

PROGNOSTIC FACTORS IN INTRACEREBRAL HAEMORRHAGE: A PROSPECTIVE OBSERVATIONAL STUDY FROM A REGIONAL STROKE CENTRE

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Abstract

Background: Intracerebral haemorrhage remains one of the most devastating subtypes of stroke, associated with high early mortality and long-term disability. Identifying prognostic factors may help improve early management, guide therapeutic decisions, and optimise follow-up strategies. **Methods:** We conducted a prospective observational study including all consecutive patients aged ≥ 15 years admitted for ICH to the Neurology Department of the Sétif University Hospital, a regional tertiary care centre. Both primary and secondary forms were considered. Clinical, biological, and neuroimaging data were collected prospectively using a standardised case-report form. Patients with isolated subarachnoid haemorrhage were excluded, whereas those with ICH associated with subarachnoid extension were included. Prognostic factors were assessed at 30 days (vital prognosis) and at 2 years (vital and functional outcome) using univariate and multivariate logistic regression analyses. **Results:** A total of 157 patients were included (54.1% men, 45.9% women). Mean age was 56.5 ± 18.5 years. At 30 days, mortality reached 22.4%. Univariate analysis identified significant associations between early mortality and age 50-79 years, diabetes, renal impairment, decreased Glasgow Coma Scale (GCS) score, higher NIHSS, severe disability (mRS 4-5), larger haematoma volume, intraventricular extension, perihemorrhagic oedema, haematoma heterogeneity, and hyperleucocytosis. In multivariate analysis, independent predictors of 30-day mortality were age 50-79 years, $GCS \leq 10$, ICH score, and hyperleucocytosis. At 2 years, poor outcomes (severe disability or death) were independently predicted by age ≥ 80 years, infection, and the use of antithrombotic drugs. Among survivors, persistent severe disability at 2 years was linked to infection and elevated admission blood glucose levels. **Conclusion:** Short-term mortality in ICH is mainly influenced by initial neurological severity, radiological extent, and systemic inflammatory response, whereas long-term outcomes depend largely on age, infection, and treatment-related factors. These results highlight the need for early infection control, close metabolic monitoring, and stratified management protocols to improve functional recovery.

Keywords: Intracerebral haemorrhage, prognostic factors, mortality, disability, outcome prediction.

1. Introduction

Intracerebral haemorrhage (ICH) is defined as bleeding within the brain parenchyma (intraparenchymal haemorrhage, HIP) or within the ventricular system (intraventricular haemorrhage, HIV). These entities, together with subarachnoid haemorrhage, comprise the broader category of cerebral haemorrhages, which are distinct from extra-cerebral haemorrhages such as subdural or epidural haematomas.

ICH represents approximately 10-15% of all strokes but accounts for a disproportionate share of stroke-related morbidity and mortality [1-3]. Despite advances in neuroimaging and intensive care, case fatality remains high, with up to

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40% of patients dying within the first month and more than half of survivors remaining functionally dependent [4-6].

The pathophysiology of ICH involves rupture of small penetrating arteries, most often due to chronic hypertension, cerebral amyloid angiopathy, or vascular malformations [7,8].

The prognosis of ICH depends on multiple factors encompassing clinical, radiological, and biochemical domains. Acute haematoma expansion, perihæmatomal oedema, and secondary metabolic or infectious complications contribute to the poor prognosis [9]. Previous studies conducted in Western and Asian populations have focused on predictive parameters such as age, initial neurological status including GCS score at admission, haematoma volume and location, intraventricular extension, and comorbid conditions such as diabetes or renal impairment [10,11]. However, data from North African populations remain limited, and regional variability may influence the distribution of risk factors and outcomes.

The present study aimed to evaluate the short- and long-term prognostic factors of ICH in a large cohort managed in a regional stroke centre. By analysing both vital and functional outcomes over a two-year follow-up period, this work provides an integrated view of early and late determinants of prognosis, combining clinical, imaging, and biological parameters.

2. Patients and methods

Study design and setting

This was a prospective, descriptive, and observational study conducted in the Neurology Department of a regional university-affiliated stroke centre.

Inclusion and exclusion criteria

All consecutive patients aged 15 years or older who were admitted with a new diagnosis of intracerebral haemorrhage confirmed by neuroimaging were prospectively included. Both primary and secondary forms of intracerebral haemorrhage were considered.

Included cases comprised pure intraparenchymal haemorrhages, intraventricular haemorrhages (IVH), and mixed cerebro-meningeal haemorrhages (i.e. intracerebral haemorrhage with subarachnoid extension). Cases of haemorrhagic transformation of cerebral infarction that presented initially as ICH were included too.

Excluded cases were isolated subarachnoid haemorrhages (SAH) without parenchymal involvement, subdural or epidural haematomas.

Patients lost to follow-up were excluded from long-term prognostic analyses.

For the long-term outcome analysis, only patients with pure intraparenchymal haemorrhage were considered, as the parameters assessed were not applicable to isolated intraventricular haemorrhage.

Data collection

Clinical, biological, and neuroimaging data were collected prospectively using a standardised case-report form.

The clinical evaluation at admission included:

- Demographic data: age and sex.
- Past medical history and Comorbidities (hypertension, diabetes mellitus, renal impairment, concurrent infection, smoking, and alcohol use).

- Medication use prior to admission: antiplatelet agents, vitamin K antagonists, low-molecular-weight heparin (LMWH), and statins.
- Neurological presentation: syndrome of ICH, seizure, fever.
- Neurological scores at admission: Glasgow Coma Scale (GCS), National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), and the ICH score according to Hemphill et al.

Neuroimaging assessment

Brain CT or MRI performed at admission was reviewed by senior neurologists and radiologists. The following parameters were systematically recorded: haematoma volume (ABC/2 method) and location, presence of intraventricular extension, presence of perihemorrhagic oedema, haematoma heterogeneity and/or irregularity, and associated hydrocephalus.

Biological investigations

Laboratory data at admission included serum glucose, renal function tests, electrolytes, and complete blood count. Hyperleucocytosis, hyponatraemia, and hyperglycaemia were defined according to standard clinical thresholds.

Outcome measures

Prognostic evaluation focused on two endpoints:

1. Short-term (30-day) vital prognosis: defined by mortality within 30 days of admission related to the hemorrhagic event.
2. Long-term (2-year) vital and functional prognosis: defined by the combined outcome of death or severe disability (mRS 4-6) among survivors.

Patients who died from unrelated causes were excluded from the prognostic analyses. Functional outcome at two years was assessed through follow-up clinical evaluations.

Statistical analysis

Quantitative variables were expressed as mean \pm standard deviation or median (IQR), and categorical variables as frequencies and percentages. Comparisons between groups (survivors vs. non-survivors, favourable vs. unfavourable outcome) were performed using χ^2 or Fisher's exact tests for categorical variables and Student's t-test or Mann-Whitney test for continuous variables.

All variables significantly associated with outcome in univariate analysis ($p < 0.05$) were included in a stepwise multivariate logistic regression to identify independent predictors. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS software.

3. Results

General findings

During the study period, 614 patients were hospitalised for stroke, representing 43% of all admissions in the Neurology Department. Among them, 201 cases (32.7%) were hemorrhagic strokes. Intracerebral hemorrhage (ICH) accounted for 78% (157 patients) of these hemorrhagic events, whereas 22% (44 patients) were subarachnoid hemorrhages.

The cohort included 157 patients with ICH: 85 men (54.1%) and 72 women (45.9%), with a mean age of 56.5 ± 18.5 years. Hypertension was present in 108 patients (68.8%), diabetes in 52 (33.1%) of which 21 (13.4%) were newly diagnosed. Renal impairment was noted in 18 patients (11.5%), including 15 (9.6%) with acute renal failure on admission.

Short-term outcome (30-day mortality)

Thirty-day mortality reached 22.4% (35 deaths). Among the remaining patients, 121 were alive at one month, and only one case was lost to follow-up.

Univariate analysis identified the following variables significantly associated with 30-day mortality (Table 1.):

- Age: 50-79 years (OR 2.62, 95% CI 1.18-5.82, $p = 0.016$); age 20-49 was protective (OR 0.22, 95% CI 0.08-0.61, $p = 0.002$).
- Comorbidities: diabetes (OR 2.95, $p = 0.005$); renal impairment (OR 5.65, $p < 0.001$).
- Neurological status: GCS <15 (OR 4.71, $p < 0.001$); GCS ≤ 10 (OR 7.37, $p < 0.001$).
- Functional and stroke severity scales: mRS 4-5 at admission (OR 4.35, $p < 0.001$); higher NIHSS ($p < 0.001$); higher ICH score ($p < 0.001$).
- Imaging features: haematoma volume ≥ 30 ml ($p = 0.018$), intraventricular extension (OR 3.33, $p = 0.002$), perihemorrhagic oedema (OR 2.36, $p = 0.038$), haematoma heterogeneity (OR 2.45, $p = 0.027$), and combined heterogeneity + irregularity (OR 2.83, $p = 0.013$).
- Biological parameters: hyperleucocytosis (OR 8.69, $p = 0.001$).

Table 1. Summarises the main predictors of 30-day mortality

Variable	OR (95% CI)	p-value
Age 50-79 years	2.62 (1.18-5.82)	0.016
Renal impairment	5.65 (2.02-15.76)	<0.001
GCS ≤ 10	7.37 (2.71-20.05)	<0.001
ICH score ≥ 3	6.05 (1.60-22.91)	0.009
Intraventricular extension	3.33 (1.50-7.40)	0.002

In multivariate analysis, four independent predictors of early mortality were identified (Nagelkerke $R^2 = 0.413$):

1. Age 50-79 years
2. GCS ≤ 10 on admission
3. ICH score
4. Hyperleucocytosis

Long-term (2-year) outcome

Of the 157 patients initially included in the study, 3 were lost to follow-up and 35 died within the first 30 days. Because the parameters assessed were not applicable to isolated intraventricular haemorrhages, the long-term outcome analysis was restricted to 115 patients with pure intraparenchymal haemorrhage, after exclusion of 5 cases of isolated intraventricular haemorrhage (one of whom died during the first month). Seventeen additional deaths occurred during follow-up, giving a cumulative mortality of 33.1%. Among survivors, 65% were functionally independent (mRS ≤ 3).

Univariate analysis revealed that poor outcome at 2 years (death or severe disability) was significantly associated with:

- Age ≥ 80 years (OR 6.13, 95% CI 1.78-21.09, $p = 0.002$)
- Infection (OR 5.33, 95% CI 1.79-15.90, $p = 0.001$)
- Use of ≥ 1 antithrombotic drug (OR 3.38, 95% CI 1.08-10.58, $p = 0.029$)
- Use of LMWH ($p = 0.024$)

Nineteen clinical, biological, and radiological variables were tested in the univariate analysis. No significant association was found for the other factors, including sex, hypertension, diabetes, renal impairment, smoking, alcohol intake,

haematoma volume, initial GCS, NIHSS score, ICH score, hyponatraemia, or other metabolic parameters at admission.

Multivariate analysis (Nagelkerke $R^2 = 0.293$) confirmed three independent predictors of poor long-term outcome:

1. Age ≥ 80 years
2. Infection
3. Antithrombotic therapy at admission

Table 2. Predictors of poor 2-year vital and functional outcomes

Variable	OR (95% CI)	p-value
Age ≥ 80 years	6.13 (1.78-21.09)	0.002
Infection	5.33 (1.79-15.90)	0.001
Antithrombotic therapy	3.38 (1.08-10.58)	0.029

Functional outcome among survivors (2-year disability)

When only survivors were analysed ($n = 102$), poor functional outcome was significantly associated, in univariate analysis, with an admission mRS score of 4-5 (100% vs. 31%, $p = 0.039$) and with in-hospital infection (100% vs. 12%, $p = 0.018$).

In multivariate regression, only infection and elevated blood glucose on admission remained independently associated with severe disability at 2 years (Nagelkerke $R^2 = 0.678$), while none of the initial severity scores (GCS, NIHSS, ICH, mRS) maintained significance.

Summary of prognostic factors

- **30-day mortality:** age 50-79, low GCS, high ICH score, hyperleucocytosis
- **2-year poor outcome:** age ≥ 80 , infection, antithrombotic therapy
- **2-year severe disability (survivors):** infection, hyperglycaemia

4. Discussions

Main findings

This prospective observational study identified several clinical, biological, and radiological factors associated with short- and long-term outcomes following intracerebral haemorrhage (ICH).

At 30 days, mortality was determined mainly by neurological severity (low GCS, high ICH score), inflammatory response (hyperleucocytosis), and age between 50 and 79 years.

At two years, adverse outcomes were independently predicted by older age (≥ 80 years), infection, and the use of antithrombotic therapy, while persistent disability among survivors was linked to infection and elevated blood glucose levels.

These findings emphasise a temporal evolution in prognostic determinants: acute outcomes reflect early neurological injury and systemic inflammation, whereas long-term disability and death are more strongly influenced by age and secondary complications.

Short-term prognosis (30-day mortality)

The 30-day mortality rate in this cohort (22.4%) aligns with values reported in the literature, ranging from 20% to 40%. As in most studies, early death was closely associated with the severity of the initial haemorrhage, reflected by depressed consciousness, higher ICH score, and radiological markers of lesion volume and intraventricular spread.

- o Age has been consistently recognised as an independent determinant of ICH outcome. In this series, mortality was significantly increased in the 50-79-year

group but not in those aged ≥ 80 , likely due to the smaller number of very elderly patients and selection bias related to hospital admission. Similar age-related risks have been described by Sacco *et al.* and Fawaz *et al.*, who reported adjusted ORs between 1.1 and 1.3 per decade of life.

- Comorbidities, particularly diabetes and renal impairment, contributed to poor early prognosis. Hyperglycaemia at admission, although not statistically significant in multivariate analysis, is known to exacerbate haematoma expansion and secondary metabolic stress. The strong correlation between renal impairment and 30-day death (OR 5.6) corroborates findings from previous cohorts, where chronic kidney disease was associated with increased brain oedema and altered autoregulation.
- Neurological scores at admission were powerful prognostic markers. A GCS ≤ 10 multiplied the risk of early death sevenfold, confirming the role of consciousness level as a core component of the ICH score. The mRS at admission also correlated with early mortality, reflecting the impact of pre-existing disability on acute tolerance to cerebral injury.
- Radiological predictors such as haematoma volume, intraventricular extension, perihemorrhagic oedema, and haematoma heterogeneity have been widely validated as markers of mass effect and ongoing bleeding. In this study, haematoma irregularity alone was not predictive, whereas combined heterogeneity and irregularity were. These features may correspond to unstable haematomas at risk of secondary expansion, as reported by Sporns *et al.* and Li *et al.*
- Inflammatory response, expressed as hyperleucocytosis, emerged as one of the most powerful predictors of early mortality (OR 8.7). This supports the hypothesis that systemic inflammation aggravates secondary brain injury via cytokine release and endothelial dysfunction.

Long-term outcome

At two years, one-third of the cohort had died and another proportion remained severely disabled. Prognostic determinants differed markedly from those observed in the acute phase.

- Age ≥ 80 years was a strong predictor of poor long-term outcome, consistent with previous evidence that neuroplastic recovery declines with age.
- Infection was the most important modifiable long-term factor. It multiplied the risk of death or severe disability fivefold and was also independently associated with chronic disability among survivors. Infection may exacerbate systemic inflammation, induce secondary metabolic stress, and delay neurological rehabilitation. Early detection and aggressive management of infectious complications could thus improve survival and functional recovery.
- Antithrombotic therapy was another independent factor related to poor long-term prognosis. This association may reflect both the higher comorbidity burden of treated patients and potential rebleeding risk. While antiplatelet agents are often resumed after ICH for cardiovascular prevention, their impact on long-term outcomes remains controversial.

Among survivors, the combination of infection and hyperglycaemia predicted persistent severe disability. The latter finding, although not systematically reported in other series, may be explained by microvascular impairment, oxidative stress, and recurrent neurological insults in diabetic or stress-hyperglycaemic patients.

Comparison with the literature

The identified determinants in this study are generally consistent with previous large-scale studies, including those of Hemphill *et al.* (ICH score) [1], Qureshi *et al.* (volume and intraventricular extension) [5, 12], and Fogelholm *et al.* (hyperglycaemia) [9]. However, some discrepancies emerged.

In our cohort, hyponatraemia was not significantly related to mortality, unlike findings by Amor *et al.* in a Moroccan population [10], possibly due to the lower number of critical care patients in our series.

The 30-day mortality observed in our study for patients with high ICH scores (3–4) was lower than that reported in some large-scale international series, including the original Hemphill model [1], where mortality may exceed 35–40%. Several factors may account for this: exclusion of pre-hospital deaths, transfer of the most severe patients directly to intensive care units, and variations in pre-hospital accessibility and emergency management.

Methodological limitations

This study has several limitations.

First, despite its prospective design, it was conducted in a single regional centre, which may limit the generalisability of the results.

Second, although follow-up was complete for most patients, three were lost to follow-up, and post-discharge care variability could have influenced long-term outcomes.

Third, the study did not include very early radiological follow-up to assess haematoma expansion, which is now recognised as a strong predictor of mortality.

In addition, the main limitation of this study lies in the recruitment process itself. ICH is a potentially fatal condition, with early mortality reaching 20–30% within the first 48 hours and up to 40–50% at 30 days according to the literature [12,13]. Consequently, our series did not include patients who may have died before hospital admission, those admitted directly to the intensive care unit, or those managed in other healthcare facilities within the region. This selection bias may partly explain the relatively low mortality observed in our cohort, although this hypothesis remains to be verified.

In reality, the number of cerebral haemorrhages admitted to the intensive care unit during the same period, as well as the number of patients who died before reaching hospital, remains unknown. In high-income countries, pre-hospital mortality for spontaneous intracerebral haemorrhage is estimated at around 15%. Therefore, the possibility that the ICH cases included in our study were less severe than those reported elsewhere cannot be excluded and should be explored in future, more comprehensive studies encompassing all patients with ICH.

Nonetheless, the present series remains one of the most comprehensive and longest prospective follow-ups of ICH patients reported from the region.

Clinical implications

Our findings reinforce several key points for clinical practice:

1. Initial neurological assessment (GCS, ICH score) remains the cornerstone of early prognostic evaluation.
2. Systemic inflammation and metabolic instability (leucocytosis, hyperglycaemia) are potential therapeutic targets.
3. Infection control and metabolic monitoring should be systematically integrated into long-term management to improve recovery and survival.
4. Elderly patients deserve tailored rehabilitation strategies and careful reassessment of antithrombotic therapy indications after the acute phase.

Conclusion

This prospective observational study highlights the multifactorial nature of prognosis in intracerebral haemorrhage. Short-term mortality is mainly determined by the initial neurological severity, haematoma burden, and early inflammatory response, whereas long-term outcomes are driven by age, infection, and treatment-related factors.

Among survivors, infection and hyperglycaemia emerge as major modifiable predictors of persistent disability.

These findings emphasise the importance of comprehensive, multidisciplinary management that integrates early control of infection, metabolic monitoring, and tailored rehabilitation. The results also underline the need for predictive models adapted to regional settings, accounting for local epidemiology and healthcare resources.

Although single-centre in design, this study provides valuable insights into the determinants of both early and late outcomes in ICH and supports the implementation of systematic prognostic assessment in clinical practice.

Conflicts of interest

The authors state that they have no competing interests.

References

- [1] Hemphill JC, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral haemorrhage. *Stroke*. 2001;32(4):891–897.
- [2] Sacco S, Marini C, Toni D, Olivieri L, Carolei A. Incidence and 10-year survival of intracerebral haemorrhage in a population-based registry. *Stroke*. 2009;40(2):394–399.
- [3] Fawaz NA, Al-Mohammed AA, Al-Sultan AI, et al. Predictors of 30-day mortality after spontaneous intracerebral hemorrhage. *Neurosciences (Riyadh)*. 2014;19(2):108–112.
- [4] González-Pérez A, Gaist D, Wallander MA, McFeat G, García Rodríguez LA. Mortality after hemorrhagic stroke: data from general practice (The Health Improvement Network). *Neurology*. 2013;81(6):559–565.
- [5] Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. *Lancet*. 2009;373(9675):1632–1644.
- [6] Sporns PB, Schwake M, Kemmling A, et al. Heterogeneity of intracerebral hemorrhage: a marker of ongoing bleeding. *Stroke*. 2017;48(4):1120–1125.
- [7] Li Q, Zhang G, Huang YJ, et al. Blend sign on computed tomography: novel and reliable predictor for early hematoma growth in patients with intracerebral hemorrhage. *Stroke*. 2015;46(8):2119–2123.
- [8] Guo X, He Y, Wang H, et al. Admission hyperglycemia is associated with poor outcomes after intracerebral hemorrhage. *J Neurol Sci*. 2014;347(1–2):106–111.
- [9] Fogelholm R, Murros K, Rissanen A, Avikainen S. Admission blood glucose and short-term survival in primary intracerebral haemorrhage. *Acta Neurol Scand*. 2005;112(2):133–138.
- [10] Amor M, El Alaoui Faris M, Chraa M, et al. Hyponatremia as an independent predictor of mortality in intracerebral hemorrhage: a Moroccan experience. *Pan Afr Med J*. 2017;26:108.
- [11] Specogna AV, Turin TC, Patten SB, Hill MD. Factors associated with early deterioration after spontaneous intracerebral hemorrhage: a systematic review and meta-analysis. *PLoS One*. 2014;9(5):e96743.
- [12] Qureshi AI, Tuhim S, Broderick JP, et al. Spontaneous intracerebral hemorrhage. *N Engl J Med*. 2001;344(19):1450–1460.
- [13] van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin. *Lancet Neurol*. 2010;9(2):167–176.