Improving Mortality: The Future of Stroke Treatment

Stroke is one of the most prevalent causes of mortality in the world today. In this review, Dr. Hussain and Dr. Shuaib explore the new directions stroke treatment can take in order to better manage and reduce the devastating effects of this condition.

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Sally's Stroke

Sally, 49, presents to the Hinton Hospital in Hinton, Alberta with a sudden onset of left-sided weakness and numbness that began 2.5 hours earlier.

The ER physician recognizes this as a stroke and obtains an immediate CT scan of Sally's head (Figure 1). The scan is interpreted by the radiologist on call as being normal and the stroke neurologist on-call is then informed of the situation.

Rather than transferring Sally to Edmonton, which would involve a costly delay of several hours, the ER physician and the stroke neurologist on-call decide to initiate thrombolytic therapy in Hinton. Tissue plasminogen activator (tPA) is given. Sally begins to improve and returns to normal within hours. She is discharged five days later, with no deficits.

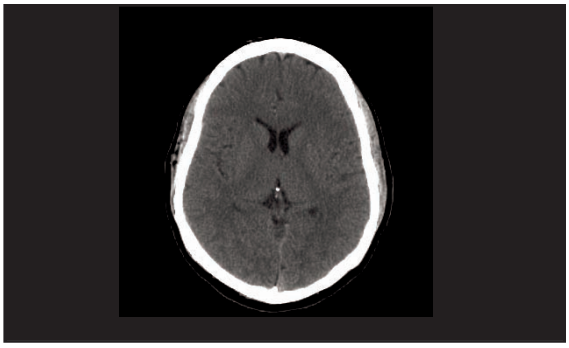

Figure 1. Sally's CT scan upon presentation.

Stroke is the third leading cause of mortality and the greatest cause of disability in the developed world.[1] Acute stroke care has improved greatly in the last decade, particularly after the discovery that tissue plasminogen activator (tPA), given within the first three hours after the onset of ischemic stroke symptoms, improved patient outcomes.[2] However, despite the availability of this acute stroke treatment, only 2% to 3% of stroke patients are given tPA in the US.[3] Many factors contribute to this low rate of administration, but with organized stroke teams and stroke care, this rate can be greatly improved (Table 1).[4,5]

Pre-hospital and in-hospital care

The majority of patients who present to the hospital with ischemic stroke are not eligible for tPA therapy as they are outside the accepted three-hour window.[6] Efficient emergency medical services (EMS), trained in dealing with acute stroke, are critical in order to improve tPA administration rates and patient outcomes. EMS staff should be trained to identify the symptoms and signs of stroke and once identified, these patients should be immediately brought to a dedicated acute stroke center. This may mean that EMS will bypass local hospitals in favor of ones offering thrombolytic therapy. Education of the general population is also crucial, as it will enable patients, families, or others present at the

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Table 1
Methods to improve administration rates of tPA

Pre-hospital factors	In-hospital factors
• Education to improve recognition of stroke symptoms • Improve emergency medical services (EMS) identification of stroke symptoms/signs • EMS bypass local hospital centers offering acute stroke therapy • Quick methods of transportation (*i.e.,* helicopter) for patients in remote areas	• Rapid identification by emergency staff of stroke symptoms/signs • Immediate involvement of dedicated acute stroke team • Immediate CT imaging

time of a stroke to quickly identify stroke symptoms and alert the EMS.

Once patients arrive to the ED, an acute stroke protocol should be instituted, including immediate bloodwork and a CT scan of the brain. Simultaneously, the acute stroke team should be alerted to:

- assess the patient,
- interpret the CT imaging and
- administer tPA therapy if appropriate.

It has been shown that this organized approach results in improved rates of administration of tPA therapy in stroke patients and also decreases the rates of complications, particularly intracerebral hemorrhage.[7]

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Future directions

With increasing education and acceptance of tPA therapy, many more centers will develop the capabilities to care for acute stroke patients.

As illustrated in Sally's case, primary care hospitals with rapid access to CT imaging may be an ideal place to deliver tPA treatment. A new initiative has been started in Northern Alberta which will utilize and advance this practice. In centers such as Hinton, the local ER physician caring for an acute stroke patient will be able to contact the on-call stroke neurologist in Edmonton. Once an acute stroke patient has a CT scan, the images can be sent via internet to the on-call neurologist, who will interpret the images and offer an opinion regarding thrombolysis. Armed with this information, local ER physicians will then be able to administer tPA themselves and thus avoid the delay in therapy that occurs with a transfer to a tertiary care hospital. Strong evidence exists that the sooner an acute stroke can be treated with tPA, the better the patient's outcome.[8]

Continued research and advancement is needed in order to develop novel therapies with larger time windows to increase the number of patients eligible for therapy and ultimately improve patient outcomes.

Tertiary care centers will offer more intensive therapy, such as:

- intraarterial therapy in selected patients,
- close observation of patients with large cerebral infarctions and
- treatment of patients who have hemorrhagic stroke.

In addition, many new, experimental therapies are being studied which can be offered at these centers. For example, neuroprotective agents, such as NXY-059, are showing promise in the treatment of acute stroke.[9] In the Stroke Acute Ischemic NXY-059 Treatment (SAINT) I trial, this agent was given within six hours of onset of stroke symptoms. The trial showed a statistically significant improvement in the disability at 90 days. This small, but significant result is quite important, as it is the first study of a neuroprotective agent that has shown to be of benefit in humans. Confirmation of the results is keenly being sought in the SAINT II trial.

New therapies are emerging for hemorrhagic stroke as well. Currently, Factor VIIa is being studied in hemorrhagic stroke patients presenting within three hours after the onset of their symptoms. In a recently published Phase II study, patients who received factor VIIa had less hematoma expansion and better outcomes than those receiving placebo.[10] However, there was an increase in myocardial and cerebral ischemic events in the treatment group. A Phase III study is still ongoing, with results expected shortly. If confirmed, this information would add a much-needed therapeutic option to the treatment of hemorrhagic stroke, but again, a limited time window exists. The expedited and efficient referral of patients with acute stroke symptoms is critical for healthcare centers to be able to offer this therapy.

Conclusion

Stroke is a devastating event, but with well thought-out and implemented strategies, healthcare centers can make a large difference in reducing the morbidity and mortality associated with this condition. Continued research and advancement is needed in order to develop novel therapies with larger time windows to increase the number of patients eligible for therapy and ultimately, improve patient outcomes.

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