Thrombolysis With Intravenous Tissue Plasminogen Activator Predicts a Favorable Discharge Disposition in Patients With Acute Ischemic Stroke

Nneka L. Ifejika-Jones, MD, MPH; Nusrat Harun, MSPH; Nareesa A. Mohammed-Rajput, MD, MPH; Elizabeth A. Noser, MD; James C. Grotta, MD

Background and Purpose—Acute ischemic stroke patients who receive recombinant tissue plasminogen activator (rt-PA) within 3 hours of symptom onset are 30% more likely to have minimal to no disability at 3 months. During hospitalization, short-term disability is subjectively measured by discharge disposition, whether to home, inpatient rehabilitation, a skilled nursing facility, or subacute care. There are no studies assessing the role of recombinant tissue plasminogen activator use as a predictor of poststroke discharge disposition.

Methods—We conducted a retrospective analysis of all patients with ischemic stroke who presented within the original three hour window for intravenous thrombolysis, and who were admitted to the University of Texas Houston Medical School Stroke Service at Memorial Hermann Hospital - Texas Medical Center between January 2004 and October 2009. Baseline demographics and National Institute of Health Stroke Scale score were collected. Cerebrovascular disease risk factors were used for risk stratification in the multivariate regression.

Results—Out of 2225 patients with acute ischemic stroke, 1019 were discharged to home, 719 to inpatient rehabilitation, 371 to a skilled nursing facility and 116 to subacute care. Patients who received recombinant tissue plasminogen activator therapy were more likely to be discharged home compared to the other levels of care (P<0.0001; OR, 1.945; 95% CI, 1.538 to 2.459). Considering post-acute inpatient rehabilitation versus skilled nursing facility/subacute care and disposition at a skilled nursing facility versus subacute care, there were no differences in disposition between patients who received recombinant tissue plasminogen activator therapy. Inpatient Rehabilitation versus Skilled Nursing Facility or Subacute Care (P = 0.123); Skilled Nursing Facility versus Subacute Care (P = 0.605).

Conclusions—Patients who receive intravenous recombinant tissue plasminogen activator as treatment for acute ischemic stroke are more likely to be discharged directly home after hospitalization. This study is limited by its retrospective nature and the undetermined role of psychosocial factors related to discharge. (Stroke. 2011;42:700-704.)

Key Words: outcomes ■ rehabilitation ■ stroke recovery ■ thrombolysis

Cerebrovascular disease is the leading cause of long-term disability in the United States, increasing costs of postacute care and caregiver burden.1,2 Outcomes research is critically important in this population, particularly related to poststroke discharge disposition. The discharge level of care after an acute stroke is directly related to clinical outcomes, including functional status, activity tolerance, and medical acuity.

Rehabilitation medicine is a relatively young and diverse field that extends from the first days of inpatient care to years of chronic treatment in a range of settings.3 The goal of stroke rehabilitation is to improve recovery in the weeks after a stroke and to decrease disability during the years that follow. For an inpatient rehabilitation facility (IRF) to be compensated by Medicare, a minimum of 60% of the facility’s total inpatient population must meet 1 of 13 medical conditions. The 13 medical conditions that qualify for the 60% rule are stroke, spinal cord injury, congenital deformity, amputation, major multiple trauma, brain injury, fracture of femur (hip), burns and neurological disorders, including multiple sclerosis, motor neuron diseases, polyneuropathy, muscular dystrophy, and Parkinson disease.4

An incarnation of the compliance rule has been part of the IRF payment criteria since the implementation of the Inpatient Prospective Payment System in 1983. Its purpose is to ensure that IRFs are primarily providing rehabilitation services to patients who cannot be served in other, less intensive rehabilitation settings such as a skilled nursing facility (SNF). Over the past 10 years, this rule has undergone significant alterations. In
2002, the Center for Medicare and Medicaid Services instructed the Fiscal Intermediaries to delay enforcement of the 75% rule because of concerns that the criteria were not enforced uniformly across the country. In 2004, the Center for Medicare and Medicaid Services reinstated the rule and expanded the compliance list to the 13 qualifying conditions. In addition, a 3-year transition period was instituted to gradually increase the compliance rate from 50% in 2004% to 75% by 2007. However, in 2007, Congress passed the Medicare, Medicaid, and SCHIP Extension Act, which set the IRF compliance rule at no more than 60% retroactive to cost-reporting periods beginning on or after July 1st. The influence of the compliance rule has been a longstanding source of concern for rehabilitation units, as Medicare accounts for approximately 70% of IRF cases with an estimated 5.6 billion dollars paid to IRFs annually.

To qualify for admission to an IRF, patients must require close medical supervision by a rehabilitation physician, 24-hour nursing care, and a coordinated multidisciplinary rehabilitation program consisting of a combination of physical therapy, occupational therapy, speech and language pathology, nursing, case management, and social work. In addition, patients must be able to participate in an intense rehabilitation regimen for a duration of a minimum of 3 hours daily and be expected to achieve significant practical improvement over a short period of time.

Patients receiving care in a SNF traditionally exhibit decreased activity tolerance; therefore, they would not be able to participate in 3 hours of therapy daily required for inpatient rehabilitation. A patient whose SNF stay is based solely on the need for rehabilitation services would meet the “daily basis” requirement, they would receive a combination of physical, occupational, and speech therapy at least 5 days a week.

Subacute care is a transitional level of treatment for medically stable patients who no longer require daily diagnostic/invasive care. Also known as long-term acute care, the patients at this level require 24-hour access to services available in an acute care hospital. In addition, the patient may require tracheotomy care and/or mechanical ventilation plus any 1 of 6 treatment procedures, including tube feeding, wound care, continuous intravenous therapy (hydration or antibiotic), frequent nebulizer treatments, total parental nutrition, and inpatient physical, occupational, or speech therapy.

Patients with stroke admitted to subacute care predominantly have severe disability due to large infarcts.

Intermediate care facilities provide treatment for individuals who are disabled, mentally handicapped, or chronically ill. To qualify for intermediate care services, a patient must have a medical condition that requires observation on an intermittent basis to prevent deterioration. Compared with the previously mentioned levels of care, neither skilled nursing nor therapy services are required in intermediate care facilities. Patients in intermediate care facilities also exhibit more independence with basic activities of daily living than those served by inpatient rehabilitation, SNFs, or subacute care.

The National Institute of Neurological Disorders and Stroke rtPA Stroke Study investigators have demonstrated that patients with acute ischemic stroke receiving intravenous tissue plasminogen activator within 3 hours of symptom onset are 30% more likely to have minimal or no disability at 3 months.10 During hospitalization, short-term disability and functional status are subjectively measured by discharge disposition, whether to home, inpatient rehabilitation (IR), a SNF, or subacute care (Sub). There are no studies assessing the role of recombinant intravenous tissue plasminogen activator (rtPA) treatment for acute ischemic stroke as a predictor of functional status evidenced by poststroke discharge disposition.

### Subjects and Methods

We conducted a retrospective analysis a prospectively collected quality assured database of all patients with ischemic stroke admitted to the University of Texas Houston Medical School Stroke Service at Memorial Hermann Hospital Texas Medical Center between January 2004 and October 2009 with discharge disposition of home, IR, a SNF, or Sub. Memorial Hermann Hospital Texas Medical Center is a tertiary care center with an in-hospital inpatient rehabilitation unit; all patients who meet admission criteria are accepted, regardless of insurance type or ability to pay. Patients were included if they presented within the original 3-hour window for intravenous thrombolysis.

Baseline demographics, including age, gender, ethnicity, and National Institutes of Health Stroke Scale (NIHSS) score on arrival, were collected (Table 1). All patients had frequent vital sign monitoring including an electrocardiogram and 24 hours of telemetry. Cardiac and cerebrovascular imaging, lipid and glucose levels were obtained as part of routine practice; all of which were used in the multivariate model for risk stratification (Table 2). Medical records were reviewed to determine presence of comorbidities that can affect outcome. Modified Rankin Scale score was obtained at discharge for all patients.

Exclusion criteria were diagnosis of intracranial hemorrhage, transient ischemic attack, and alternate disposition (discharge to other service or left against medical advice). Discharge to home for custodial/hospice care and death were included in the analysis to determine whether there was increased morbidity or mortality in the rtPA versus the non-rtPA group. Cerebrovascular disease risk factors were used for risk assessment and stratification; the presence of multiple medical comorbidities increase the likelihood of poststroke
Table 2. Independent Variables Collected for Risk Stratification

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>Presence of atrial fibrillation, congestive heart failure, coronary artery disease, history of myocardial infarction, peripheral vascular disease</td>
</tr>
<tr>
<td>DM</td>
<td>History of diabetes mellitus or serum glucose &gt;200 on arrival</td>
</tr>
<tr>
<td>HTN</td>
<td>History of hypertension or elevated blood pressure on arrival</td>
</tr>
<tr>
<td>HLD</td>
<td>History of hyperlipidemia or total cholesterol &gt;200 on arrival</td>
</tr>
<tr>
<td>Hx stroke</td>
<td>History of cerebrovascular event (transient ischemic attack, acute infarct, intracerebral hemorrhage, epidural hematoma, subdural hematoma, subarachnoid hemorrhage)</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; Hx, history of.

Table 3. Independent Risk Stratification Variables ± Intravenous rtPA Therapy

<table>
<thead>
<tr>
<th>rt-PA (866)</th>
<th>No rt-PA (1890)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV, %</td>
<td>43</td>
<td>34</td>
</tr>
<tr>
<td>DM, %</td>
<td>27</td>
<td>34</td>
</tr>
<tr>
<td>HTN, %</td>
<td>70</td>
<td>76</td>
</tr>
<tr>
<td>HLD, %</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>Hx stroke, %</td>
<td>77</td>
<td>77</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; Hx, history of.

Table 4. Effects of Independent Variables plus Intravenous rt-PA Therapy – Discharge Disposition to Home vs. Other Level of Care (Inpatient Rehabilitation, Skilled Nursing Facility or Subacute Care)

<table>
<thead>
<tr>
<th></th>
<th>P</th>
<th>OR</th>
<th>95% CI, Lower</th>
<th>95% CI, Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>rtPA</td>
<td>&lt;0.0001</td>
<td>1.945</td>
<td>1.538</td>
<td>2.459</td>
</tr>
<tr>
<td>NIHSS on arrival</td>
<td>&lt;0.0001</td>
<td>0.822</td>
<td>0.805</td>
<td>0.840</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;0.0001</td>
<td>0.967</td>
<td>0.960</td>
<td>0.974</td>
</tr>
<tr>
<td>CV</td>
<td>0.187</td>
<td>1.156</td>
<td>0.932</td>
<td>1.434</td>
</tr>
<tr>
<td>DM</td>
<td>0.041</td>
<td>0.803</td>
<td>0.650</td>
<td>0.991</td>
</tr>
<tr>
<td>HTN</td>
<td>0.177</td>
<td>0.850</td>
<td>0.671</td>
<td>1.076</td>
</tr>
<tr>
<td>HLD</td>
<td>0.016</td>
<td>0.774</td>
<td>0.628</td>
<td>0.954</td>
</tr>
<tr>
<td>Hx stroke</td>
<td>0.023</td>
<td>1.311</td>
<td>1.037</td>
<td>1.658</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; Hx, history of.

Results

Out of our study sample size of 2459 patients with discharge disposition to home, inpatient rehabilitation, skilled nursing facility or subacute care, nine percent of the patients were excluded secondary to missing data for the explanatory variable (Table 1). This has been attributed to the merging of data fields from earlier forms of the University of Texas Houston Medical School Stroke Registry, a common quandary with outcomes studies. During secondary analysis, we discovered the missing fields were evenly distributed uniformly between primary independent and dependent variables. The administration of IV rt-PA for acute ischemic stroke is correlated with increased mortality (12% vs. 5.4% in the no rt-PA group; P = <0.0001; Table 1); there were no statistically significant differences in the likelihood of discharge to home for hospice care (2.5% vs. 4% in the no rt-PA group; P = 0.1638; Table 1). A total of 2756 patients were included in the independent risk stratification analyses (Tables 2 and 3); this was narrowed by 0.65% during assessment of demographic information due to missing variables for ethnicity.

Discharge Disposition to Home Versus Other Level of Care (IR, SNF, or Sub)

Of the remaining 2225 patients, 1019 were discharged home, 1206 to IR, a SNF, or Sub. After accounting for all effects in the multivariate regression, patients who received rtPA for acute ischemic stroke were more likely to be discharged home (P<0.0001; OR, 1.945; 95% CI, 1.538 to 2.459; Table 4). Both increased age (P<0.0001; OR, 0.967; 95% CI, 0.960 to 0.974) and NIHSS on arrival (P<0.0001; OR, 0.822; 95% CI, 0.805 to 0.840) were associated with discharge disposition to another level of care.

The odds ratio was higher for acute ischemic stroke patients treated with IV rt-PA in relation to discharge disposition than several cerebrovascular disease risk factors, including cardiovascular disease (P=0.187; OR, 1.156; 95% CI, 0.932 to 1.434), diabetes mellitus (P=0.041; OR, 0.803; 95% CI, 0.650 to 0.991), hypertension (P=0.177; OR, 0.850; 95% CI, 0.671 to 1.076), hyperlipidemia (P=0.016; OR, 0.774; 95% CI, 0.628 to 0.954), and history of stroke (P=0.023; OR, 1.311; 95% CI, 1.037 to 1.658).

Discharge Disposition to IR Versus Other Level of Care (SNF or Sub)

Of the remaining 1206 patients with acute ischemic stroke, 719 patients were discharged to acute IR and 487 to either a SNF or Sub. After accounting for all effects in the multivariate regression, there were no statistically significant differences in disposition between patients who received and did not receive rtPA (P=0.123; OR, 1.255; 95% CI, 0.940 to 1.675; Table 5).
Table 5. Effects of Independent Variables plus Intravenous rt-PA Therapy – Discharge Disposition to Inpatient Rehabilitation vs. Skilled Nursing Facility or Subacute Care

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI, Lower</th>
<th>95% CI, Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>rtPA</td>
<td>0.123</td>
<td>1.255</td>
<td>0.940</td>
</tr>
<tr>
<td>NIHSS on arrival</td>
<td>0.913</td>
<td>0.896</td>
<td>0.930</td>
</tr>
<tr>
<td>Age</td>
<td>1.026</td>
<td>1.045</td>
<td>1.007</td>
</tr>
<tr>
<td>CV</td>
<td>0.741</td>
<td>0.564</td>
<td>0.973</td>
</tr>
<tr>
<td>DM</td>
<td>0.806</td>
<td>0.608</td>
<td>1.067</td>
</tr>
<tr>
<td>HTN</td>
<td>0.905</td>
<td>1.744</td>
<td></td>
</tr>
<tr>
<td>HLD</td>
<td>0.888</td>
<td>1.579</td>
<td></td>
</tr>
<tr>
<td>Hx stroke</td>
<td>2.424</td>
<td>1.784</td>
<td>3.293</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; Hx, history of.

The presence of advanced age predicted discharge to a SNF or subacute level of care ($P<0.0001$; OR, 0.948; 95% CI, 0.938 to 0.958). Unlike the first analysis, cardiovascular disease predicted discharge to a SNF or Sub, which corroborates the importance of activity tolerance when determining poststroke discharge disposition ($P=0.031$; OR, 0.741; 95% CI, 0.564 to 0.973).

Increased NIHSS on arrival predicts discharge disposition to a SNF or Sub independent of rtPA use ($P<0.0001$; OR, 0.913; 95% CI, 0.896 to 0.930). History of stroke is also predictive of discharge disposition to either a SNF or Sub; these patients are more likely to have a physical impairment at baseline ($P<0.0001$; OR, 2.424; 95% CI, 1.784 to 3.293). There were no significant differences in disposition to IR versus a SNF or Sub for patients with diabetes mellitus, hypertension, or hyperlipidemia (Table 5).

Discharge Disposition to a SNF Versus Sub

Of the remaining 487 patients with acute ischemic stroke, 371 were discharged to a SNF and 116 to Sub. After accounting for all effects in the multivariate regression, there were no significant differences in disposition between patients who received rtPA for acute ischemic stroke ($P=0.605$; OR, 0.884; 95% CI, 0.554 to 1.410; Table 6). Advanced age is predictive but not as strongly associated with discharge disposition to subacute care ($P=0.006$; OR, 1.026; 95% CI, 1.007 to 1.045). It is known that patients with larger infarcts are more likely to be discharged to Sub than a SNF due to the severity of their deficits; in addition, there is significantly higher mortality of older patients in this group compared with the previous analyses.

Increased NIHSS on arrival ($P<0.0001$; OR, 0.945; 95% CI, 0.919 to 0.971) and history of stroke ($P<0.0001$; OR, 2.77; 95% CI, 0.153 to 5.01) both predict discharge disposition to Sub independent of rtPA use. There were no significant differences in disposition for patients with cardiovascular disease, diabetes mellitus, hypertension, or hyperlipidemia (Table 6).

Discussion

To our knowledge, this study is the first to provide a direct link between the administration of intravenous rtPA for treatment of patients with acute ischemic stroke and improved short-term outcomes evidenced by discharge disposition to home versus another level of care. The association between this short-term outcome and long-term disability has not been studied; this will be the focus of future research. Patients who received rt-PA tended to have higher NIHSS on arrival than the non-treatment group, lower age, normal cholesterol values and no prior history of stroke.

The variability of the 60% rule during the study time period has a potential confounding effect on patients admitted to IRFs. Although Congress passed the Medicare, Medicaid, and SCHIP Extension Act in 2007, it only applied to reimbursement of payments to IRFs; it has no bearing on our analyses and the appropriateness of the discharge level of care during that time period. Future studies will further be impacted by the new Center for Medicare and Medicaid Services 2010 IRF coverage requirements. The Center for Medicare and Medicaid Services 2010 guidelines are an effort to determine whether individual IRF claims are reasonable and necessary. The new coverage requirements document whether the patient is medically stable to benefit from IR admission, specify the need for coordinated multidisciplinary rehabilitation care, and outline benefit from the intensity of treatment provided in an IRF. The impact of these new guidelines on IR admissions is yet to be seen, and it will be the subject of future studies.

Consistent with previous studies, we found that low NIHSS on arrival has the strongest correlation with discharge to home; however, the conclusion that rtPA use has a stronger correlation to favorable discharge disposition than several cerebrovascular disease risk factors has a significant impact on the role of rtPA as a prognostic indicator in this population. Our analysis is based on data collected within the traditional 3-hour window of intravenous thrombolysis; future studies will extrapolate the data to 4.5 hours.

There are considerable barriers to care in the IR, SNF, and Sub groups. Although organized stroke care with timely multidisciplinary IR is associated with improved outcomes, many patients are unable to access postacute rehabilitation services secondary to lack of insurance or underinsurance. Use and accessibility of postacute services vary with age, race/ethnicity, and geographic region.

Advanced age can be used as both an outcome predictor and a screening tool for Medicare eligibility in populations that may otherwise be uninsured. Postacute care facilities predominantly serve patients who have the financial means to pay for care, whether through insurance or independently. This study was conducted at a tertiary care center with an

Table 6. Effects of Independent Variables plus Intravenous rt-PA Therapy – Discharge Disposition to Skilled Nursing Facility vs. Subacute Care

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI, Lower</th>
<th>95% CI, Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>rtPA</td>
<td>0.604</td>
<td>0.884</td>
<td>0.554</td>
</tr>
<tr>
<td>NIHSS on arrival</td>
<td>&gt;0.0001</td>
<td>0.945</td>
<td>0.919</td>
</tr>
<tr>
<td>Age</td>
<td>1.026</td>
<td>1.007</td>
<td>1.045</td>
</tr>
<tr>
<td>CV</td>
<td>0.924</td>
<td>0.641</td>
<td>1.633</td>
</tr>
<tr>
<td>DM</td>
<td>0.911</td>
<td>0.565</td>
<td>1.470</td>
</tr>
<tr>
<td>HTN</td>
<td>1.037</td>
<td>0.593</td>
<td>1.814</td>
</tr>
<tr>
<td>HLD</td>
<td>0.676</td>
<td>1.910</td>
<td></td>
</tr>
<tr>
<td>Hx stroke</td>
<td>&gt;0.0001</td>
<td>0.153</td>
<td>0.501</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; Hx, history of.
in-hospital IRF; therefore, all patients who meet criteria for admission are accepted. The results of this study may not be extrapolated to centers in which patients have to undergo financial screening as a part of eligibility.

Disposition after postacute hospitalization is a factor in admission to each prospective level of care. If a candidate is IR-appropriate but needs supervision for safety, cognitive impairment, or physical limitations, it is recommended that a caregiver be identified before transfer of care is completed. These patients may be transferred to a SNF, which traditionally has a longer length of stay, until a caregiver becomes available. It is estimated that 25% to 74% of stroke survivors require assistance with activities of daily living from informal caregivers, often family members.\(^\text{15}\) Although the physical, psychological, emotional, and social consequences of caregiving and its economic benefit to society are well recognized, caregivers’ needs are often given low priority in stroke management and many caregivers feel inadequately trained, poorly informed, and dissatisfied with the level of support provided after discharge.\(^\text{16}\) A key determinant of whether a patient can be discharged home is the competency and physical ability of the caregiver, which is unrelated to the status of the patient. These patients may be appropriate for discharge home, but are instead admitted to an IRF or a SNF if their caregiver is unable to meet their functional needs.

We cannot comment on patients with ischemic stroke who transition to another level of care after IR. There is a percentage of patients who were determined to be appropriate for IR that are unable to tolerate 3 hours of therapy daily; therefore, they are transferred to a SNF. In the future, we will track the disposition of patients with acute stroke after IR to capture these outliers.

This analysis is retrospective; we endeavored to stratify the data for age, stroke severity, and known risk factors that suggest worse outcomes. In addition, the use of retrospective data makes it difficult to collect missing variables, which accounted for 9% loss of data in this study. There is potential confounding related to whether intravenous rtPA truly predicts better outcomes or are there other unknown causes. This possibility is best addressed with a prospective observational study of this patient group.

In summary, patients with acute ischemic stroke who received intravenous rtPA within the traditional 3-hour window were more likely to be discharged home and not require postacute hospitalization. Improvements in treatment of acute stroke frequently bring net health expenditure savings by reducing rehabilitation, postacute care, and lost productivity costs.\(^\text{3}\) Traditional rehabilitation is one of the therapeutic tools to augment the poststroke recovery process. There remains considerable scope for improvement in access to postacute stroke care and continued evolution in response to patient and caregiver needs and the changing environment of healthcare provision.

Although traditional rehabilitation medicine helps patients, a better understanding of its scientific basis could further increase its impact.\(^\text{17}\) The characteristics of the rtPA group that increase the likelihood of favorable disposition will be the subject of future studies, including demographics, medical acuity, comorbid conditions, and poststroke complications. In addition, optimal timing of rtPA therapy within the window needs to be defined to quantify the potency of treatment effect on discharge disposition.

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Disclosures

None.

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背景与目的：在症状发生 3 小时内接受重组型组织纤溶酶原激活物 (rt-PA) 溶栓的急性缺血性卒中患者有 30% 的机会在 3 个月时无或有轻的功能障碍。在住院期间，短期功能障碍是由出院时的状况主观进行判断的，决定是直接回家、住院康复、转至专业护理机构或接受亚急性期治疗。目前尚无研究评估 rt-PA 溶栓在预测卒中后出院安置中的作用。

方法：我们对 2004 年 1 月至 2009 年 10 月间在德克萨斯大学休斯顿医学院的赫尔曼纪念医院 - 德州医学中心的卒中中心收治的发病 3 小时溶栓治疗时间窗内的所有缺血性卒中患者进行了回顾性分析，收集人口统计学基线资料及 NIHSS 评分。脑血管疾病的危险因素在多元回归分析中用于危险分层。

结果：总共 2225 例急性缺血性卒中患者，其中 1019 例出院回家，719 例继续住院康复，371 例转至专业的护理机构及 116 例进行亚急性治疗。与对照组相比，接受 rt-PA 溶栓治疗的患者出院后直接回家的可能性要高于出院时的其他级别的照料 (P<0.0001；OR，1.945；95% CI，1.538-2.459)。rt-PA 溶栓治疗的患者与未溶栓患者之间，急性期后继续住院康复与转至专业的护理机构/接受亚急性治疗之比无显著差异 (P=0.123)；转至专业的护理机构与进行亚急性治疗之比亦无显著差异 (P=0.605)。

结论：接受 rt-PA 溶栓治疗的急性缺血性卒中患者在经住院治疗后更有可能直接回家。研究的局限性在于回顾性研究且未明确心理社会因素对出院的影响。

关键词：结局，康复，卒中恢复，溶栓

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较大幅度的调整。2002 年，医疗保险 (Medicare) 中心和医疗补助服务 (Medicaid Service) 通过财政中介延迟执行规定的 75%，主要是担心该规则并未在全国范围内统一实行 [9]。2004 年，医疗保险和医疗补助服务再次重申了规则，并将适用标准扩大到 13 个病种的符合情况。另外，设立 3 年的过渡期以逐渐提高适用比例，从 2004 年的 50% 增加到 2007 年的 75%。然而，2007 年，国会通过了医疗保险、医疗补助及 SCHIP 扩大法案，设置了 IRF 适用规则为不超过追溯自 7 月 1 日开始的费用报告期的 60%。适用规则的影响是康复单位长期担忧的一个原因，因为医疗保险 (Medicare) 要为每年总计约 56 亿美元的 IRF 患者支付其中的 70% [6]。

为了满足 IRF 的条件，患者必须接受康复医生，24 小时看护，由物理治疗、职业治疗、语言训练、护理、病例管理及社会工作者组成的协调的多学科康复治疗的严密医学观测。此外，患者必须有能力进行每日至少 3 小时的相当强度的康复锻炼，并能预期在短期内达到有实际意义的改善 [4]。

亚急性照料是指每日不再需要诊断性或侵入性治疗且病情相对稳定患者的过渡阶段治疗，也称为长期急性照料。这个阶段的患者在急性期治疗医院需要有 24 小时随时可以提供的服务。此外，患者可能需要气管切开或机械辅助通气的照料，也可以是 6 种下列照料中的任意一种，如胃管进食、伤口护理、持续静脉治疗 (营养支持或抗生素)、频繁雾化治疗、完全肠外营养、及住院的物理、职业和语言治疗 [8]。需要进行亚急性期治疗的卒中患者主要是由大面积脑梗死造成的严重功能障碍者。间断护理设施主要为功能障碍、精神残疾或慢性病患者提供治疗 [9]。需要间断观察以防止病情恶化的情况存在。比较上述不同层次的照料，在间断照料设施中不需要专业护理也不需要治疗服务。在间断照料设施中照料的患者，与接受住院康复、SNF 或亚急性照料患者相比，表现出更多的基本日常生活的独立。

国家神经功能缺损和卒中研究所的 rtPA 卒中研究 (NIDSS) 已经证实，在症状发生 3 小时内接受 rt-PA 静脉溶栓的急性缺血性卒中患者，30% 者更有可能在 3 个月内无或仅有轻微的功能障碍 [10]。在住院期间，短期功能障碍和功能状态的判断是根据出院时的去向而主观评估，去向包括直接回家、住院康复、转至专业的护理机构或接受亚急性照料。目前尚无研究评估急性缺血性卒中 rt-PA 静脉溶栓在预测卒中后出院去向所提示的功能状态中的作用。

### 对象与方法

我们对前瞻性收集的可靠的缺血性卒中资料库进行回顾性分析，该库有 2004 年 1 月至 2009 年 10 月间在德克萨斯大学休斯顿医学院的赫尔曼纪念医院 - 德州医学中心的卒中中心收治的所有缺血性卒中的卒中者出院时的去向为直接回家、住院康复 (IR)、SNF、亚急性照料 (Sub)。赫尔曼纪念医院 - 德州医学中心是一个具有院内康复单元的三级医疗中心 ; 接收满足入院标准的所有患者，不考虑其保险类型或支付能力。纳入在发病 3 小时内溶栓治疗时问窗内住院的患者。收集患者的人口统计学基线资料，包括年龄、性别、种族及就诊时的 NIHSS 评分 (表 1)。所有患者都有频繁的生命体征监测包括心电图和 24 小时动态监测。常规行心脏和脑的影像学、血脂和血糖水平检查 ; 这些常规检查用于多变量模型进行危险因素分层 (表 2)。对医疗记录进行检查以确定存在会影响预后的合并症。收集所有的患者出院时的改良

<table>
<thead>
<tr>
<th>表 1 是否 rt-PA 静脉溶栓的急性缺血性卒中患者的人口学资料</th>
<th>rt-PA (865)</th>
<th>rt-PA (1873)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>年龄，岁，均数 ± 标准差</td>
<td>65.32 ± 15.02</td>
<td>64.12 ± 14.83</td>
<td>0.6648</td>
</tr>
<tr>
<td>就诊时 NIHSS 评分</td>
<td>12 (6-18)</td>
<td>5 (2-12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>中位数 (IQR)</td>
<td>53.18</td>
<td>51.35</td>
<td>0.3725</td>
</tr>
<tr>
<td>性别，男性 %</td>
<td>30</td>
<td>36.5</td>
<td>0.0059</td>
</tr>
<tr>
<td>种族，%</td>
<td>13</td>
<td>13.5</td>
<td>0.0059</td>
</tr>
<tr>
<td>白人</td>
<td>55</td>
<td>48</td>
<td>0.0059</td>
</tr>
<tr>
<td>其它</td>
<td>2</td>
<td>2</td>
<td>0.0059</td>
</tr>
<tr>
<td>死亡，% (例数)</td>
<td>12 (104)</td>
<td>5.4 (102)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>不同安置去向，% (例数)</td>
<td>3.35 (25)</td>
<td>2.40 (45)</td>
<td>0.1638</td>
</tr>
<tr>
<td>去向 (%)</td>
<td>0.2699</td>
<td></td>
<td></td>
</tr>
<tr>
<td>回家 ± 门诊</td>
<td>43 (314)</td>
<td>46 (792)</td>
<td></td>
</tr>
<tr>
<td>SNF</td>
<td>33 (239)</td>
<td>32 (551)</td>
<td></td>
</tr>
<tr>
<td>IRF</td>
<td>17 (127)</td>
<td>17 (292)</td>
<td></td>
</tr>
<tr>
<td>Sub</td>
<td>7 (52)</td>
<td>5 (92)</td>
<td></td>
</tr>
</tbody>
</table>

IQR 指的是四分位间距。
Stroke  March 2011

排除标准为颅内出血、短暂性脑缺血发作和出院后其他去向（出院后至其他服务中心或者不能遵医嘱）。出院后在家或在临终关怀医院接受临终关怀及死亡的患者亦纳入分析，以确定是否rtPA组的发病率或死亡率较非rtPA组增加。脑血管病的危险因素被用于风险评估和分层。存在多种合并症会增加卒中后死亡及出院后转入体现患者功能状态较差的照料单位的似然值（表3）。

主要自变量是急性缺血性卒中应用rtPA，主要因变量是患者的功能状态。我们用出院后的去向体现患者的功能状态。对出院后去向进行配对分组（直接回家对其他水平的照料，住院康复对转至专业的护理机构或亚急性照料，转至专业的护理机构对亚急性照料）。NIHSS评分是很好的临床结局和出院后去向的预测[11,12]。在多变量回归分析中，我们将就诊时NIHSS评分作为连续变量。急性缺血性卒中患者的NIHSS评分低预示卒中后转入体现功能状态较好的照料单位。

统计分析采用SAS 9.2（Cary, NC）。连续变量呈正态分布以均数±标准差表示，呈非正态分布以中位数和范围表示。NIHSS评分用四分位距的中位数表示。在适当的时候分类变量用χ²检验和Fisher确切检验进行分析。我们用t检验评估均数之间的差异，用Wilcoxon检验评估中位数之间的差异。在校正接受rtPA溶栓治疗急性缺血性卒中患者的脑血管病的危险因素后，我们用logistic回归分析来明确卒中后去向的差异性。

结果

本研究共有2459例患者出院后直接回家、住院康复、转至专业的护理机构或接受亚急性照料，9%的患者因作为解释变量的数据丢失而被剔除（表1）。这是德克萨斯大学休斯顿医学院的卒中中心早期形式数据集的合并造成的，这也是所有结局研究的共同难题。在二次分析中，我们发现丢失的数据集都一致地平均分布于主要的自变量和因变量之间。急性缺血性卒中rt-PA静脉溶栓与死亡率增加相关（12%对5.4%[无rt-PA组]；P≤0.0001；表1）; 出院后回家接受临终关怀的似然值无显著统计学差异（2.5%对4%[无rt-PA组]；P=0.1638；表1）。共有2756例患者被纳人独立危险因素分层分析（表2和3）。在评估人口统计学信息时由于缺少种族变量信息而减少0.65%

表2 用于危险分层的自变量

<table>
<thead>
<tr>
<th>变量</th>
<th>定义</th>
</tr>
</thead>
<tbody>
<tr>
<td>心血管疾病</td>
<td>房颤，充血性心力衰竭，冠心病，心梗史，周围血管病</td>
</tr>
<tr>
<td>糖尿病</td>
<td>糖尿病史或就诊时血糖&gt;200</td>
</tr>
<tr>
<td>高血压</td>
<td>高血压病史或就诊时血压升高</td>
</tr>
<tr>
<td>高脂血症</td>
<td>高脂血症史或就诊时总胆固醇&gt;200</td>
</tr>
<tr>
<td>卒中史</td>
<td>脑血管事件病史（短暂性脑缺血发作、急性梗死，脑出血，硬膜外血肿，硬膜下血肿，蛛网膜下腔出血）</td>
</tr>
</tbody>
</table>

表3 是否rt-PA静脉溶栓治疗患者的危险因素

<table>
<thead>
<tr>
<th></th>
<th>rt-PA (866)</th>
<th>无rt-PA (1890)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>心血管疾病，%</td>
<td>43</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>糖尿病，%</td>
<td>27</td>
<td>34</td>
<td>0.0002</td>
</tr>
<tr>
<td>高血压，%</td>
<td>70</td>
<td>76</td>
<td>0.0004</td>
</tr>
<tr>
<td>高脂血症，%</td>
<td>26</td>
<td>30</td>
<td>0.0489</td>
</tr>
<tr>
<td>卒中史，%</td>
<td>77</td>
<td>77</td>
<td>0.9719</td>
</tr>
</tbody>
</table>

表4 自变量加入rt-PA静脉溶栓结果—出院后直接回家对比转入其他照料单位（IRF、SNF、Sub）

<table>
<thead>
<tr>
<th></th>
<th>P</th>
<th>OR</th>
<th>95% CI 下限</th>
<th>95% CI 上限</th>
</tr>
</thead>
<tbody>
<tr>
<td>rt-PA</td>
<td>&lt;0.0001</td>
<td>1.945</td>
<td>1.538</td>
<td>2.459</td>
</tr>
<tr>
<td>就诊时NIHSS评分</td>
<td>&lt;0.0001</td>
<td>0.822</td>
<td>0.805</td>
<td>0.840</td>
</tr>
<tr>
<td>年龄</td>
<td>&lt;0.0001</td>
<td>0.967</td>
<td>0.960</td>
<td>0.974</td>
</tr>
<tr>
<td>心血管疾病</td>
<td>0.187</td>
<td>1.156</td>
<td>0.932</td>
<td>1.434</td>
</tr>
<tr>
<td>糖尿病</td>
<td>0.041</td>
<td>0.803</td>
<td>0.650</td>
<td>0.991</td>
</tr>
<tr>
<td>高血压</td>
<td>0.177</td>
<td>0.850</td>
<td>0.671</td>
<td>1.076</td>
</tr>
<tr>
<td>高脂血症</td>
<td>0.016</td>
<td>0.774</td>
<td>0.628</td>
<td>0.954</td>
</tr>
<tr>
<td>卒中史</td>
<td>0.023</td>
<td>1.311</td>
<td>1.037</td>
<td>1.658</td>
</tr>
</tbody>
</table>

出院后回家与到其他照料单位（IRF、SNF或Sub）比较

剩余的2225例患者，1019例出院后回家，1206例患者则转入IRF、SNF或Sub。在多变量回归回归分析中分析所有效应后，发现接受rtPA溶栓的急性缺血性卒中患者出院后更有可能直接回家（P<0.0001；OR，1.945；95% CI，1.538-2.459；表4）。增龄（P<0.0001；OR，0.967；95% CI，0.960-0.974）和就诊时NIHSS评分（P<0.0001；OR，0.822；95% CI，0.805-0.840）及卒中后转入其他照料单位相关。

对于急性缺血性卒中患者，静脉内rt-PA与出院后去向关系的OR值要比脑血管病的危险因素高，如心血管疾病（P=0.187；OR，1.156；95% CI，0.932-1.434）、糖尿病（P=0.041；OR，0.803；95% CI，0.650-0.991）、高血压病（P=0.177；OR，0.850；95% CI，0.671-1.076）、高脂血症（P=0.016；OR，0.774；95% CI，0.628-0.954）及卒中史（P=0.023；OR，1.311；
在剩下的 1206 例急性缺血性卒中的患者中，719 例患者出院后转至 SNF 或 Sub，在多变量回归分析调整所有效应后，接受 rt-PA 治疗或未接受 rt-PA 治疗的患者在出院后的去向上无显著的统计学差异（P=0.123；OR，1.255；95% CI，0.940-1.675；表 5）。高龄提示出院后易转至 SNF 和 Sub（P<0.0001；OR，0.948；95% CI，0.938-0.958）。与首次分析结果不同，合并心血管疾病预示出院后转至 SNF 和 Sub，这证实活动耐力在决定卒中出院后安置中的重要性（P=0.031；OR，0.741；95% CI，0.564-0.973）。不受 rt-PA 应用的影响，就诊时 NIHSS 评分高预示出院后转至 SNF 和 Sub 的可能性高（P<0.0001；OR，0.913；95% CI，0.896-0.930）。卒中史也与出院后转至 SNF 和 Sub 相关，这些患者更容易在基线时有躯体功能损害（P<0.0001；OR，2.424；95% CI，1.784-3.293）。糖尿病、高血压和高脂血症对卒中后的安置无显著影响（表 5）。

出院后转至 SNF 与 Sub 的比较

在剩下的 487 例急性缺血性卒中患者中，371 例患者转至 SNF，116 例患者接受 Sub。在多变量回归分析调整所有效应后，发现是否接受 rt-PA 治疗与卒中后在 SNF 或 Sub 这两种单位的安置上无显著差异（P=0.605；OR，0.884；95% CI，0.554-1.410；表 6）。高龄与卒中后接受 Sub 有关，但影响并不显著（P=0.006；OR，1.026；95% CI，1.007-1.045）。大面积脑梗死的患者由于损伤较严重，出院后更易接受 Sub 而非转至 SNF。此外，与之前的分析相比，此组高龄患者的死亡率显著升高。

讨论

据我们所知，这是首个有关急性缺血性卒中患者静脉 rt-PA 溶栓治疗与出院后回家或转入其他照料单位所反映的短期预后改善直接联系的研究。短期结局与长期残疾之间的联系尚未被研究，将是未来研究的焦点。与未行 rt-PA 溶栓治疗的患者相比，接受 rt-PA 溶栓治疗的患者倾向于更年轻， NIHSS 评分高、年龄轻、胆固醇水平正常、无卒中病史。在进行本研究期间，前述有关 60% 的规则有变异，对接受 IRFs 的患者有潜在的混杂效应。尽管 2007 年国会通过了医疗保险、医疗补助及 SCHIP 扩大法案，也只有用于 IRF 的费用报销，它对这段时期的出院去向并无影响。今后的研究将受到新的 2010 年医疗保险和医疗补助服务中心的 IRF 覆盖要求的影响。医疗保险和医疗补助服务中心 2010 年指南目的是致力于确定 IRF 的个人申请是否合理和必需。新的覆盖要求提供患者病情确实稳定且可从 IRF 获益，特别是对协调的多学科康复治疗的需要，并指出某个 IRF 所能提供的治疗获益 [13]。这些新指南对转入 IRF 的影响还有待观察，也将是未来研究的课题。
溶栓能真正地预示良好结局，也可能存在还
未知的原因。对此，最好是采用前瞻性的观察研究。

总之，在规定的 3 小时时间窗内接受静脉
rt-PA 治疗的急性缺血性卒中患者出院后更有可能直接
回家而不需要急性期后的住院治疗。急性卒中治疗的
改进通过减少康复、急性期后照料及损失劳动力的
成本，使得净卫生费用减少[3]。传统的康复是促进
卒中后恢复进程的一个治疗手段。在卒中急性期后
照料提高、继续改进患者和照料者的需求、改进健
康保健环境等方面还有相当大的空间

尽管传统的康复治疗药物对患者有帮助，但对
其科学基础的更好了解将进一步提供其影响[17]。关
于 rt-PA 治疗增加有利结局的特点将是未来研究的内
容，包括人口统计学、疾病严重程度、共病及卒中
并发症。此外，需要确定 rt-PA 治疗时间窗内的最佳
时机，以量化其治疗效应对出院后去向的影响。

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