

In-hospital stroke

Kolja Schürmann¹ and Arno Reich^{1*}

¹Department of Neurology, University Hospital Rheinisch-Westfälische Technische Hochschule [RWTH] Aachen, Aachen, Germany

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*Correspondence:

Arno Reich (MD), Department of Neurology, RWTH Aachen University, Pauwelsstrasse 30, D-52074 Aachen, Germany
Email: areich@ukaachen.de

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ABSTRACT

In-hospital stroke (IHS), which represents between 2.2% and 17% of all strokes, differs from community-onset stroke (COS) in etiology, treatment approaches and outcome. Patients hospitalized for cardiac disease are especially vulnerable to predominantly cardioembolic IHS. Stroke severity, functional outcome and mortality compare unfavorably to COS. Difficulties in symptom recognition, intra-hospital delays, various stroke mimics, critical underlying diseases and contraindications against standard systemic thrombolysis represent difficulties in IHS treatment. Quality of care may be improved by educating medical staff, implementing a code stroke and a CT-rendezvous system, providing access to specialized care (e.g. on stroke units) and endovascular reperfusion therapy as well as neuromonitoring, where applicable.

Epidemiology and Definition

Stroke is generally known to be among the leading causes for death and acquired disability worldwide^{1,2}. It is less known that between 2.2% and 17% of all strokes occur in hospitalized patients, with a lower percentage reported in smaller hospitals and multicenter studies^{3,4} and higher rate in tertiary clinics^{5,6}. This difference is presumably due to a higher percentage of critically ill patients in larger hospitals, more frequent high-risk procedures and, possibly, a lower rate of reported cases in some participating centers in multicenter studies. In-hospital stroke (IHS) is most commonly defined as stroke, that occurs during hospitalization in a patient originally admitted for another diagnosis, provided that neuronal tissue damage due to infarction or hemorrhage is confirmed by cerebral imaging (usually computed tomography (CT) or magnetic resonance imaging (MRI))^{3,7}. This definition usually excludes recurrent stroke⁸, progressive community-onset stroke (COS), global cerebral hypoperfusion and periprocedural complications of reperfusion therapies for patients with acute ischemic stroke (AIS). It includes complications of non-stroke related interventions such as percutaneous coronary interventions (PCI). Inpatient hemorrhagic stroke is widely regarded as subtype of IHS and has been reported to be less common than ischemic IHS (between 2% and 11% of all IHS)^{9,10}.

Etiology, Risk factors and Outcome

Patients who are hospitalized for cardiac disease are especially vulnerable to IHS⁷. Most ischemic IHS occur on cardiological or cardiosurgical wards¹¹ after coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI)^{9,12} or, more generally, after invasive procedures (70%)¹³. Accordingly, most patients with IHS are hospitalized because of myocardial infarction (MI) or CABG¹⁴.

Stroke etiology according to TOAST criteria¹⁵ is more often reported to be cardioembolic or undetermined in comparison to COS^{12,14}. Inflammation, diabetes, dehydration, hypertension or instable blood-pressure, reduced renal function, reduced left ventricular ejection fraction, newly detected atrial fibrillation and previous MI or stroke have been described as independent risk factors for IHS¹⁶⁻²⁰. Although IHS patients generally have a higher vascular burden³, the dominant etiology of IHS is cardioembolism. This special vulnerability may be the consequence of a general prothrombotic state due to inflammatory reactions and reduced organ function in critically ill patients or of necessary withdrawal of anticoagulation. The high incidence of IHS on cardiological wards suggests that direct injury or interventional manipulation of the heart further enhances the risk of cardioembolism. The closer in time the index event, the higher the IHS risk: four out of five strokes after MI occur during the first five days²¹. The absolute periprocedural or -operative risk to suffer from IHS is about 0.25% in PCI¹⁷, 0.9% after acute coronary events²² and about 1.4% after CABG²³.

Truly iatrogenic IHS due to plaque rupture during PCI or accidental embolisation during cerebral angiography or coiling of aneurysms – approximately 11.8% of all IHS¹¹ – are often difficult to determine, since the interventions themselves enhance the risk for cardioembolism. Most studies refer to the TOAST criteria for stroke etiology, which do not specifically identify iatrogenic causes. Thus, iatrogenic IHS may be underreported.

IHS is associated with unfavorable outcome. The mortality in IHS is higher than in COS, reaching up to 33%¹¹. Stroke after MI or CABG is a serious complication and increases in-hospital mortality significantly^{24,25}. IHS patients are less likely to be discharged home (27.7% (IHS) vs 49.9% (COS)) or to be functionally independent (31.0% (IHS) vs 50.4% (COS))³ and remain hospitalized for a longer time (mean 19.5 (IHS) vs 12.1 days (COS))¹². They are more likely to experience incontinence, dysphagia, a lower level of consciousness and higher grade of motor deficit²⁶. The differences in the course of disease and outcome are foremost attributed to the underlying disease⁵, but also to the greater stroke severity³ and possibly to a higher rate of large vessel occlusions (LVO)¹²) as well as due to delays in treatment.

Diagnosis and Treatment

Despite omission of the pre-hospital phase in IHS, longer time intervals between symptom recognition and start of reperfusion therapy⁹, as well as longer in-hospital delays^{3,12} have been reported. While in COS patients symptoms are usually recognized by spouses or relatives, IHS is most often recognized by medical personnel (80%), especially nurses (64%)¹⁴. In case of an emergency call,

COS are usually taken to the emergency department by emergency medical services, where they are neurologically evaluated and immediately treated²⁷. The COS rescue chain is a well-established multidisciplinary process, which constantly aims to reduce time intervals to ensure early diagnostics and treatment (e.g. pre-hospital notification of the neurologist before admission²⁸). In IHS, however, stroke symptoms are often not recognized as an emergency¹¹ and thus treated with significant delay. Since success of reperfusion treatment is time-dependent²⁹ and must be initiated within the first hours after onset of symptoms, any delay can be detrimental to the patient's outcome⁷.

Besides reliable recognition of stroke symptoms, identification of onset time can be challenging, even in alert and otherwise healthy patients. Critically ill hospitalized patients, however, often are not able to notice and/or to communicate their deficits due to medication and/or underlying illness. Hence, IHS presents with reduced or altered level of consciousness more often than COS^{9,26}. This may impair the neurological evaluation by the attending staff immensely, or render it impossible, even for specialists. Thus, despite professional medical surroundings, uncertainties regarding the time of symptom onset of IHS are frequently reported (20% to 33,5% of patients)^{7,12}. The percentage of IHS with unknown onset is comparable to the one of COS (21% wake-up stroke, 14% unknown onset)³⁰.

Correct and timely diagnosis is furthermore complicated by a high rate of in-hospital stroke mimics. Sudden changes in mental status (most commonly seizures, hypotension or delirium) account for about 50% of suspected IHS^{31,32}. This diagnostic uncertainty surely is in many cases the reason, why IHS workup is not adequate for a potentially treatable emergency¹⁴.

If IHS is recognized in time, various contraindications that are frequently present in hospitals, limit the use of standard reperfusion therapy with intravenous recombinant tissue plasminogen activator (IVRTPA). The most common contraindications are recent major surgery, current and sufficient anticoagulation, recent bleeding or terminal illness^{5,11}. In patients who can receive IVRTPA, however, IVRTPA has been shown to be equally safe in IHS and in COS³. In recent years, endovascular approaches significantly improved the outcome of COS patients with LVO and should be considered whenever possible³³. This holds even more true for IHS, where modern stent-assisted neurothrombectomy is a safe, effective and practicable treatment option^{12,34}.

In COS, specialized neurological treatment on stroke units (SU) is well-established and proven to improve outcome and survival³⁵. IHS are transferred to SU less often than COS^{10,26}. This leads to a lower rate of adequate

secondary prevention, assessment of deficits (e.g. dysphagia) and rehabilitation. Overall, IHS treatment shows lower adherence to treatment guidelines. For example, early use of rtPA, antithrombotic treatment, dysphagia screening and smoking cessation counselling were applied less often³.

Recommended Treatment Approach

Increased awareness, education and training of medical staff are fundamental for timely symptom recognition, especially on (identified) high risk wards, for example cardiological plus intensive and intermediate care units. While general knowledge about stroke symptoms is generally sufficient, specific knowledge about time-dependent treatment options is often lacking³⁶. Educational programs can enhance “code stroke” activations³⁷. Patient with a high risk for IHS should be identified and closely clinically monitored for stroke symptoms (paralysis, numbness, diplopia, vision loss, changes in language and/or speech, non-orthostatic dizziness³⁸). If possible, antithrombotic treatment should be started early (<48h) after MI¹⁸ and paused anticoagulation resumed. After CABG, the risk of early anticoagulation in case of atrial fibrillation, however, seems to outweigh the benefit³⁹.

In case of suspected IHS, we recommend a clearly structured code stroke protocol. Protocol-driven approaches have been shown to significantly improve response times in COS⁴⁰. In IHS, this has been achieved by appointing a specialized stroke response team that could be called by any staff member. By doing so, the median time from symptom recognition to CT could be reduced radically (74min compared to 271min before the implementation)⁴¹. The goal of a protocol-driven approach is to create unambiguous responsibilities and to perform tasks simultaneously instead of sequentially whenever possible (detailed pocket-card by E. Cumber)⁴². If an acute IHS is suspected, we furthermore suggest a CT- rendezvous system¹²: the attending physician immediately contacts a vascular neurologist and neuroradiologist while transporting the patient to the CT and checking the relevant time points, medical history, contraindications against contrast agents and rtPA. The patient then receives a neurological evaluation and multimodal stroke CT at the (neuro-)radiological diagnostic site. In case of IHS, an interdisciplinary decision is then reached and treatment initiated. Due to contraindications against IVRTPA and a high rate of LVO in IHS, endovascular approaches should always be considered, especially in severely affected patients (NIHSS ≥ 7 within 3 hours of symptom onset, NIHSS ≥ 9 within 3-6 hours)⁴³. Hospitals without interventional stroke treatment options need to participate in neurovascular networks and establish pragmatic referral algorithms⁴⁴.

Patients with IHS should, whenever possible, be treated on a SU or neurological ICU. Specialized stroke care is not limited to reperfusion therapy, but includes diagnostics and initiation of secondary prevention, physiotherapy, dysphagia assessment, logopedic treatment, rehabilitation assessment and planning as well as counselling for patients and family members⁴⁵.

For patients undergoing procedures with high IHS-risk, neuromonitoring should be considered. Continuous EEG- and Doppler/Duplex ultrasound monitoring have been shown to effectively detect perioperative brain ischemia during vascular surgery^{46,47}. However, these approaches have not routinely been established in longer-term monitoring due to personnel costs and practical constraints⁴⁸. Continuous EEG has been shown to reduce mortality on ICUs⁴⁹, though, and could potentially overcome the limitations in clinical assessment of sedated and/or ventilated patients.

Conclusion

While generally regarded as the same disease, IHS differs from COS in distribution of etiology, risk factors and treatment options. Certain caveats demand special attention in recognizing and treating IHS. Staff education, a code stroke and CT- rendezvous system, specialized care and therapy and, in some cases, neuromonitoring are recommended to improve quality of care.

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