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Journal of Brain and Neurological Disorders

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Research Article

Frequency and Factors Associated with Symptomatic Hemorrhagic Transformation in the Acute Phase of Cerebral Infarctions in the Ouagadougou University Hospitals in Burkina Faso

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Received Date: September 21, 2024 | **Accepted Date:** October 17, 2024 | **Published Date:** October 25, 2024

Citation: Lompo D. Labodi, Kere M. Fabienne, Zoungrana Alassane, Gnampa Melody Z, Napon Christian, et al., (2024). Frequency and factors associated with symptomatic hemorrhagic transformation in the acute phase of cerebral infarctions in the Ouagadougou University Hospitals in Burkina Faso, *J. Brain and Neurological Disorders*, 7(3): **DOI:10.31579/2642-973X/122**

Abstract

Background/Aim: Hemorrhagic transformation (HT) of cerebral infarction (CI) is one of the complications arising in the acute phase of CI, which significantly increases mortality and worsens the functional prognosis of patients. However, the HT of CI is little studied in our context. The aim of our study was to assess the frequency and identify the factors associated with HT in the acute phase of CI in the university hospitals (UH) of Ouagadougou in Burkina Faso.

Materials and Methods: It was a descriptive and analytical cross-sectional study, with prospective data collection, of HT in the acute phase of CI in Ouagadougou's teaching hospitals (UH Yalgado Ouédraogo, UH-Tingandogo, UH-Bogodogo), from July 1, 2022 to September 30, 2022.

Patients aged over16 years were included, admitted to the 3 UHs for CI diagnosed on CT and/or MRI and dating back no more than 24 hours, during the study phase. Symptomatic hemorrhagic transformation (SHT) was diagnosed at follow-up CT performed as part of the investigation of neurological deterioration, corresponding to a recent increase in baseline neurological deficit ≥ 4 points at initial NIHSS. The frequency, clinical, paraclinical and evolutionary data of CI with SHT were described. Univariate and then multivariate analysis with Cox logistic regression identified sociodemographic, clinical and paraclinical characteristics independently associated with the occurrence of SHT, with p value < 0.05.

Results: Twenty-one (21) patients presented with SHT out of a total of 211, representing a frequency of 9.9% with a M/F sex ratio of 1.1. The mean age of patients was 58.7 years (±19.6 years). Increased neurological deficit was the main clinical feature of SHT, with 13 cases (61.9 %). The CI was large in 9 patients (42.9%); mass effect in 17 cases (80.9%), extensive cerebral edema with 12 cases (57.1%) were the main associated neuroradiological abnormalities. The in-hospital mortality rate was 61.9%. The variables independently associated with the occurrence of SHT, present at admission, identified were: history of diabetes (OR=1.27; p=0.001), initial severe neurological deficit (NIHSS≥ 17) (OR=1.41; p=0.041), hyperglycemia on admission (OR=2.31; p=0.004); large CI on admission (OR=12.4; p=0.0001), brain involvement on admission (OR=10.61; p=0.001), extensive cerebral edema on admission (OR=29.0; p=10-4); cardio-embolic etiology of the CI (OR=2.23; p=0.013).

Conclusion: SHT complicates 1 in 10 CI in the hospital phase, and is associated with an appalling prognosis, with death in 3/5 of patients and loss of autonomy in most survivors. Markers of early CI severity, initial hyperglycemia and cardioembolic etiology are the risk factors for its occurrence. The establishment of dedicated stroke care networks, the implementation of stroke units, and the availability of thrombolysis and mechanical thrombectomy in our hospitals, would contribute to improving the vital and functional prognosis of stroke patients.

Key Words: cerebral infarction; symptomatic hemorrhagic transformation; in-hospital mortality; risk factors; ouagadougou

Introduction

Hemorrhagic transformation is a fairly frequent complication of CI. It may be symptomatic, manifesting clinically as worsening neurological deficit, impaired alertness or headache, or asymptomatic **[1].** It is diagnosed by neuroimaging (brain CT or MRI). Its mechanism may involve the influence of reperfusion (revascularization of an occluded vessel, involvement of pie-meridian anastomoses, blood-endothelium interaction), vascular rupture, the size of the ischemia, but also an increased blood pressure, the type of embolus (infective endocarditis), age, antithrombotic treatment (antiplatelet aggregator, anticoagulant or fibrinolytic) **[2, 3].** According to a Western series, the incidence of HT in the post-CI is variously reported depending on whether it is spontaneous or induced by intravenous recombinant tissue plasminogen activator (rtPA), asymptomatic or symptomatic: 4.5% to 39.6% for asymptomatic HT and 5.2% to 7.3% for symptomatic HT (SHT), for CI after fibrinolysis with rtPA. In contrast, for spontaneous HT, the rates of asymptomatic HT and SHT varied respectively from 13% to 43% and from 0.6% to 20 **% [4].** HT is one of the most serious and fatal complications of CI. It increases the risk of death and disability post-CI, multiplying the risk of death by 8 **[2, 3, 5, 6].** To our knowledge, no study has yet focused on HT in the acute phase of CI in sub-Saharan Africa, specifically in Burkina Faso. We are therefore carrying out the present inaugural study to assess the frequency and identify the factors associated with SHT in CI in Ouagadougou, through a prospective cross-sectional hospital study. Given the high morbidity and mortality of CI, particularly in sub-Saharan Africa and Burkina Faso, the identification of risk factors for SHT could help improve patients prognosis.

Matérials and Methods

It was a descriptive and analytical cross-sectional study, with prospective data collection, of SHT in the acute phase of CI in the university hospitals of Ouagadougou (UH Yalgado Ouédraogo, UH Tengandogo, UH Bogodogo), inBurkina Faso, conducted over 3 months, from July 1 to September 30, 2022. Our study population was made up of patients aged over 16 years, admitted to the said UH for recent CI dating back no more than 24 hours, diagnosed on cerebral CT performed no more than 12 hours after admission, then followed up throughout the hospitalization phase and reviewed at least 3 months after the occurrence of the stroke, having given their consent to participate in the study or consent obtained from the family (patients with aphasia, impaired vigilance, or non-lucid). Not included in our study were patients who died on arrival, patients whose CIs were more than 24 hours old at the time of hospitalization, patients who did not undergo neuroimaging or whose diagnostic neuroimaging was performed more than 12 hours after admission, patients aged <16 years, patients for whom consent was not obtained. Depending on the clinical situation, some patients were treated with anti-platelet agregation monotherapy to prevent recurrence of CI and with low-molecular-weight heparin (LMWH) in isocoagulant doses to prevent venous thromboembolic complications, while others received anticoagulant treatment with LMWH followed by vitamin K anticoagulant (VKA) or direct oral anticoagulants (DAO) in hypocoagulant doses, particularly CI of cardio-embolic origin. No patient was treated with thrombolytics or mechanical thrombectomy.

HT was defined as any degree of spontaneous hemorrhagic-type hyperdensity observed within the area of hypodensity on brain CT corresponding to IC. HT was classified as hemorrhagic CI (HCI) or intra-CI parenchymal hemorrhage (intra-CIPH). HCI was defined by the presence of small hemorrhagic petechiae along the margins of the CI (HCI-1) or by the presence of more confluent hemorrhagic petechiae within the CI but without mass effect (HCI-2). Intra-CIPH was subdivided into hemorrhage occupying less than 30% of the infarcted cerebral area with mild mass effect (Intra-CIPH-1) or hemorrhage occupying 30% or more of the infarcted cerebral area with significant mass effect (Intra-CIPH -2) [7].

SHT of CI was diagnosed by the demonstration of ICH (ICH-1 or ICH-2) or Intra-CIPH (Intra-CIPH-1 or Intra-CIPH-2) on follow-up brain CT, performed as part of the investigation of neurological deterioration (ND) corresponding to a permanent increase in baseline neurological deficit (≥4 points on baseline NIHSS), appeared during hospitalization, after exclusion of other possible causes of ND (post-critical neurological deficit, major metabolic disorders, additional infectious syndrome, etc.). The time to onset of SHT was defined as the time elapsed between the onset of CI and the onset of persistent HT-related DN. [8]

For all patients meeting the inclusion criteria [7, 8], a cerebral CT scan was rapidly performed on admission and interpreted jointly by radiologists and neurologists. Admission times, vascular risk factors (VRFs) and comorbidities were systematically recorded, as were blood pressure (BP), temperature and oxygen saturation. Initial neurological and general clinical evaluation by a senior neurologist, a standard ECG, initial biological exams (blood glucose, creatinine, blood count, blood ionogram, protidemia), blood lipid exams (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides), a transthoracic cardiac ultrasound and, if necessary, a 24-hour ECG holter, were also carried out.

Other complementary examinations were carried out on a case-by-case basis : standard chest X-ray if bronchopneumonia was suspected, repeat metabolic examinations to monitor the treatment of any metabolic disorders, thick blood drop (SG) if malaria was suspected, urine cytobacteriological examination (UCBE) if urinary tract infection was suspected, blood culture if sepsis was suspected. Patients were monitored on a daily basis during hospitalization, by means of a clinical assessment, possibly supported by additional tests on a case-by-case basis, and any complications were regularly recorded in the medical record until the end of hospitalization.

After discharge, patients were seen in a neurology outpatient clinic to assess their clinical outcome at 1 and 3 months post-stroke ; for those who could not be seen again for various reasons (lost to follow-up, deceased, intercurrent conditions, etc.), information on clinical outcome was obtained by telephone and/or by a visit to the patient's home or to the re-hospitalization health service, etc. Complications sought included those observed on admission or which appeared during hospitalization. On discharge, patients were subdivided according to discharge status, into surviving and deceased patients. Patients were managed according to revised ESO 2009 guidelines. Intravenous fibrinolysis or mechanical thrombectomy were not available.

Operational definitions :

The National Institute of Health Stroke Scale (NIHSS) was used to assess the clinical severity of stroke in the acute phase of stroke (NIHSS ≤ 4 : mild neurological deficit; NIHSS between 5 and 14: moderate neurological deficit; NIHSS between 15 and 20: severe neurological deficit; NIHSS > 20: very severe neurological deficit) [9].

The modified Rankin score (mRS) was used to assess post-stroke functional outcome (mRS 0 -2 : autonomy or independence; mRS 3 - 5: moderate to severe or major disability; mRS 6: patient deceased) [10, 11].

The Glasgow score was used to assess alertness (≤ 8 : coma ; 9 -14 : impaired alertness; 15: normal alertness).

The CI was classified on cerebral CT as small CI if the ischemic lesion involved less than half a cerebral lobe or was located in the brain stem ; medium CI if the ischemic lesion involved half a lobe or a cerebral lobe or the brain stem or a cerebellar hemisphere; large CI when the ischemic lesion involved more than one cerebral lobe [12].

The variable of interest was the occurrence of SHT during hospitalization designated as the acute phase of CI, confirmed on brain imaging.

The explanatory variables were :

- Sociodemographics: age, gender, occupation, marital status
- Clinical : vascular risk factors, comorbidities, admission time, state of alertness on admission (Glasgow score), constants on admission (temperature, blood pressure), neurological deficit on admission (NIHSS),
- Paraclinical :
    - Neuroimaging on admission : CI topography, CI size, early signs of cerebral ischemia, old scar lesions, radiological neurological complications (HT, cerebral edema, cerebral involvement, mass effect, hydrocephalus, etc.).
    - Biologicals on admission : blood glucose, hemoglobin, white blood cell count, platelet count ; natremia, kalemia, calcemia; creatinemia; glomerular filtration rate
- Evolving :
    - Clinical and neuroradiological in-hospital neurological complications : epileptic seizures, confusional syndrome, SHT, recurrent stroke, malignant sylvian infarction;
    - Intra-hospital extra-neurological complications : metabolic, infectious, venous thrombo-embolic, cardiac, etc;
    - Status at end of hospitalization (alive or deceased) ;
    - Clinical outcome at 3 months post-stroke (mRS).
- Etiology of CI

Data analysis was performed using Epi Info 7.2.5.0 and IBM SPSS Statistic 25 software. For the descriptive study, data were expressed as frequencies (qualitative variables) and means +/- standard deviation (quantitative variables). For the analytical study, we identified factors associated with the occurrence of SHT after univariate and then multivariate analysis with logistic regression using Cox's proportional hazards model. The occurrence of SHT (yes/no) was the dependent variable, and patient characteristics present on admission (sociodemographic, clinical paraclinical) were the independent variables. We used the chi-square (χ^2) test to compare proportions, and the Odd Ratio (OR) was calculated with a 95% CI. A value of $p< 0.05$ was considered significant.

Ethical procedures were followed from data collection to dissemination of results. Data were collected and processed anonymously. Data collection was obtained after authorization from the administrations of the various university hospitals.

Results

Descriptive study

During the study period, 247 patients were consecutively hospitalized for CI, 211 of whom met the inclusion criteria for our study. The mean age of the patients was 63.6 years (±14 years) (extremes 22 and 91 years), with a median age of 64 years. There were 115 men (54.5%) and 96 women (45.5%), i.e. a M/F sex ratio of 1.20. The average emergency admission time was 18.8 hours (±4.8 hours) (extremes 1 to 24 hours). The median admission time was 19 hours; 42 deaths were recorded, giving an in-hospital mortality rate of 19.9%. During hospitalization, SHT was diagnosed in 21 patients, with a frequency of 9.9%. The mean age of patients with SHT was 58.7 years (±19.6 years), (extremes 22 and 90 years) ; the median age was 60 years. There were 11 men and 10 women, i.e. an M/F sex ratio of 1.1. The neurological deterioration characteristic of SHT was represented by an increase in pre-existing neurological deficit in 13 cases (61.9%), impaired alertness or worsening of pre-existing impaired alertness in 11 cases (52.4%), associated with unusual headaches in 10 cases (47.6%), occurring during hospitalization. According to the brain CT aspect of SHT, we noted 6 cases of intra CIPH-1 (2.8%) and 15 cases of intra CIPH-2 (7.1%), there were no cases of ICH. On admission, the mean Glasgow score was 13.9 (±3.4), (extremes 9 and 15) and 4 patients (19%) had early impairment of vigilance ; the mean NIHSS score on admission was 14.7 points (±6.3 points), (extremes 4 points and 26 points), and 11 patients (55%) had a severe initial neurological deficit (NIHSS ≥ 17). The Middle cerebral artery (MCA) territory with 14 cases (66.7%) was the most represented. The large CI with 12 cases (57%) was the most represented. Large mass effect and extensive cerebral edema with 17 cases (80.9%) and 12 cases (57.1%) respectively were the neuroradiological abnormalities most frequently associated with SHT. Etiologies were dominated by emboligenic heart disease, mainly cardiac arrhythmia due to atrial fibrillation, with 10 cases (47.6%).

Antiplatelet aggregators were initially used in all patients (100%), before being replaced by low-molecular-weight heparins (LMWH) in curative doses, then direct oral anticoagulants (DOACs) or Vitamin K Antagonists (VKAs) in 10 patients (47.6%) within an average of 14 days of the onset of CI (extremes 7 and 18 days).

Other in-hospital complications associated with the onset of SHT in CI were marked neurologically by seizure and confusional syndrome in 9 cases each (42.9%), and extra-neurologically by urinary incontinence, bronchopulmonary infection, hyperglycemia and respiratory distress, respectively in 19 cases (90.47%), 18 cases (85.71%), 13 cases (61.9%) and 13 cases (61.9%).

The clinical, paraclinical and evolutionary characteristics of patients with SHT are summarized in Table I below.

Admission variables	Numbers (n=21)	Percentages (%)
Vigilance status		
• Normal (Glasgow score = 15)	17	80.9
• Disturbed alertness (Glasgow score between 14 and 9)	4	19.1
Neurological deficit		
• Minor (NIHSS ≤ 5)	1	4
• Moderate (NIHSS 6-16)	11	50
• Severe (NIHSS > 17)	9	46
Arterial territory of CI		
• Middle cerebral artery	14	66.7
• Anterior cerebral artery	3	14.3
• Posterior cerebral artery	2	9.5
• Stepped vertebro-basilar	1	4.8
• Multi territorial	1	4.8
CI size		
• Large IC	12	57

• Medium-sized IC	8	38
• Small IC	1	5
Other associated neuroradiological abnormalities		
• High mass effect	17	80.9
• Severe cerebral edema	12	57.1
• Brain engagement	11	52.4
• Acute hydrocephalus	5	23.8
Biological abnormalities on admission		
• Hyperglycemia	15	71.4
• Hyperleukocytosis	12	57.1
• Anemia	9	42.8
• Hypokalemia	6	28.6
• Thrombocytosis	5	23.8
• Hyponatremia	4	19.0
Antithrombotic treatment		
• Antiplatelet aggregator	11	52.4
• Anticoagulant in curative doses	10	47.6
Etiologies of CI		
• Emboligenic heart disease (ACFA)	10	47.6
• Cervicocephalic atherosclerosis	8	38.1
• Undetermined	3	14.3
In-hospital neurological complications		
• Epileptic seizures	9	42.9
• Malignant sylvian infarction	12	57.1
• Confusion syndrome	9	42.9
Extra-neurological intercurrent complications		
• Hyperglycemia	13	61.9
• Fever	9	42.9
• Bronchopulmonary infection	18	85.7
• Urinary tract infection	4	19
• Sepsis	2	9.5
• Cardiac complications (MI, cardiac arrhythmias, congestive heart failure)	9	42.8
• Pulmonary embolism	2	9.5

Table I : Distribution of patients with SHT according to in-hospital clinical, paraclinical and evolutionary data.

The mean time to onset of SHT was 5.6 days ± (2 and 29 days) ; the majority of SHT cases, 10 (47.6%), occurred between day 3 and day 5 after stroke onset.

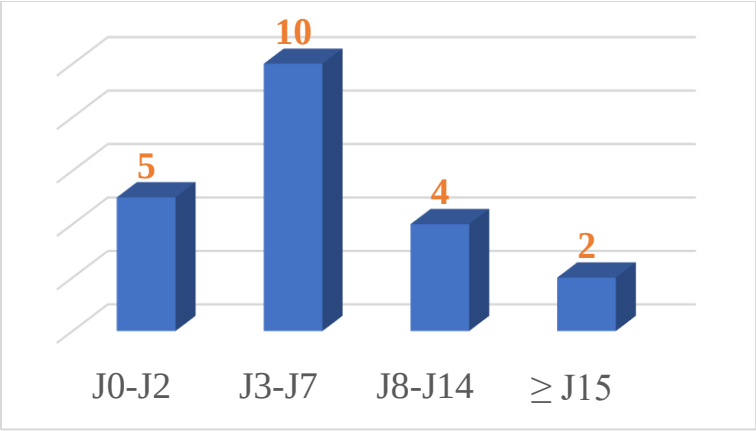

Figure 1 : Distribution of patients by time of onset of SHT

The average length of hospital stay was 16.4 days (+/- 9.9 days), with extremes of 2 days and 35 days; 13 patients died during the in-hospital phase, giving an in-hospital mortality rate of 61.9%. Immediate causes of death were dominated by intracranial hypertension. Survivors numbered 8 (38.1%), all with severe to very severe disability (mRS 4 and 5).

Analytical study

In univariate analysis, the factors significantly associated with the occurrence of SHT were:

1. Vascular risk factors: diabetes (p=0.002), history of stroke (p=0.0093), history of heart disease (p=0.01);

2. Clinical signs on admission : severe neurological deficit (p=0.033) ;
3. Biological signs on admission : hyperglycemia (p=0.0045), hypokalemia (p=0.004) ;
4. Neuroradiological signs of severity on admission : large CI (p=0.00001), extensive cerebral edema ($p=10^{-8}$), significant mass effect (p=0.005), cerebral involvement ($p= 10^{-5}$) ;
5. Cardio-embolic etiology of CI (p=0.0001).

In multivariate analysis with logistic regression : A story of type 2 diabetes [OR=1.27; 95% CI (1.11-1.32) p=0.001], severe neurological deficit on admission [OR=1.41; 95% CI (1.08-10.03); p=0.041], hyperglycemia on admission [OR=2.31; 95% CI (1.28-10.03) p=0.004], a large CI on admission [OR=12.4; 95% CI (9.15-16.38); p=0.0001]; early cerebral involvement [OR=10.61; 95% CI (2.14-14.69); p=0.001], extensive cerebral edema on admission [OR=29; 95% CI(18.14-66.1); $p=10^{-6}$] and cardioembolic etiology of the CI [OR=2.23; 95% CI(1.54-6.87); p=0.013], were the variables significantly and independently associated with the occurrence of SHT (see Table II).

Variables	SHT		P-value	OR (95%IC)	P adjusted
	Yes	No			
Age					
≤60 years	10	73	0,48		73
>60 years	11	117			117
Arterial hypertension					
Yes	15	170			
No	6	20	0,39		
History of stroke					
Yes	1	32			
No	20	158	0,21		
Tobacco					
Yes	08	54	0,45		
No	13	136			
Diabetes mellitus					
Yes	9	25	**0,002**	1,27(1,11-1,32)	**10^{-3}**
No	12	165			
Obesity					
Yes	04	44	0,79		
No	17	146			
Sedentary lifestyle					
Yes	18	7	0,89		
No	3	183			
Oral contraception					
Yes	2	18	1,00		
No	19	172			
Alcohol					
Yes	9	88	0,82		
No	12	102			
Hypercholesterolemia					
Yes	7	43	0,28		
No	14	147			
History of heart disease					
Yes	8	27	**0,01**	1,96(1,02-7,)	**0,016**
No	13	163			
Blood pressure					
High	12	38	**10^{-3}**	1,30(1,00-2,58)	**0,03**
Normal	09	152			
Glasgow score					
≤14	4	48	**0,124**		
=15	17	142			
NIHSS					
≤16	12	149			
≥17	9	41	**0,033**	1,41(1,08-3,4)	**0,041**
Blood glucose					
Normal	6	131			
Hyperglycemia	15	59	**4.10^{-4}**	2,31(1,28,10,03)	**0,004**
Leukocytes					
Normal	09	90			
Hyperleukocytosis	12	100	0,82		
Hemoglobin					
Normal	12	123			
Anemia	09	67	0,48		
Platelets					

1,46(0,60-3,60)

Normal *Augmented*	16 05	186 04	**5.10^{-4}**	0,41(0,33-0,86)	0,05
Natraemia *Normal* *Hyponatremia*	17 4	159 31	0,76		
Kalemia *Normal* *Hypokalemia*	15 6	178 12	**0,004**	3,91(0,97-8,1)	0,061
Large IC *Yes* *No*	9 12	7 183	**10^{-5}**	12,4(9,15-16,38)	**10^{-4}**
Medium-sized CI *Yes* *No*	8 13	101 89	0,25		
Small size CI *Yes* *No*	1 20	69 121	**0,002**	0,01(0,001-0,39)	0,11
Brain engagement *Yes* *No*	11 10	16 174	**10^{-5}**	10,61(2,14-14,69)	**10^{-3}**
Extensive cerebral edema *Yes* *No*	12 09	7 183	**$<10^{-8}$**	29,01(18,14-66,1)	**10^{-6}**
Hydrocephalus *Yes* *No*	5 16	12 178	**0,02**	4,45(0,47-12,19)	0,19
High mass effect *Yes* *No*	17 04	91 99	**0,005**	2,15(0,15-3,3)	**0,032**
cardio-embolic etiology *yes* *no*	10 11	29 161	**10^{-4}**	2,23(1,54-6,87)	**0,013**
atheromatous etiology *yes* *no*	8 13	39 151	0,094		

Table II : Factors associated with the occurrence of SHT in CI after univariate and multivariate analysis

A comparative study of clinical outcome at discharge and at 3 months post-stroke in patients with and without SHT showed an in-hospital mortality rate of 61.9% in patients with SHT versus 16.3% in patients without SHT (p=0.0001), and a raté of independence or autonomy at 3 months post-stroke of 28.6% in patients with SHT versus 74.2% in patients without SHT (p=0.013) (see table III).

Post-stroke clinical course	SHT	No SHT	P-value
Discharge status *Living* *Deceased*	 08 13 (61.9%)	 159 31 (16.3%)	 **10^{-4}**
Length of hospital stay *≤10days* *>10days*	 12 (37.5%) 09 (5.0%)	 20 (62.5%) 170 (95%)	 **$<10^{-8}$**
3-month post-stroke mortality *Survivors* *Deceased*	 7 (4.1%) 14 (22.6%)	 163 (95.9%) 48 (77.4%)	 **6.10^{-8}**
Functional status at 3 months post-stroke *Independent* *Dependants*	 2 (28,6%) 5 (71,4%)	 121 (74,2%) 42 (28,6%)	 **0,013**

Table III : Comparative study of the clinical course of patients with and without SHT.

Discussion

The frequency of post-CI HT varies from 10 to 40% overall, but is reported differently in different contexts. Considering the time to onset, some studies distinguish between early HT (≤ 48 hours) and late HT (>48 hours). HT can occur spontaneously after physiological reperfusion as part of the natural course of CI, but can also occur after thrombolytic therapy such as recombinant tissue plasminogen activator (tPA or rtPA) and/or mechanical reperfusion therapies such as thrombectomy **[13].** Two different pathophysiological mechanisms explain spontaneous HT : early reperfusion via leptomeningeal anastomoses, following secondary thrombus displacement (early HT) ; increased vascular permeability and blood flow after reduction of vasogenic cerebral edema (late HT) **[14, 15]**. In our series, the mean time to onset of post-CI HT was 5.6 days, reflecting a predominance of late HT.

When referring to the diagnostic method, HT diagnosed by neuroimaging (brain CT or MRI) is reported at a frequency of 13 to 46%, whereas this frequency reaches 38 to 71% in autopsy series **[16]**.

When considering the clinical manifestations associated with HT, the incidence of SHT is variably reported between 0.6 and 20% **[3, 16, 17, 18].** Indeed, in a Dutch series, the incidence of SHT was 7.3% **[19]**, close to the 9.9% incidence reported in our study. Various risk factors for SHT, such as initial clinical severity of stroke represented by an initial NIHSS score ≥ 17 and/or initial impairment of alertness, the presence of early signs of cerebral ischemia, and/or a large size of the CI on initial CT, a cardioembolic etiology of the CI and hyperglycemia on admission or a history of diabetes mellitus, identified in the literature **[3, 19, 20],** were indeed found in our study.

Initial CI severity is a powerful risk factor for HT. In our series, as in other series in the literature, it refers clinically to the initial severe neurological deficit (admission NIHSS >17) with or without early impairment of vigilance ; and neuroradiologically to the initial large size of the CI, as well as to early signs of cerebral ischemia (cerebral edema, mass effect, ...) **[3, 21]**. A close link has been demonstrated between the duration of cerebral ischemia, the severity of CI and the risk of HT in CI patients and in experimental stroke models. Indeed, a long duration of exposure to cerebral ischemia results in larger volumes of CI, associated with a high degree of blood-brain barrier (BBB) disruption, via activation of the immune system. Similarly, with or without thrombolytic therapy, a long delay between the onset of cerebral ischemia and reperfusion has been associated with an increased risk of HT **[3, 22]**, whereas early reperfusion is associated with a reduced risk of HT.

Emboligenic heart disease is also a powerful risk factor for HT, as reported in the literature **[3, 19, 20]**, as it was in our series. In general, emboligenic heart disease, dominated by Cardiac arrhythmia due to atrial fibrillation, is more frequent in older subjects **[23]**. They more often lead to occlusion of the large cerebral vessels, resulting in severe CI with serious consequences: large ischemic lesions, extending to the white matter, putting them at increased risk of HT **[24]**; early signs of cerebral ischemia, impaired alertness and/or major neurological deficits, which are recognized markers of post-CI HT **[3, 21]**. Furthermore, the use of anticoagulants in hypocoagulant doses, such as LMWH or vitamin K antagonists or direct oral anticoagulants, often indicated in patients with cardioembolic CI to reduce the risk of ischemic recurrence, however also carries an increased risk of HT **[7, 15, 25].** In our series, curative anticoagulant treatment for embolism-related heart disease was performed in 47.6% of patients, constituting an additional risk factor for the occurrence of HT, hence the interest in delaying anticoagulant treatment by at least 14 days in cases of cardioembolic CHF associated with risk factors for HT, as recommended by the American Stroke Association **[26].**

Hyperglycemia on admission, linked to pre-existing diabetes or in response to post-stroke stress, usually described in 28 to 40% of acute CI patients **[3, 27]**, was indeed found in 33.5% of patients in our series. It is a risk factor for HT of stroke with or without thrombolysis, frequently reported in the literature. Its mechanism involves expansion of the ischemic lesion volume and potentiation of inflammation, resulting in increased BBB rupture and HT **[27, 28]**. Hyperglycemia on admission was also identified in our series.

Other risk factors for HT inconsistently identified in the literature were not found or not investigated in our study, such as advanced age, hypertension, insufficient cerebral arterial collaterals on brain imaging, thrombocytopenia, use of antithrombotic drugs and reperfusion therapies **[7, 21].**

In the literature, intra-CI parenchymal hemorrhage is associated with an increased risk of death or disability, and has been identified as a major risk factor for early and 3-month death and unfavorable functional prognosis in post-CI, multiplying the risk of death by 8 **[5, 6]**. Similarly, in our study, SHT dominated by intra-CI parenchymal hemorrhage multiplied the rate of in-hospital mortality by 4 (p=0.0001) and multiplied the rate of unfavourable functional prognosis at 3 months by 2.5 (p=0.013), confirming the negative impact of SHT on vital and functional post-CI prognosis.

Thus, the establishment of dedicated stroke care networks, the implementation of stroke units, and the availability of thrombolysis and mechanical thrombectomy in our hospitals, by ensuring the prevention and early management of HT risk factors and other neurological and extra-neurological post-stroke complications, would contribute to improving the vital and functional prognosis of stroke patients.

Our study has certain limitations, in particular methodological biases, which do not, however, call into question its validity : the unaffordability of follow-up brain CT scans for most of our patients meant that we had to restrict our study to cases of SHT, thus excluding cases of asymptomatic HT ; similarly, some probable cases of SHT were not included for the same reason.

Conclusion

SHT, essentially of the intra-IC parenchymal hemorrhage type, complicates one IC in ten in the hospital phase, occurring mostly during the first week post-stroke, associated with an appalling prognosis, with death in 3/5 of patients and loss of autonomy in most survivors. Risk factors include severe stroke, initial hyperglycemia and cardioembolic etiology. The establishment of dedicated stroke care networks, the implementation of stroke units, and the availability of thrombolysis and mechanical thrombectomy in our hospitals, by ensuring the prevention and early management of risk factors for HT and other neurological and extra-neurological post-stroke complications, would contribute to improving the vital and functional prognosis of stroke patients.

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DOI:10.31579/2642-973X/122