

Intraventricular Bleeding and Hematoma Size as Predictors of Infection Development in Intracerebral Hemorrhage: A Prospective Cohort Study

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Background: Acute intracerebral hemorrhage (ICH) is associated with increased susceptibility to bacterial infection. The physiopathology of this phenomenon is not very clear. We conducted a prospective observational study investigating the correlation and independent predictors of infections in patients with ICH. **Patients and methods:** Patients admitted between April 1997 and June 2013 with ICH diagnosis were evaluated for inclusion and exclusion criteria. **Results:** Two hundred twenty-two patients were included in this study. Ninety four patients (42.6%) presented with an infection during hospitalization being more common than pneumonia (30%) and urinary tract infections (14%). Intraventricular hemorrhage (IVH) (95% confidence interval [CI], 62.7% versus 39.3%; $P < .001$) and higher ICH score (95% CI, 2.31% versus 1.67%; $P = .0014$) were more common in patients who had infections. We found the following risk factors for having an infection in patients with ICH: IVH (odds ratio [OR] 2.3; 95% CI, 1.3-4.1), each point of ICH score (OR 1.3; 95% CI, 1.1-1.6), and having a hematoma volume larger than 30 cc (OR 2.0; 95% CI, 1.1-3.5). The localization of the hematoma was not found to be relevant. **Conclusions:** ICH score, size of the hematoma, and presence of IVH are independent risk factors for having an infection after ICH. **Key Words:** Intracerebral hemorrhage—ICH—hemorrhagic stroke—stroke inflammation—immune response—infections.

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Introduction

Acute stroke is associated with increased susceptibility to bacterial infection,¹ pulmonary and urinary tract infections being the most frequent, with a prevalence of up to 33% during the acute phase of the stroke.² Pneumonia accounts for almost 20% of in-hospital deaths and poor outcomes at discharge.³ Nearly all pneumonias occur

within the first week after stroke.⁴ The physiopathology of this phenomenon is not very clear. Impairment of consciousness and reduced bulbar reflex facilitate aspiration and are responsible for most pneumonias in stroke patients. However, there is increasing evidence that this is not the only mechanism; a transient immunodeficiency syndrome encompassing innate and adaptive immune cells has been observed in murine large ischemic stroke models and extensive damage in stroke patients.⁵

Experimental mice stroke models and large clinical series have shown an association with the development of infections within 24 hours after stroke, leading to high mortality.⁶ Infections are preceded by a rapid suppression of peripheral cellular immune responses, which is mainly characterized by lymphocyte apoptosis and altered lymphocytic cytokine production.^{5,7}

Intracerebral hemorrhage (ICH) accounts for 15%-25% of acute stroke. About 20% of patients suffering from a

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large intracerebral hematoma die within 30 days after ICH as a consequence of pneumonia or sepsis.⁸ There are few studies characterizing the systemic immune response after ICH, all of them in animal experimental models.⁹

Although the characteristics of hematoma in ICH such as size, localization, and ventricular drainage are associated with global prognosis,¹⁰ there are only a few studies investigating these variables and the risk of infection.¹¹ It is possible that the characteristics of the hematoma are determinant in both neurological impairment and immunosuppression syndrome, and could be related to the risk of infection after an ICH. We conducted a prospective observational study investigating the correlation and independent predictors of infections in patients with ICH.

Patients and Methods

Clínica Alemana is a teaching nonprofit private hospital of 350 beds in the Northeast of Santiago, Chile. Patients with suspected stroke are rapidly evaluated by a neurologist on call and a stroke fellow. Acute neurological assessment includes a neuroimaging protocol consisting of a noncontrast computed tomography (CT) scan and brain computed tomography angiography (CTA) or magnetic resonance angiography (MRA). CTA is offered to and performed in all patients without contraindications such as known allergies to iodized contrast mediums or renal failure. If CTA is contraindicated, patients undergo MRA.

After acute neurological assessment, patients are admitted in a stroke unit and followed up by a vascular neurologist. All patients are evaluated by a speech therapist before they receive oral feeding. Patients with trouble swallowing are fed by enteral route and are followed up by the speech therapy team until they can be fed by oral route or when the patient has had a gastrostomy in the more severe cases. Patients also receive physiotherapy within 24 hours of being admitted.

The data for this study were extracted from the Clínica Alemana Acute Stroke Registry (RECCA). RECCA is a prospectively database kept since 1997 in our institution for quality control of the Stroke Program and includes clinical assessment (National Institutes of Health Stroke Scale [NIHSS]), neuroimaging (brain CT, CTA or MRA, diffusion-weighted imaging–magnetic resonance imaging, and digital subtraction angiography), time from symptom onset, affected vascular territory, risk factors, treatments, complications, and outcome. All data were collected before the present study was planned.

Participants and Variables

All consecutive patients with acute nontraumatic ICH admitted to Clínica Alemana de Santiago between November 1997 and August 2013 were evaluated to determine whether they meet inclusion and exclusion criteria. Inclusion criteria for the present study were all consecutive patients with a clinical syndrome of stroke and brain CT

compatible with ICH. Exclusion criteria were patients without complete data. ICH was diagnosed in patients with history, clinical examination results, and evolution typical of focal vascular brain damage with signs of brain hemorrhage on CT scan.

Prespecified variables included in the analysis were age, sex, hematoma characteristics such as size, localization, ventricular drainage, and ICH score.¹²

CTA scans were obtained with a multislice CT scanner Siemens Somatom Definition AS 128 (Erlangen, Germany) channels. Images were analyzed by a neuroradiologist. Volume was calculated from the first CT scan using the $A \times B \times C \times .5$ method.¹³ Each patient was followed up by a second CT scan 24–36 hours after being admitted.

Infection was defined by the combination of the following 2 criteria during in-hospital stay: (1) presence of suggestive clinical and laboratory or radiological signs of infection (e.g., urinary tract symptoms, productive cough, pleuritic pain, dyspnea, tachypnea, fever, cultures positive for a pathogen, leukopenia [$<4/L$] or leukocytosis [$>12/L$], and chest X-ray infiltrate) and (2) serum C-reactive protein level of more than 40 mg/mL.

Standard Protocol Approval, Registrations, and Patient Consent

All aspects of the RECCA registry have been approved by the Ethics Committee of Universidad del Desarrollo—Clínica Alemana de Santiago prior to the initiation of the research. The Ethics Committee is the institutional review board of both institutions.

Analysis

The present study is reported according to the STROBE initiative. The cases were divided into 2 groups, depending on whether or not they had an infection during their hospitalization, and were compared for clinical, laboratory, and radiological variables in univariate analysis. Chi-square and Student *t*-test analyses were performed when appropriate and 95% confidence intervals (CIs) were obtained.¹⁴ Multivariate logistic regression with 95% CIs was performed to investigate independent risk factors associated with an infection during the hospitalization in these patients.

Results

Between November 1997 and August 2013, 309 patients with a suspected ICH were admitted in our center of which 221 met the inclusion criteria. The general characteristics of the patient population are shown in Table 1. Ninety-four patients (42.6%) presented with an infection during hospitalization being more common than pneumonia (30%) and urinary tract infections (14%). As shown in Table 2 where we compared the 2 groups,

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