reduces morbidity and mortality after AMI.<sup>1-6</sup> Optimizing "door-to-needle time" is becoming increasingly critical for best practice and poses unique challenges in northwestern Ontario where communities are isolated and distributed over vast areas.

Current Canadian clinical practice guidelines recommend administration of thrombolysis within 30<sup>7</sup> to 60<sup>8</sup> minutes after patients' arrival at an emergency department. The guidelines also recommend providing emergency medical services to assess patients' needs and paramedics' ability to provide thrombolysis before patients reach hospital.<sup>7</sup> There is, as yet, no Canadian literature on prehospital administration of thrombolytics for treatment of AMI.

International studies on prehospital thrombolysis have been conducted since the mid-1980s. Most of the literature comes from centres in Europe,<sup>9-14</sup> the United States,<sup>15-17</sup> Scotland,<sup>1,18</sup> Israel,<sup>19</sup> and Russia.<sup>20</sup> Almost all have demonstrated that prehospital thrombolysis is feasible, safe, and results in faster treatment for AMI. In most of the studies, thrombolytic agents were administered by emergency paramedics in the field.

The obvious benefits of early intervention particularly challenge rural caregivers in isolated regions of Canada. The air ambulance based in Sioux Lookout, Ont, services a geographic area the size of France and is called upon to treat and evacuate patients with AMIs once or twice a month from any of the 26 northern First Nations communities without road access. Transportation time is measured in hours. Distances can exceed 700 km one way. The availability of planes and varying weather conditions cause further delays and give a whole new meaning to door-to-needle time.

This article examines the issue of prehospital administration of thrombolytics in a remote setting and describes development of a program in northwestern Ontario to meet clinical needs.

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**Dr Kapasi** is a medical student at the University of Ottawa. **Dr Kelly** practises family medicine in Sioux Lookout, Ont, and is a Sioux Lookout base hospital physician. **Dr Morgan** practises family medicine in Sioux Lookout and is Medical Director of the Sioux Lookout Base Hospital Program.

### Objective of program

The Sioux Lookout prehospital thrombolysis program was developed to provide more rapid therapy to northern patients experiencing AMIs. Thrombolytics are administered by air-ambulance paramedics flying to remote communities.

### Program

Because of the high prevalence of coronary artery disease (CAD) and diabetes and the increasing incidence of AMIs in First Nations communities,<sup>21,22</sup> the Sioux Lookout base hospital developed a program for prehospital administration of streptokinase by air ambulance paramedics. In spring 1995, the base hospital Medical Director received approval from the Emergency Health Services Branch of the Ontario Ministry of Health and the Provincial Base Hospital Air Advisory Committee for adding streptokinase to the "B list" of drugs: drugs paramedics could administer to patients under physicians' orders. Reteplase has since been added.

Diagnosis of AMI is made by the on-call physician at the Sioux Lookout Zone Hospital after speaking with nursing station staff and reviewing patients' histories, results of physical examinations, and faxed 12-lead electrocardiograms (ECG). Standard ECG criteria<sup>6</sup> are used for diagnosis of AMI: ST elevation >1.5 mm and ST segment elevation in at least two contiguous limb leads, or ST elevation >2 mm in two contiguous precordial leads, or evidence of new-onset left bundle branch block.

Air ambulances are dispatched with full resuscitation equipment and two critical care flight paramedics, whose training includes advanced emergency courses (Advanced Cardiac Life Support [ACLS], Advanced Trauma Life Support, Perinatal Advanced Life Support, Neonatal Advanced Life Support, and Advanced Life Support in Obstetrics) and ongoing mandatory continuing medical education (CME) programs.

Upon arrival, paramedics review an exclusion criteria checklist (**Table 1**) with a community nurse and a Sioux Lookout base hospital physician by telephone and then administer thrombolytics according to the *Sioux Lookout District Health Centre/Base Hospital Policy and Procedure Manual*. This involves placing patients under a continuous cardiac monitor; establishing two saline intravenous lines; drawing blood for complete blood count, electrolyte, blood urea nitrogen, glucose, and enzymes levels, and prothrombin time (PT)/partial thromboplastin time (PTT); and then administering thrombolytics.

Table 1. **Inclusion and exclusion criteria checklist****INCLUSION CRITERIA**

- Chest pain of at least 30 minutes' duration that is consistent with cardiac ischemia and unresponsive to nitroglycerin therapy
- Onset of pain, preferably within 6 hours before treatment (thrombolysis may be given up to 12 hours if chest pain persists)
- ST elevation >1.5 mm in two contiguous leads; new-onset left bundle branch block

**EXCLUSION CRITERIA**

- Intracranial or intraspinal surgery within 2 months
- Documented intracranial bleeding within 2 months
- Cardiovascular accident within 2 months
- Age more than 75 years
- Previous use of streptokinase or reteplase within 6 months
- Bleeding diathesis
- Prosthetic valve
- Documented pre-existing atrial fibrillation
- Active internal bleeding (within 10 days)
- Brain metastasis
- Pregnancy
- Documented hemorrhagic retinopathy
- Severe uncontrolled hypertension (diastolic  $\geq$  110, systolic  $\geq$  180 mm Hg)
- Known major surgery within 10 days
- Gastrointestinal bleeding within 2 months

Initially, 1.5 million U of streptokinase were used, but two 10-mL boluses of reteplase are now given, followed by heparin. Reteplase is given in two boluses half an hour apart: the first in the nursing station, the second while on board. Acetylsalicylic acid (325 mg orally) is also given if a station nurse has not already given it. These procedures are performed on the ground due to chancy flying conditions and unreliable airborne communications. Patients are then flown to receiving hospitals in Sioux Lookout; Winnipeg, Man; or Thunder Bay, Ont.

In the program's first year, 10 patients received prehospital thrombolysis and two other AMI patients met exclusion criteria. All the treated patients were transferred without complication from their northern communities to hospital.

Time from receiving calls from nursing stations to start of paramedic-administered thrombolysis varied from 2 h and 25 min to 5 h and 20 min. Average was 4 h and 5 min.

**Evaluation**

The program was developed in response to clinical need in our region. The pilot phase included only 10 patients. All were First Nations men between 30 and 50 years old. All were transported safely to hospital. Two other patients met exclusion criteria and were not offered thrombolysis. The pilot phase was continued until we were able to work out the many difficulties encountered.

As rural physicians know, introducing thrombolysis to rural areas is a challenge. This program attempted to address the long times many patients waited for definitive diagnosis and treatment of AMI. A second phase of the program is being developed with improved documentation of patients' progress from nursing stations to base hospital and receiving hospitals.

Initially, funding for thrombolytic medication was a problem, but that has been addressed during the last 2 years. In the beginning, medication had to be "borrowed" from either the Sioux Lookout Zone Hospital or the Sioux Lookout District Health Centre formularies. Paramedics required locally developed CME and ACLS certification for safe treatment protocols. Federal nurses in our region's nursing stations provide acute care diagnosis and treatment with telephone advice from doctors on call at the Sioux Lookout Zone Hospital, yet are, in fact, historically mandated to provide preventive health care. They are not currently equipped to administer thrombolytic medications, nor is it currently within their scope of practice.

During this initial period, and for the foreseeable future, the program will rely on paramedics to administer thrombolytic medication. If only one ACLS-certified paramedic is available for the trip, a physician must make the trip north, a drain on scant physician resources. The pilot phase is now completed, and a patient-outcome study is currently being designed. We believe that we have shortened the door-to-needle time by at least the time of a one-way trip to a remote community (a matter of hours) and

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have established that appropriately trained paramedics, with physician and nursing support, can safely deliver thrombolytic therapy in the field.

#### Discussion

Ample data in the international literature have established the safety and feasibility of prehospital thrombolysis, but evidence of better outcomes is somewhat equivocal. Some authors reported smaller infarcts, lower morbidity and mortality rates, shorter durations of pain and ischemia, and higher ejection fractions,<sup>13,14,18</sup> while others found no significant differences between patients treated before they got to hospital and those treated in hospital.<sup>12,16</sup> These data come from programs conducted almost universally in cities where tertiary care centres were close by. In the literature we reviewed, the smallest reported gain in treatment time was 33 minutes<sup>16</sup>; most studies reported gains of 40 to 55 minutes. Although all authors concluded that earlier treatment resulted in better outcomes overall, it is clear that outcomes might not differ significantly in settings relatively close to tertiary care centres.

The most relevant data to our context in northwestern Ontario comes from northeast Scotland, from the Grampian Region Early Anistreplase Trial (GREAT),<sup>1,18</sup> which reported the greatest time gain for prehospital thrombolysis in the studies we reviewed. The trial involved tissue-type plasminogen activator (t-PA) administered at home by a physician. It decreased average time to treatment after symptom onset from 4.0 to 1.8 hours, shortening door-to-needle time by 2.2 hours. These researchers also demonstrated the greatest improvement in outcomes, reducing the 1-year mortality rate to 10.4% from 21.6%<sup>1</sup> and the 5-year mortality rate to 25% from 36%.<sup>18</sup>

**Hours count, not minutes.** The relatively minor time gains reported in many studies limit their applicability and relevance to our context in northwestern Ontario. For northern patients, hours count, not minutes. In this respect, the Sioux Lookout program is distinct from others reviewed in the literature. It addresses a variety of unique issues not faced by most prehospital programs around the world that operate within, or in close proximity to, urban centres. The necessity of making long-distance diagnoses, absence of physicians in small northern First Nations communities, use of air versus ground ambulance, vast distances, limited hospital resources, and extremely long delays between onset of symptoms and treatment in hospital result in a very different context for prehospital thrombolysis.

We estimate that the Sioux Lookout prehospital thrombolysis program has cut several hours (the time of an average one-way trip) off the wait for thrombolysis. According to preliminary data accumulated from the program's pilot phase, average time to treatment was 4.1 hours from receipt of nurses' calls. If time from symptom onset to presentation and evaluation at a nursing station are factored in, it becomes clear that many patients will not receive thrombolysis within 6 hours, even with prehospital administration. Clearly, we have taken just the first step.

Benefit from thrombolysis has been demonstrated for patients treated within 6 to 12 hours<sup>2,5,20,23,24</sup>; residual benefit has been reported for those treated up to 24 hours.<sup>25</sup> Although the exact mechanism of benefit after 6 hours is uncertain, reduced cardiac expansion, reduced electrical instability, and improved healing of the infarcted site have been postulated.<sup>25,26</sup>



**Chancy flying conditions and unreliable airborne communications:** *Patient is boarded for transfer to hospital once thrombolysis is begun on the ground.*

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We are confident that prehospital administration of thrombolysis by air ambulance staff is a necessary addition to the paramedics' role in treatment of AMI in our region and an important addition to overall health care in rural Canada. The program brings northern populations one step closer to timely thrombolysis, but still hours from recommended in-hospital treatment.<sup>7</sup> The program begins to address Canadian recommendations<sup>7</sup> that emergency medical services assess the need for and ability to provide prehospital



**Following procedure:** Paramedics administer pre-hospital thrombolysis.

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thrombolysis in light of current evidence on safety, feasibility, and improved outcomes.

So far, the program has resulted in administration of thrombolysis to 10 patients. Enrolment has been low in this pilot phase due to the delay in adequate funding for thrombolytic medications, a problem that has since been resolved. All 10 patients were flown without complication from their northern communities to hospital centres after administration of streptokinase at nursing stations. Future program evaluation and follow-up studies should assess longer-term clinical outcomes and establish reliable recording methods for tracking patients through other facilities.

**Choice of thrombolytic agent.** The choice of thrombolytic agent for the air ambulance program was based on clinical efficacy and cost. Some authors have shown a faster rate of coronary artery patency and reperfusion<sup>5,6,27-29</sup> and slightly lower mortality<sup>5,6,29</sup> among patients treated with t-PA compared with those treated with streptokinase. Other trials, however, have found no significant difference between the two medications in terms of mortality and major outcomes.<sup>30,31</sup> Most investigators concur that early therapy is the

key to better prognosis and much more important than the specific treatment used, especially for patients presenting several hours after symptom onset. Given these considerations, the air ambulance program initially used streptokinase as the drug of choice. Tissue-type plasminogen activator, however, has just recently become part of the air ambulance formulary, and newer agents are under review. In January 2000, reteplase became the agent of choice.

The program also considered ease of administration, given the sometimes extreme conditions and less than ideal circumstances facing paramedics and northern nursing stations. Reteplase, a newer recombinant t-PA, has recently been shown by some investigators to be as effective as streptokinase and alteplase and easier to administer in two bolus injections.<sup>31-33</sup> Such advances warrant close inspection by prehospital programs.

**Research and reevaluation.** Ultimately, we hope to conduct a larger study examining short- and long-term outcomes of patients treated in the field, and gain more data on time savings and complications. Patient education to reduce time from symptom onset to nursing assessment is another important area for development.

The program is also constantly being reevaluated in terms of staff capabilities and duties. While most nursing stations have experienced outpost nurses providing acute medical care, their role is currently defined as providing public health care. Not all nursing stations



**Reducing response time:** Paramedic readies air ambulance for the next trip.

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are equipped with defibrillation equipment and a full complement of cardiac medications. Newly developing point-of-care serology testing technology and expanded nursing roles, training, equipment, and physician support might one day further simplify treatment of AMI in such isolated settings.

### Conclusion

The Sioux Lookout prehospital thrombolysis program's pilot phase has shown promise, and further development and evaluation are planned. The field of AMI thrombolytic therapy is rapidly changing, and we anticipate many developments in the future. A direct relationship between time to thrombolysis and improved outcomes exists for in-hospital patients. Our task in managing prehospital care is to apply best possible practice in a context that poignantly reflects the realities and challenges of delivering health care in rural and remote regions of Canada. This prehospital care program is unique in the world due to the great distances involved. It is the first program of its kind described in Canada. ❀

**Correspondence to:** Dr Len Kelly, The Clinic, PO Box 489, Sioux Lookout, ON P8T 1A8

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### Key points

- This is the first prehospital thrombolysis program reported in Canada.
- The program was established to cope with the unique circumstances of the Sioux Lookout area: high prevalence of diabetes and coronary artery disease and long delays in reaching hospital.
- Critical care flight paramedics are trained to fly to patients' communities, check exclusion criteria, and give thrombolytics according to an established protocol. Then patients are flown to hospital.
- In this pilot phase, 10 patients were successfully treated, and "door-to-needle time" was reduced by at least the duration of a one-way flight to a remote community.

### Points de repère

- Il s'agit du premier programme de traitement thrombolytique avant l'admission à l'hôpital à être rapporté au Canada.
- Le programme a été mis sur pied pour surmonter les circonstances particulières à la région de Sioux Lookout: une forte prévalence de diabète et de coronaropathies, et les longs délais avant d'atteindre l'hôpital.
- Le personnel paramédical des soins intensifs en avion est formé pour se rendre dans les collectivités des patients, vérifier les critères d'exclusion et administrer le traitement thrombolytique conformément à un protocole établi. Les patients sont ensuite transportés en avion vers l'hôpital.
- Durant cette étape expérimentale, 10 patients ont reçu un traitement avec succès et le délai d'administration a été réduit d'au moins la durée d'un voyage aller simple vers une collectivité éloignée.

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