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Clinical Study

International benchmarking for acute thrombolytic therapy implementation in Australia and Japan

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ABSTRACT

Although a wide range of strategies have been established to improve intravenous tissue plasminogen activator (IV-tPA) treatment rates, international benchmarking has not been regularly used as a systems improvement tool. We compared acute stroke codes (ASC) between two hospitals in Australia and Japan to study the activation process and potentially improve the implementation of thrombolysis. Consecutive patients who were admitted to each hospital via ASC were prospectively collected. We compared IV-tPA rates, factors contributing to exclusion from IV-tPA, and pre- and in-hospital process of care. IV-tPA treatment rates were significantly higher in the Australian hospital than in the Japanese (41% *versus* 25% of acute ischaemic stroke patients, p = 0.0016). In both hospitals, reasons for exclusion from IV-tPA treatment were intracerebral haemorrhage, mild symptoms, and stroke mimic. Patients with baseline National Institutes of Health Stroke Scale score ⩽5 were more likely to be excluded from IV-tPA in the Japanese hospital. Of patients treated with IV-tPA, the door-to-needle time (median, 63 *versus* 54 minutes, p = 0.0355) and imaging-to-needle time (34 *versus* 27 minutes, p = 0.0220) were longer in the Australian hospital. Through international benchmarking using cohorts captured under ASC, significant differences were noted in rates of IV-tPA treatment and workflow speed. This variation highlights opportunity to improve and areas to focus targeted practice improvement strategies.

1. Introduction

Intravenous tissue plasminogen activator (IV-tPA) for acute ischaemic stroke (AIS) patients improves the likelihood of good clinical outcome [1]. However, IV-tPA is only administered to a small proportion of all AIS patients internationally, for example only 7% in Australia [2] and 5% in Japan [3]. Single centre audits have demonstrated treatment rates of up to 20% can be achieved with streamlining of systems and there has been increasing interest recently in benchmarking and adopting strategies that have been demonstrated to be effective across international boundaries [4].

The most common barrier to IV-tPA administration is the narrow therapeutic time window of 4.5 hours. International guidelines recommend door-to-imaging time ⩽25 minutes and door-to-needle (DTN) time ⩽60 minutes [5]. Door-to-imaging time and imaging-to-needle times are reported to be contributing factors of delays in DTN time [6].

For several years, our institutes (John Hunter Hospital, Australia [JHH] and Saiseikai Kumamoto Hospital, Japan [SKH]) have implemented acute stroke codes (ASC) to reduce potential delays in patient assessment and to improve the efficacy of IV-tPA treatment. Previously, we and other researchers have shown that ASC increased rates of IV-tPA [7–10] and decreased DTN time [8,9]. However, there are relatively few detailed comparative analyses of the process of care at different hospitals internationally, and limited information on differential rates of IV-tPA internationally [10]. We could not find any other studies attempting a direct comparative analysis of acute stroke cohorts identified by ASC at the time of writing.

We aim to compare the process of care via ASC activation between tertiary hospitals in Australia and Japan with the aim of this international benchmarking being to improve the current process of care.

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2. Methods

This study used prospective stroke registries of ASC at JHH and SKH. This study was approved by the Institutional Review Board of each hospital.

2.1. Regional and "ASC" characteristics

JHH is the tertiary referral hospital for Hunter region of New South Wales, Australia. JHH is a university hospital, having seven full-time equivalent stroke neurologists, and covering a metropolitan catchment (approximately 500,000 people, 2920 km^2) and a large rural area (140,000 people, 20,330 km^2) [11]. It is the only comprehensive stroke centre in the area with the capacity to deliver recanalisation therapy for AIS. ASC was devised in 2006 and has undergone occasional refinement. Currently, patients suspected of hyperacute stroke and who have a known time of onset or time last seen normal and projected time of arrival at hospital within 3.5 hours are assessed by paramedics in the field and the ambulance operation centre is notified. A pre-hospital acute stroke triage tool, including glucose level, arm drift of grip strength, speech disturbance, and onset time [7], is used by paramedics in the field. A mobile phone text message is used to notify on-call stroke neurologists of a potential thrombolysis case in transit to JHH, and to seek approval to bypass local non-thrombolysis capable hospitals.

SKH is the teaching hospital of Kumamoto University in Kumamoto, Japan, one of five stroke centres of the area, having seven full-time equivalent stroke neurologists, and serves a population of approximately one million in an area of 1812 km^2. ASC was devised in 2005 and has undergone refinement. Currently, people suspected of hyperacute stroke who have a known onset time or time last seen normal and projected time of arrival at hospital within 4 hours are identified by ambulance or emergency department (ED) staff. The hospital is notified of any suspected acute stroke patients assessed in the field before arrival. Emergency physicians in direct contact with paramedics then contact stroke neurologists to determine whether the ASC protocol should be activated.

In both hospitals, ASC activation causes the stroke team, which comprises at least one stroke neurologist, at least one ED medical staff member, at least one ED nursing staff member and one stroke expert radiographer, both within and out-of-hours, to rapidly deploy and prepare for potential reperfusion therapy to rapidly deploy and prepare for patient arrival. As the patient arrives in the ED, the stroke neurologist performs the clinical assessment, the patient is sent for immediate brain imaging, and blood samples are sent for first-priority laboratory examination. In JHH, patients are generally directly transferred from the ambulance bay to CT scan, keeping the patient on the ambulance trolley while the stroke neurologist assesses the patient. Standard protocol is perfusion CT scan. Patients are transferred back to and thrombolysed in the ED. In SKH, the stroke neurologist generally assesses the patients in the ED bed, and patients are transferred to CT scan, MRI, then to the intensive care unit and thrombolysed there. MRI is the standard protocol if no intracranial haemorrhage (ICH) is seen on non-contrast CT scan. In both hospitals, imaging is interpreted by the stroke neurologists without waiting for formal imaging reports (Fig. 1).

2.2. Patients and data collection

All patients suspected of AIS who arrived at each hospital for whom ASC were activated between October 2012 and May 2014 were included. We assessed onset-to-door (OTD) time, door-to-CT scan time (DCTT), and door-to-MRI-time (DMRIT). Of the patients treated with IV-tPA, stroke severity was assessed by National Institutes of Health Stroke Scale (NIHSS) score, and bolus IV-tPA (needle) time, onset-to-needle time, CT scan-to-needle-time (CTNT) and MRI-to-needle-time (MRINT) were recorded. Diagnoses were classified as AIS, transient ischaemic attack, ICH, subarachnoid haemorrhage, or stroke mimics.

IV-tPA was defined as standard intravenous alteplase treatment based on existing guidelines in each country [12,13]. Reasons for exclusion from IV-tPA treatment in patients with AIS were categorized as follows: "too mild" (including rapid improving), "too severe", "medically unsuitable" (contraindication/comorbidity), "unsuitable onset time", "recent stroke", "large ischaemic changes" (on CT scan and/or MRI), "no penumbra" (on CT perfusion), "recanalization" (of the relevant artery before treatment on images), "treated with experimental protocol", and patient or their family "refused therapy". In cases where a patient had more than one factor excluding them from treatment, Australian and Japanese neurologists re-assessed their cases and retrospectively ascertained the most pressing reason. In the absence of standardised criteria, clinical judgment on behalf of the attending stroke neurologist was used to define patients who presented with too mild or too severe symptoms, and who had large ischaemic changes or no penumbra. Patients who had stroke symptoms while in hospital were excluded.

2.3. Statistical analysis

ASC were compared according to their institution. Patients treated with IV-tPA were compared according to their clinical characteristics and time intervals. We used the Wilcoxon rank-sum test for continuous variables and chi-square test for categorical variables. $p < 0.05$ was considered significant. Statistical analysis was performed using the JMP10 package (SAS Institute, Cary, NC, USA).

3. Results

3.1. All patients via ASC

The ASC was activated 232 times in JHH and 413 in SKH (Table 1). The rate of AIS was significantly higher in JHH than SKH, and the rate of ICH was significantly lower in JHH than SKH. OTD and DCTT were significantly shorter in SKH than JHH. The three most frequent reasons for exclusion from IV-tPA at both hospitals were ICH, mild symptoms, and stroke mimics (Table 1, 2).

3.2. Patients treated with IV-tPA

Sixty-two patients were treated with IV-tPA at JHH, as were 60 individuals at SKH (Table 1). IV-tPA treatment rate was significantly higher at JHH than SKH (41% *versus* 25% of AIS received tPA, $p = 0.0016$; 27% *versus* 15% of ASC received tPA, $p = 0.0001$). Ninety-five percent of patients arrived within 3.5 hours at each hospital, but OTD time tended to be shorter in SKH than JHH (Table 3). Onset-to-needle time, DTN time and DCTT were significantly shorter at SKH than JHH. MRINT in SKH was significantly shorter than CTNT in JHH (median, 27 *versus* 34 minutes, $p = 0.0022$). Of patients treated with IV-tPA, baseline NIHSS score was higher in SKH than JHH, and the rate of baseline NIHSS score $\leqslant 5$ was significantly lower in SKH than JHH (Table 3). However, of patients with AIS who were not treated with IV-tPA, baseline NIHSS score (median, 6 in JHH *versus* 7 in SKH, $p = 0.2662$) and the rate of baseline NIHSS score $\leqslant 5$ (46% in JHH *versus* 41% in SKH, $p = 0.5135$) had no significant difference. Of patients deemed as having too mild symptoms, baseline NIHSS score was significantly higher in SKH than JHH (median 3, range 0–10, *versus* 2, 0–6, $p = 0.0253$).