管理脑梗死的住院阶段：第二部分

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背景：急性脑梗死在住院医师中较为常见。近年来，对这些患者的急性管理和二级预防能力有了显著提升。美国医院联合委员会（JCAHO）对主要脑梗死中心（primary stroke center）的认证变得越来越重要，该认证强调了住院阶段和出院过程中的许多要素。

目的：患者入院后，重点转向避免并发症和适当启动联合治疗以及二级预防。

数据来源：主要试验、当前指南。

结论：住院医师在一个对脑卒中人群有重大学习和实践能力的环境中，可以发挥重要作用。

关键词：脑血管疾病，指南，住院，脑卒中。

住院阶段的脑梗死管理包括许多要素，在急性阶段同样重要。这部分内容在第一部分中有所涉及。进一步的诊断评估依赖于患者入院时的风险因素。同样，进一步的治疗，无论是住院治疗还是二级预防，都基于识别脑梗死的机制。住院医师在脑卒中管理和预防复发方面具有独特的地位。

案例呈现

76岁的右利手男性，有高脂血症和心肌梗死病史，于早上7点被发现右半身瘫痪和反应迟钝。在急诊科时，患者出现部分性失语、右侧肢体瘫痪和向左偏视，医生对左中脑动脉（MCA）卒中的可能性有很高的怀疑。不幸的是，他被排除在使用静脉溶栓（tPA）或任何其他急性治疗之外，因为最后一次被确认为神经功能正常时是前一天晚上，该时间点被认定为卒中的起病时间。抗血小板药物被继续使用，并将患者收入院进行进一步的检查。

住院阶段

当急性脑梗死患者被收入院时，应放在标准化的急性脑卒中流程中（也称为标准流程、路径、临床路径等），这一流程多由住院医师/神经科医生及多学科团队创建，并收入脑卒中病房。脑卒中病房可能以物理上分离的单元形式存在，特别是在有充足患者入院的医院，也可以是入院患者较少的楼层。多学科的护理人员在脑卒中病房接受特殊培训。多学科团队在脑卒中患者中表现出显著的降低病死率和改善功能结果。1 干预的几个基本要素包括心电图监测、保持体温和血糖在正常水平、密切监测血压和神经状态、主动避免并发症、启动二级预防治疗、早期介入康复服务和患者教育。

体温调节可能通过在前48小时内给患者服用定时的泰诺来辅助，但并没有证据支持这种做法。2 虽然体温和血糖水平的提高与急性卒中患者的不良结局相关。3–5

血压管理

正常情况下，大脑血管的自动调节机制可以在一定程度上保持大脑血流稳定。在急性脑卒中患者中，这种自动调节机制可能失效。患者在急诊科的就诊时间，伴有部分性失语、右侧肢体瘫痪和左视。尽管如此，患者被排除在使用静脉溶栓（tPA）或任何其他急性治疗之外。然而，患者被问及脑中动脉（MCA）卒中的可能性。不幸的是，他被排除在使用静脉溶栓（tPA）或任何其他急性治疗之外，因为最后一次被确认为神经功能正常时是前一天晚上，该时间点被认定为卒中的起病时间。抗血小板药物被继续使用，并将患者收入院进行进一步的检查。

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中枢性眩晕可能由病史中的高脂血症和心肌梗死引起，这是患者被收入院的背景。患者入院时，症状为部分性失语、右侧肢体瘫痪和左视。尽管如此，患者被排除在使用静脉溶栓（tPA）或任何其他急性治疗之外。然而，患者被问及脑中动脉（MCA）卒中的可能性。不幸的是，他被排除在使用静脉溶栓（tPA）或任何其他急性治疗之外，因为最后一次被确认为神经功能正常时是前一天晚上，该时间点被认定为卒中的起病时间。抗血小板药物被继续使用，并将患者收入院进行进一步的检查。

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autoregulate is diminished or absent in regions of and surrounding an acute ischemic stroke; as the area becomes ischemic, autoregulation opens the local vasculature maximally in an effort to draw in as much blood as possible. Maximally dilated arterioles are perfused in direct correlation with systemic blood pressure, thus any drop in the systemic blood pressure leads to direct decreases in blood flow specifically in the area of ischemia; if there is a penumbra of marginally perfused tissue, such systemic blood pressure drops risk extending the area of fatal ischemia (increasing the size of the ischemic stroke). Thus in the acute period of an ischemic stroke, the American Heart Association (AHA)/American Stroke Association (ASA) “Guidelines for the Early Management of Adults With Ischemic Stroke” (referred to herein as the “Guidelines”) suggest avoid treatment unless systolic blood pressures are >160 prior to recommending treatment.

Higher-quality Inpatient Stroke Care and Harmonized Performance Measures

Beginning in January 2008, a set of 10 performance measures (Table 1) for inpatient acute stroke care have been agreed upon (“harmonized”) by 3 major stakeholders including the Joint Commission, the ASA’s “Get with the Guidelines–Stroke” quality improvement program, and the Center for Disease Control and Prevention’s (CDC’s) Paul Coverdell Acute stroke registries. These performance measures were selected to help avoid complications (deep vein thrombosis [DVT], aspiration pneumonia), encourage appropriately aggressive care (tPA administration), optimize secondary prevention (antithrombotics, cholesterol lowering, smoking cessation, education), and facilitate functional recovery (early rehabilitation). All 10 measures are appropriate for consideration in every ischemic stroke patient, and 5 are appropriate for the hemorrhagic stroke types.

Further Workup

After the ischemic stroke patient has had their computed tomography (CT) scan, possibly a computed tomography angiography (CTA), been admitted to the stroke unit, started on an antithrombotic medication, and had their blood pressure appropriately treated, attention then turns to defining the pathophysiology related to the stroke and starting an optimal regimen for secondary prevention. Imaging of the cerebral vasculature including both extracranial and intracranial large vessels is a vital first step in understanding the cause of ischemic stroke. There are multiple potential modalities (magnetic resonance angiography [MRA], CTA, and duplex/transcranial Doppler), the choice of which depends on local availability and expertise as well as the specific clinical situation. Magnetic resonance imaging (MRI) of the brain for all ischemic stroke patients is standard of care at most stroke centers; per the “Guidelines,” MRI is better at distinguishing acute, small cortical, small deep, and posterior fossa infarcts; at distinguishing acute from chronic ischemia; and at identifying subclinical satellite ischemic lesions that provide information on stroke mechanism.

TABLE 1. Harmonized Acute Inpatient Stroke Care Performance Measures

<table>
<thead>
<tr>
<th>Performance measure*</th>
<th>Definition*</th>
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<tbody>
<tr>
<td>1. DVT prophylaxis¹</td>
<td>Patients who are nonambulatory should start receiving DVT prophylaxis by end of hospital day 2 (can be either compression devices or any low-dose heparin)</td>
</tr>
<tr>
<td>2. Discharged on antithrombotic therapy</td>
<td>Antiplatelet agent(s) or warfarin anticoagulation</td>
</tr>
<tr>
<td>3. Patients with atrial fibrillation receiving anticoagulation therapy</td>
<td>A proven approach to secondary prevention in such patients; practice at Harborview varies time of warfarin initiation based on infarct size with larger infarcts waiting up to 2 weeks before initiating warfarin (the best randomized trial showed no benefit for full-dose low-molecular-weight heparin over aspirin in the first 2 weeks)²⁰</td>
</tr>
<tr>
<td>4. Thrombolytic therapy administered</td>
<td>In ischemic stroke patients who arrive at the hospital within 120 minutes (2 hours) of time last known well, for whom IV tPA was initiated at this hospital within 180 minutes (3 hours) of time last known well, and who qualify under strict criteria</td>
</tr>
<tr>
<td>5. Antithrombotic therapy by end of hospital day 2</td>
<td>Usually just antiplatelet agents, a minimal standard of care for ischemic stroke patients; should be started as early as possible, usually in ER</td>
</tr>
<tr>
<td>6. Discharged on statin medication</td>
<td>If LDL &gt;100, or not measured or if on a statin drug prior to admission; to reduce risk of subsequent ischemic stroke</td>
</tr>
<tr>
<td>7. Dysphagia screening⁰</td>
<td>Prior to any PO food, fluids or medications; to reduce the chances of aspiration pneumonia</td>
</tr>
<tr>
<td>8. Stroke education⁰</td>
<td>Including for families if patient unable to participate, must include “personal risk factors for stroke, warning signs for stroke, activation of emergency medical system, need for follow-up after discharge, and medications prescribed”</td>
</tr>
<tr>
<td>9. Smoking cessation/advice/counseling</td>
<td>For any patient who has smoked in the last year</td>
</tr>
<tr>
<td>10. Assessed for rehabilitation¹</td>
<td>Or received therapy services; to facilitate progress to an optimal function outcome</td>
</tr>
</tbody>
</table>

NOTE: Active January 1, 2008.
Abbreviations: DVT, deep vein thrombosis; ER, emergency room; IV, intravenous; LDL, low-density lipoprotein; PO, by mouth; tPA, tissue plasminogen activator.
*Available at: http://www.jointcommission.org/CertificationPrograms/PrimaryStrokeCenters/stroke_pm_edition_2_ver_2a.htm.
*Applies to both ischemic and hemorrhagic stroke types; if not so marked, only applies to ischemic stroke patients.
specific therapies, but are not yet widely available nor have they been shown to alter outcomes.

An electrocardiogram is indicated for all stroke patients, as is admission to a cardiac telemetry bed for at least 24 hours to document any arrhythmias, the most common being atrial fibrillation (“Guidelines,” p. 1666, 1673). An echocardiographic study (ECHO) of the heart with bubble fraction that, such as low cardiac ejection fraction, atrial septal aneurysm, patent foramen ovale (PFO), or a cardiac thrombus. The bubble study increases the sensitivity of detecting a PFO, which could serve as a gateway for venous embolization to the cerebral arteries. Assuming a large PFO is discovered, other studies such as lower extremity Doppler may be warranted to investigate other potential sources of thrombi (ie, DVT).

Regarding laboratory testing, fasting lipids should be checked as hyperlipidemia is a common modifiable risk factor for ischemic stroke. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial included ischemic stroke patients that had low-density lipoprotein (LDL) cholesterol between 100 mg/dL and 190 mg/dL and randomized them to receive atorvastatin 80 mg/day vs. placebo. Results showed a 16% relative risk reduction in recurrent stroke; however, there was a small increased risk of intracranial hemorrhage. As shown in Table 1, use of a statin on discharge is now a national performance measure for ischemic stroke.

Dissection is a common cause of stroke in young patients without traditional risk factors. Other serologies, such as hypercoagulable studies, may be warranted in patients with no other risk factors for strokes, paradoxical embolus, or of young age (eg, 45 years and under). The arterial hypercoagulable panel consists of antiphospholipid antibody panel, homocysteine levels, lupus anticoagulant levels, and prothrombin time/partial thromboplastin time (PT/PTT). The venous hypercoagulable panel consists of the laboratory values checked, with the arterial hypercoagulable and activated protein C (APC) resistance, Factor VIII activity, Factor II DNA, Factor V DNA if the APC resistance is positive, antithrombin III activity, and activity of proteins C and S. If a patient is found to have a hypercoagulable state, long-term therapy often involves careful consideration of the choice of antiplatelet therapy vs. anticoagulation with warfarin.

Initiating Secondary Prevention

Upon admission, the clinician faces a variety of treatment choices for secondary stroke prevention. The proper choice depends on the results of the workup and the presumptive pathophysiology.

Noncardioembolic/Atherothrombotic/Lacunar

The Antithrombotic Trialists’ Collaboration meta-analysis found that patients with a prior stroke or transient ischemic attack (TIA) had a highly significant decrease in the rate of subsequent vascular events (over about 3 years) on antiplatelet therapy (17.8% vs. 21.4%, P < 0.0001) and were unable to find a significant difference between low-dose and high-dose aspirin for secondary prevention. Thus, it is reasonable to place an acute stroke patient naive to antithrombotic therapy on 81 mg of aspirin or 325 mg for long-term prevention (325 mg is specifically recommended in the acute setting). Several studies such as the WARSS and ESPRIT trials have shown antiplatelet agents to be at least as effective as anticoagulation in noncardioembolic ischemic strokes. Guidelines from Europe, the American College of Chest Physicians, and the AHA/ASA all state it is acceptable to choose either aspirin monotherapy, aspirin/extended release dipyridamole combination therapy, or clopidogrel monotherapy as first-line agents for long-term secondary prevention in noncardioembolic ischemic stroke. There is no clear evidence that patients who suffer an ischemic stroke while on aspirin will derive additional benefit from increasing the aspirin dose. The newer guidelines go on to recommend aspirin/extended release dipyridamole (ER-DP) combination therapy or clopidogrel monotherapy over aspirin monotherapy, the former with a stronger level of recommendation based on the results of 2 randomized trials. These recommendations were all published without knowledge of the results of the Prevention Regimen For Effectively Avoiding Second Strokes (PROFESS) study, which directly compared aspirin/extended release dipyridamole combination therapy to clopidogrel monotherapy for long-term secondary prevention. The rate of first recurrent stroke was not significantly different between the 2 therapies (9.0% ER-DP plus aspirin, 8.8% clopidogrel; hazard ratio [HR], 1.01; 95% confidence interval [CI], 0.92–1.11). Other outcomes also showed few differences, although there were more major hemorrhagic events in the ER-DP plus aspirin group (4.1% vs. 3.6%; HR, 1.15; 95% CI, 1.00–1.32; P = 0.06).

The ASA Stroke Prevention Guideline from 2006 states, with continued relevance, “The selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, tolerance, and other clinical characteristics.” Of note, both the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) and Management of Atherothrombosis with Clopidogrel in High-risk patients with recent TIA or ischemic stroke (MATCH) trials found a significant increased risk for hemorrhage complications with long-term use of the aspirin and clopidogrel combination, and the 2008 update to the ASA Stroke prevention guidelines state that “the addition of aspirin to clopidogrel increases the risk of hemorrhage. Combination therapy of aspirin and clopidogrel is not routinely recommended for ischemic stroke or TIA patients unless they have a specific indication for this therapy (i.e., coronary stent or acute coronary syndrome).”

Atrial Fibrillation

Though our case patient did not have atrial fibrillation, this condition deserves mention. About 15% to 20% of
ischemic stroke patients have atrial fibrillation. The overall risk for stroke in patients with atrial fibrillation is about 5% per year; however, patients who have a history of stroke increase their risk factors for subsequent strokes to about 12% per year. In most cases, anticoagulation has proven to be the superior agent for primary and secondary stroke prevention with warfarin reducing the risk by 67% compared to aspirin, which only reduces the risk of stroke by 20%. A meta-analysis from 2002 showed that patients who had a prior stroke or TIA decrease their risk of subsequent strokes to 4%/year on oral anticoagulation therapy, resulting in an 8% absolute risk reduction. Patients on aspirin therapy only decrease their risk to 10%/year, or a 2% reduction in stroke events. Unless there is a strong contraindication (eg, bleeding diathesis, history of life threatening gastrointestinal [GI] bleeding, history of fall with subdural hematoma, etc.), virtually all ischemic stroke patients with atrial fibrillation should be anticoagulated for life. Anticoagulation in the setting of atrial fibrillation is seriously underutilized. The highest quality study on early anticoagulation for ischemic stroke associated with atrial fibrillation suggested that there was no benefit to starting anticoagulation earlier than 2 weeks after a stroke, and there may actually be a higher complication rate (compared to aspirin). Other cardiac indications for anticoagulation include left ventricular thrombus and mechanical valves.

**Carotid Stenosis**

Significant ipsilateral stenosis of the internal carotid artery in a patient with ischemic stroke is a strong indication for intervention, usually a standard carotid endarterectomy (CEA). Stenosis of 70% to 99% is the strongest indication for CEA, and may be of greatest benefit in men, those 75-years of age, and if surgery is done <2 weeks after the most recent symptoms. In patients with minor stroke or TIA, recent recommendations and our practice is to admit to the hospital and perform endarterectomy as soon as possible (those with major stroke may have a greater risk of complications with early CEA). Stenting should only be considered instead of CEA if high risk (for surgical complications) criteria are present. These high risk criteria include patients having “significant comorbidities and/or anatomic risk factors (ie, recurrent stenosis and/or previous radical neck dissection), and [who] would be poor candidates for CEA in the opinion of a surgeon.” For stenoses of 50% to 69%, intervention is not as compelling, and decisions should be individualized based on patient characteristics; in this group, stenting should only be considered in the setting of a clinical trial or if an investigational device exemption (IDE) exists at your institution.

**Dissection of the Carotid or Vertebral Arteries**

This is a common cause of stroke in younger adults. It should be suspected in patients without other clear causes of stroke and significant disease of the extracranial arteries. Diagnosis can usually be made with CTA or MRA, though it is suggested that the best modality may be “T1-fat-saturated” MRI images of the neck. Debate exists as to the best approach to treatment of dissections due to the absence of randomized trials. A recent comprehensive review suggested anticoagulation for 3 to 6 months followed by indefinite antiplatelet therapy for symptomatic dissections and antiplatelet therapy alone for asymptomatic dissections.

**PFO-related Stroke**

If the patient is found to have a PFO, its role in comparison to traditional risk factors must be weighed carefully. Epidemiological studies suggest that PFO may be most relevant in younger patients, those with cryptogenic stroke (no obvious cause and lack of traditional risk factors), those with higher risk associations including interatrial septal aneurysm, larger PFOs or history of previous cryptogenic stroke. The best medical therapy for seemingly PFO-related ischemic stroke is also unclear; a reasonable approach might be aspirin if neither high-risk associations nor a hypercoagulable state is present, and warfarin if either are present. Transcatheter closure of PFO is approved by the U.S. Food and Drug Administration (FDA) only under an IDE for patients who have had a recurrent event on maximally tolerated medical treatment, and requires approval from the human research committee (internal review board [IRB]) at your hospital. It is not known if closure is superior or inferior to best medical therapy, and a practice parameter from the American Academy of Neurology strongly encourages appropriate patients to consider participation in ongoing randomized trials. Further information on these trials is available at:

- http://www.closurei.com/physician

Our patient underwent a CTA of the head and neck in the emergency room to see if he would be a candidate for other interventions; unfortunately, he did not meet the time criteria. CTA showed complete occlusion of the left internal carotid artery at the bifurcation with heterogeneous retrograde filling (Supporting Figure 1). Complete occlusion of the proximal third of the left M1 segment was also seen with relative oligemia in the left MCA distribution, though several small peripheral M3/M4 vessels were opacified in the territory indicating collateralization (Supporting Figure 2). A MRI showed a large area of diffusion-weighted abnormality (Figure 1). Interestingly, the patient’s transthoracic echocardiography (TTE), which did not show evidence of a PFO, did reveal a calcified thrombus in the left ventricle. Though no arrhythmias were captured on telemetry, this thrombus does serve as a potential source of cardioembolic emboli to the cerebral vasculature. It was felt that the most likely source of the patient’s acute infarct was from artery-to-artery emboli from his internal carotid occlusion given the infarct location and the lack of infarction in other vascular distributions (as one might see from a cardiac embolic source). Therefore, his medical management consisted of an
antiplatelet regimen for 2 weeks followed by a transition to warfarin alone 2 weeks after his acute infarct as secondary stroke prevention due to the cardiac thrombus. Given the complete occlusion of the internal carotid artery and M1 segment, there was concern that the penumbra might be at risk of infarction (supporting standard guidelines of permissive hypertension). By the end of his hospitalization, the patient had improved and was transferred to inpatient rehabilitation.

The guidelines for acute stroke management continue to rapidly evolve. Certainly, there are effective treatments for acute ischemic stroke, with variation based on the timing of patient arrival at the hospital, the underlying pathophysiology, and the treatment capabilities of the individual hospital. Secondary stroke prevention is extremely important and has been emphasized during inpatient admissions with the establishment of an appropriate medication regime, given that patients are more likely to stay on treatment that is initiated around the time of a diagnosis.29 Evidence strongly suggests that management of acute stroke is improved by an organized approach to care, including the expertise of a multidisciplinary team in a specialized stroke unit. Hospitals committed to high quality of care for acute stroke patients should strongly consider the Joint Commission certification process or an analogous local certification. Such certification demonstrates a hospital’s commitment to providing high-quality care, what every stroke patient wants and deserves.

References


