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Decompressive Hemicraniectomy for Malignant Middle Cerebral Artery at the Regional University Hospital of Besançon, France: Mortality and Functional Outcome at Six Months and 12 Months

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Abstract

Introduction: Malignant infarction of the middle cerebral artery territory is a serious clinical form with a mortality rate of approximately 80%. Several large studies have demonstrated the effectiveness of decompressive hemicraniectomy in reducing mortality and functional impairment following malignant infarction of the middle cerebral artery. The aim of this work was to assess the mortality and functional prognosis of patients who underwent decompressive hemicraniectomy surgery for malignant infarction of the middle cerebral artery from 2009 to May 2016 at the Regional University Hospital of Besançon.

Methodology: This was a retrospective study with a prospective, descriptive and analytical part, on patients hospitalized at the Regional University Hospital of Besançon, from 2009 to May 2016, and having undergone a decompressive hemicraniectomy for sylvian malignant infarction. The demographic, clinical and neuroradiological characteristics before surgery, as well as the treatments administered, intercurrent complications in the hospital phase, deaths and functional outcome at 6 months and 12 months after surgery, were analyzed. The factors influencing functional outcome and mortality at 12 months were identified by bivariate analysis. For the determination of factors influencing functional outcome, we included data from 16 additional patients who had undergone decompressive hemicraniectomy for malignant sylvic infarction, in the same hospital and under the same conditions, from 2000 to 2008. The data were analyzed using Excel software and SPSS software. The different tests used to find the association between two variables were the Student test (for the quantitative variables), the Fisher test or the Chi-square (for the qualitative variables). The significance level was $p \leq 0.05$.

Results: A decompressive hemicraniectomy for malignant sylvian infarction was performed in 46 patients among 13,284 patients hospitalized from 2009 to May 2016, ie 0.34%. The mean age of the patients was 54.8 years. The mean NIHSS score used for the surgical decision was 21.8. The mean lesion volume was 207.1cm3. The rate of patients initially treated with thrombolysis alone or associated with thrombectomy was 57.2%. The time to craniectomy was 48.1 hours. Osmotherapy associated with craniectomy was performed in 34.8% of patients. The modified Rankin score was ≤ 3 at 6 months and 12 months respectively in 41.3% and 45.6% of patients; this score at 12 months was found in 8/18 patients aged> 60 years

and in 4/15 patients treated surgically after 48 hours. The 12-month mortality rate was 30.4%. High age was significantly associated with mortality at 12 months.

Conclusion: Decompressive hemicraniectomy for malignant sylvian infarction effectively improves functional outcomes and significantly reduces patient mortality. Patients over the age of 60 and those whose surgery time exceeds 48 hours also benefit, although to a lesser extent, from this therapy.

Keywords: Malignant Sylvian Infarction; Cerebral Edema; Decompressive Hemicraniectomy; Death; Becoming Functional

Introduction

The malignant infarction of the middle cerebral artery (MCA) or "malignant sylvian infarction" (MSI) is a cerebral infarction (CI) extended to the territory of the MCA [1], secondary to the occlusion of the internal carotid artery (ICA) and / or the proximal branch of the MCA, which in the absence of revascularization therapy or in the event of failure, is very often complicated by cerebral edema initially cytotoxic, then vasogenic which sets in 12 to 72 hours [2,3]. This edema is responsible for intra cranial hypertension (ICH) which is life-threatening and worsens the functional prognosis [2]. It is one of the most serious forms of CI, occurring in approximately 10% of cases of substantial infarction, leading to death in 70 to 80% of patients, by brain death secondary to compression of the brainstem [1]. The management of cerebral edema has long been controversial. Drug treatments have no beneficial effect on reducing mortality and functional impairment [4]. Before 2007, several studies suggested the superiority of decompressive hemicraniectomy (DHC) in the management of cerebral edema, but remained controversial because it was not randomized [5,6]. In 2007, three controlled, multicenter and randomized European studies confirmed the absolute superiority of surgical treatment with DHC over drug treatment for cerebral edema, both in terms of reducing the mortality rate and reducing functional disability. These studies, Decimal in France, Destiny in Germany, Hamlet in Holland [7-9], were then the subject of a meta-analysis [2] of individual data from 93 patients, including 42 randomized in the arm. medical and 51 in the surgical arm. Said meta-analysis clearly demonstrated that DHC reduced mortality by more than 50% compared to drug treatment ; among the survivors, the number of bedridden patients remained low and practically identical in each group (about 5%); the rate of survivors with mild disability was almost double in the surgical group versus the drug group. These three studies have thus made it possible to support the indication of early DHC, within 48 hours after an MSI, in patients aged 60 years or less, without associated severe pathology and without pre-existing disability.

However, many questions remained unanswered about the benefits of DHC in patients over 60 years of age and in MSIs older than 48 hours. A lot of studies have looked at this subject.

Among these studies, In the German, randomized, prospective, multicenter study (Destiny II) [10], the mean age of patients was 70 years and 39% of patients who underwent DHC had a modified Rankin score (mRS) ≤ 4 versus 18 % of patients in the drug arm. The survival rate represented 67% in the surgical arm versus 31% in patients treated with the drugs. In the Hamlet study [9], there was no significant difference at 12 months in the functional prognosis between the group of patients with MSI who underwent DHC> 48 hours from the onset of signs and the group of patients with DHC within 48 hours of onset of signs.

As part of the evaluation of medical practices concerning the DHC of MSIs at the Besançon regional university hospital center (RUHC), we carried out this work, compared to the results of major international studies devoted to this subject. The objectives of our study were on the one hand to determine the mortality and functional prognosis at 6 months and 12 months in patients having undergone DHC surgery for an MSI and on the other hand, to identify the associated factors that affect them.

Patients and Methods

We conducted a retrospective study with a prospective component (post stroke clinic outcome) on patients hospitalized at the Besançon RUHC for MSI, who received surgical treatment with DHC, between 2009 and May 2016. We did not exclude any identified patient and meeting these criteria.

For our study, we identified all patients who received surgical treatment with DHC for an MSI during the period 2009 - May 2016. For this, we searched the hospitalized stroke recording software in Neurology. To identify patients who had not yet been registered on the database, we completed a systematic search for the PMSI coding of patients hospitalized at the Besançon RUHC using the keywords (sylvian infarction, stroke, craniectomy, hemicranectomy, surgery). For all the selected files, we noted the demographic and clinical characteristics of the patients (age of onset of MSI, sex, risk factors for stroke, existence of vigilance disorders, "National Institute of Health Stroke Score" (NIHSS) before the surgical decision, etiology of the MSI), the imaging data (side of the lesion, nature of the occluded artery, volume of the lesion), the management (initial place of management, revascularization treatment, osmotherapy, time to craniectomy, time to cranioplasty), evolution and complications (assessment of residual disability at six months and one year by mRS, complications related to MSI and its treatment, death), the terms of discharge and follow-up of patients (length of hospitalization, referral of the patient on discharge, average time to neurological follow-up, place of residence one year after the MSI).

We did a telephone interview to obtain the clinical outcome at 12 months post stroke.

Calculation of the infarct volume was performed on diffusion images (DWI) on the patient's first admission exam, which was most often less than 24 hours; either manually, by circling the hypersignal cut by cut, or using semi-automatic software. Then, the sum of the measured areas was multiplied by the section thickness (6 mm) to obtain the total volume. If there were several non-contiguous lesions, they should all be surrounded. Any hemorrhagic transformation into hypointense was included in the volume. For the identification of the factors influencing the clinical outcome (functional prognosis and mortality at 12 months) of the patients, and in order to increase the statistical power of our sample, we took into account 16 additional patients, corresponding to the 1st cohort of patients having undergone surgical treatment with DHC for MSI at the RUHC of Besançon, from 2000 to 2008 [11]. There was no significant difference between the two cohorts in demographic variables, vascular risk factors, etiologies of MSI, lesion volume, time to DHC; the only difference concerned revascularization therapies previously performed in 50% of patients in the 2009 to 2016 cohort versus 1 patient / 16 in the 2000 to 2008 cohort.

All the data collected was then noted on a data collection sheet, then transcribed into an Excel database for statistical analysis which was carried out using Excel software and SAS software. The different tests used to find the association between two variables were the Student test (for quantitative variables), Fisher's test or Chi-square (for qualitative variables). Our results were compared to the results of large studies. The main variables were compared with each other.

Results

During the study period, 13,284 cases of cerebral infarction were hospitalized, among which 46 cases of DHC for MSI were identified, or 0.3%, including 28 patients / 46 (60.9%) admitted by the through telemedicine. The mean age was 54.8 years ± 12.4 (range 20 and 74 years), the age group ≥ 60 years with 18 patients accounted for 39.1%, there was a male predominance (60.9%). The mean NIHSS score used for the surgical decision was 21.8 ± 2.5 (range 17 and 27); a NIHSS score <20 was found in 13 patients (28.3%). Altered vigilance was present in 43/46 patients, or 93.5%.

The main risk factors for stroke were represented by hypertension (41.3%), active smoking (39.1%), hypercholesterolemia (15.2%), diabetes (13.0%), alcohol (10.9%). The aetiologies were mainly represented by arterial dissection (26.1%), embologenic heart disease (21.7%) and atheromatous causes (17.4%).

A right hemispherical MSI was present in 30 patients (65.2%). Arterial occlusion was found in 43/46 patients (93.5%): occlusion of MCA with 18 cases (39.1%), ICA with 14 cases (30.4%) and ICA + MCA with 11 patients (23.9%). The mean lesion volume before the surgical decision was 207.1 cm3, and 82.6% of patients had a volume greater than 145cm^3.

DHC was performed after failure of revascularization therapy in 24/46 patients, or 52.2% of patients, or 13 failures of thrombolysis alone and 11 failures of thrombolysis associated with thrombectomy. The mean time to craniectomy was 48.1 ± 7.8 hours (range 6-168 hours); 16 patients (34.8%) had been managed surgically 48 hours from the start of the MSI. The average time to cranioplasty was 7.5 months, and 16 of 46 patients had not yet had cranioplasty. Osmotherapy had previously been performed in 16/46 patients, or 34.8% of patients.

The demographic, clinical, neuroradiological and therapeutic characteristics are presented in Table 1 below.

Patient characteristics	Numbers (%)
Age (years)	
Mean, standard deviation	54.8 +/- 12.4
Median	58
Extreme	20-74
Age over 60	18 (39.1)
Male	28 (60, 9)
NIHSS Score	
Mean, standard deviation	21.8 +/- 2.5
Extreme	17-27
Median	22
Altered vigilance	43 (93.5)
Risk factors for stroke	
Arterial hypertension	19 (41.3)
Active smoking	18 (39.1)
Hypercholesterolemia	7 (15.2)
Diabetes	6 (13.0)
Alcohol	5 (10.9)
Sleep apnea syndrome	3 (6.5)
Atrial fibrillation	2 (4.3)
History of stroke or TIA	2 (4.3)
Etiologies of ISM	
Arterial dissection	12 (26.1)
Cardioembolic	10 (21.7)
Atheromatous	8 (17.4)
Other causes	2 (4.4)
Unspecified	14 (30.4)
§ includes mainly haematological causes. Early deaths before the end of the etiological assessment and etiologies not found after complete etiological assessment	

Right side		30 (65.2)
Occluded artery	**Internal carotid artery (ICA)**	14 (30.4)
	Middle cerebral artery (MCA)	18 (39.1)
	ACI + ACM	11 (23.9)
	Not found	3 (6.5)
Lesion volume (cm^3)	**Mean, standard deviation**	207.1 ± 62.6
	Extreme	87-339
	Median	213
	Volume < 145 cm^3	8 (17, 4)
	Volume ≥ 145 cm^3 (%)	38 (82.6)

Traitly revascularization	
Thrombolysis alone	**13 (28, 3)**
Thrombolysis + thrombectomy	**11 (23.9)**
Thrombectomy alone	**0 (0)**
Others†	**22 (47.7)**
Time to craniectomy (hours)	
Mean	**48.1**
Extreme	**6-168**
Median	**48**
Craniectomy in the first 48 hours	**30 (65.2)**
Craniectomy after 48 hours	**16 (34, 8)**
Pre- osmotherapy‡	**16 (34, 8)**
† Includes antiplatelet and anticoagulant therapy. ‡ Treatment with mannitol.	

† Includes antiplatelet and anticoagulant therapy.

‡ Treatment with mannitol.

Table 1: Demographic, clinical, neuroradiological and therapeutic characteristics and etiologies of ISM in the 46 patients who had HCD for ISM

At 6 months post-ISM, 19 patients / 46 (41.4%) had an mRS ≤ 3, and at 12 months post-ISM, 21 patients / 46 (45.7%) had an mRS ≤ 3 (Figure 1).

Figure 1: Distribution of the 46 patients treated surgically by DHC for an MSI according to the mRS, at six months and 12 months

In our cohort, 11 patients received DHC after 48 hours, with a mRS ≤ 3 at 12 months in four (4) / 11 patients (36.4%); 18 patients had had DHC after the age of 60 years, with an SRM ≤ 3 at 12 months in 8/11 patients (44.4%). Table 2 below shows the evolutionary characteristics of the 11 patients who had DHC after 48 hours and the 18 patients who had DHC after the age of 60 years.

Craniectomy after 48 hours	
mRS	**Number = 11 not (%)**
mRS ≤ 3	4 (36, 4)
mRS 4-6	7 (63, 6)
mRS = 6 †	4 (36, 4)
Craniectomy in patients over 60 years of âge	
mRS	**Workforce = 18 Not (%)**
mRS = 0-2	1 (5.6)
mRS = 3	4 (22.2)
mRS = 4	3 (16.7)
mRS = 5	1 (5.6)
mRS = 6 †	9 (50, 0)

†Deceased patients

Table 2: Evolutionary characteristics of the 11 patients who had DHC after 48 hours and of the 18 patients who had DHC after the age of 60 years

Lung disease (67.7%), hemorrhagic rearrangement (67.7%) and complications associated with craniectomy and cranioplasty (52.9%) were the most frequently encountered complications. Complications associated with the craniectomy or cranioplasty were represented mainly by infections, intra cerebral hemorrhages, heavy blood loss during surgery (Figure 2).

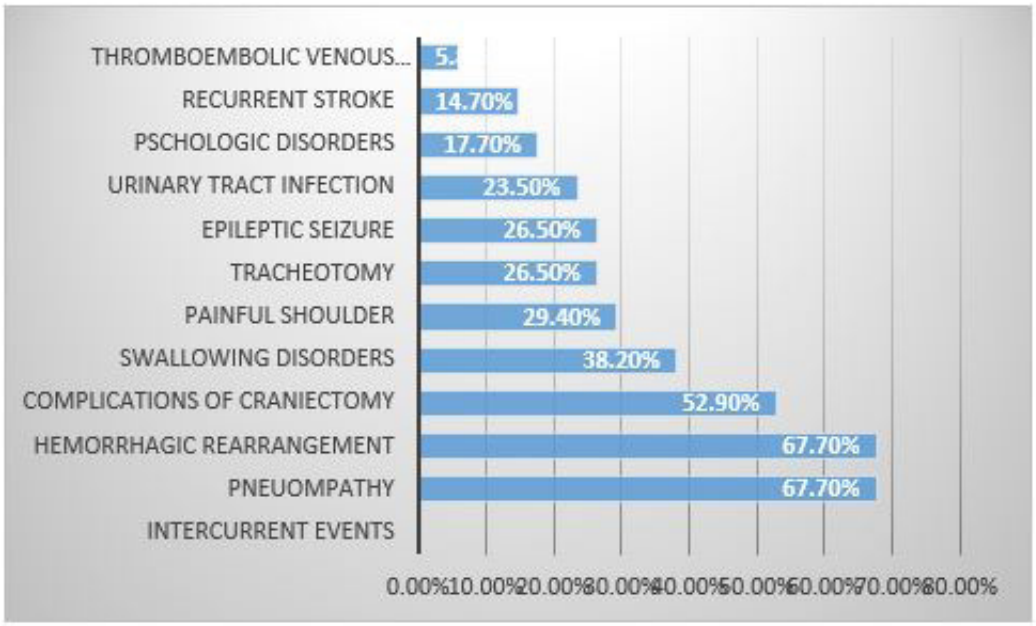

Figure 2: Main complications during hospitalization in patients treated surgically by DHC for an MSI

The average length of hospitalization was 50.6 days; 14 patients had died within the first year, and 1 patient after one year. The causes of death linked to MSI were mainly the recurrence of stroke in another territory, or the extension of the lesion in adjacent territories, responsible for intra cranial hypertension refractory to any treatment. Two patients died of cardiogenic shock. At the end of the hospital stay, the surviving patients were referred either to a rehabilitation center (50%) or to a peripheral neurology department (45%). Two patients (5%) had returned via medical transfer to their countries of origin. After one year, 22 patients had returned home, two patients were living in a retirement home, and two other patients in a specialized center for the disabled.

In univariate analysis of factors associated with overall mortality after one year in patients who had DHC for MSI, there was an association between deaths and high patient age (p = 0.00021). There was no association between deaths and high NIHSS score, lesion size or time to completion of DHC (Table 3).

After univariate analysis, by combining the data from our cohort from 2009 to 2016 with those from the previous cohort from 2000 to 2008, the factors associated with a favorable clinical outcome (mRS ≤ 3) at 12 months were age ≤ 60 years, NIHSS ≤ 20, ischemic lesion volume <145 cm3, time to DHC ≤ 48 hours (Table 4).

Independent variables	**Deceased patients n = 15 Mean**	**Living patients n = 31 Mean**	**p- value †**
Age (in years)	56.14	51.13	0.00021
Volume of the lesion (in cm^3)	210.64	206.31	NS §
NIHSS ‡	22.29	21.31	NS §
Time to surgery (in hours)	65.14	45.00	NS §

* Total number of deceased patients in our cohort

† p- value in the STUDENT test, the link is established if P value is less than 0.05

‡ National Institute of Health Stroke Score

§ No significant difference between the two cohorts for this variable

Table 3: Factors Influencing Death in DHC Surgically Managed Patients for MSI

Patient characteristics (n = 62)		mRS ≤ 3 (n)	p- value †
Age	**≤ 60 years (n = 39)**	**22**	**0.0000000029**
	> 60 years old (n = 23)	**5**	
NIHSS	**< 20 (n = 9)**	**5**	**0.00000011**
	≥ 20 (n = 53)	**22**	
Lesion volume	**<145 cm^3 (n = 8)**	**5**	**0.000000005**
	≥ 145 cm^3 (n = 56)	**22**	
Surgery time	**≤ 48 hours (n = 41)**	**23**	**0.0006**
	> 48 hours (n = 21)	**4**	

†There is a significant difference if p-value is less than 0.05

Table 4: Factors influencing clinical outcome according to mRS in the 62 patients treated surgically by HCD for an MSI in the two cohorts 2000 to 2008 and 2009 to May 2016

Discussion

The main limitation of our study is the small size of our cohort (46 patients), which could have an influence on the results. However, published randomized studies of DHC generally face the same limitations.

MSI more often affect young people [1]. The most frequent aetiologies are represented by embologenic heart disease and arterial dissections [12]. High blood pressure and smoking are the most common risk factors encountered in patients [7]. Brain edema secondary to MSI usually occurs in the absence or failure of early revascularization therapy. In our cohort, 24 cases of failed thrombolysis or thrombolysis followed by thrombectomy were reported. This edema is responsible for a mass effect on the adjacent brain structures, a deviation of the midline and a temporal engagement, within two to five days after the MSI, responsible for death in 80% of patients [13]. The DHC, "treatment of last resort" then offered at this time is not a cure. Its objective is to prevent complications linked to cerebral edema, and thus to limit the rate of mortality and functional handicap.

Several randomized and non-randomized studies have suggested or proven the superiority of DHC surgery over drug treatment for cerebral edema [7-9]. However, there are currently no well-established recommendations on the indications and contraindications for this surgery in MSIs. But the release of the major European studies, Decimal, Destiny and Hamlet, allowed each medical team to collegially decide on the indication of DHC in the MSI for each patient. The notion of collegiality is important and must involve at least neurologists, neurosurgeons, resuscitators and anesthetists [12]. It is important to have an interview with the family and their written consent [12]. Despite this prerequisite in our patients, two families complained in the late aftermath of the surgery of relentless treatment.

According to the results of these three large European studies and their meta-analysis, the ideal patient to be proposed for surgery is a patient aged 60 years or less, without associated severe pathology and without pre-existing disability, with cerebral edema secondary to an MSI, evolving for 48 hours at most. In our cohort, 60.9% of patients were ≤ 60 years old and 65.2% of patients had been managed surgically by DHC within the first 48 hours, meeting the above criteria.

However, it should be noted that these three studies and their meta-analysis did not consider age> 60 years. This concern was addressed by Jüttler et al in the Destiny II study published in March 2014 [10]. It evaluated the functional prognosis of patients with DHC within 48 hours following an MSI versus drug treatment in 112 patients aged 61 to 82 years. The 49 patients included in the surgical arm were aged 62 to 82 years, and at 12 months, 18/47 (38%) patients had an mRS ≤ 4, and 20/47 (43%) patients had died. The results found in our study are almost similar, because among the 18 patients aged> 60 years (39.1%), 8 patients (44.5%) had an mRS ≤ 4 at 12 months and 9 patients (50%) patients had died at 12 months. This study demonstrates that DHC in MSI is beneficial in patients over 60 years of age in terms of improved functional prognosis, although the beneficial effect on reducing the death rate cannot be demonstrated.

Some studies have identified clinical, biological and imaging predictors of cerebral edema in MSI [14]. The clinical predictive factors identified are a NIHSS score> 20, the presence of nausea and vomiting, impaired alertness [15,16]. In our study, 71.7% of patients had an NIHSS score> 20 and 93.5% of patients had impaired vigilance. The biological predictive factors are represented by hyperleukocytosis in the blood count and the positivity of S100B within 12 to 24 hours during the blood test [15-17]. However, the predictive values of these clinical and biological variables remain low. The predictive factors of MSI on brain imaging are the presence of a thrombus located in the terminal portion of the internal carotid artery, an MCA infarction associated with another territory (ACA and / or PCA) [15,16]. Extensive infarction of the MCA territory associated with involvement of the anterior choroidal territory (temporal lobe uncus) may be responsible for rapid temporal engagement [18]. The volume of the lesion calculated early on the diffusion sequence on cerebral magnetic resonance imaging (MRI), or on a cerebral perfusion scanner remains the most precise marker, due to its strong positive predictive value [19]. A diffusion-sequence brain MRI volume> 82 cm3 by six hours of onset of symptoms, or> 145 cm3 within 14 hours of onset, had 100% sensitivity and 94% specificity in a small cohort [20,21]. In our study, the volume> 145 cm3 was present in 82.6% of patients.

Regarding the non-surgical management of cerebral edema in MSI, osmotherapy has no beneficial effect on reducing the rate of mortality and functional impairment [22]. The combination of surgery and osmotherapy may have a better result in reducing cerebral edema and its damage. This hypothesis remains to be studied in humans. However, an experimental study published in 2015 was carried out on an animal model (rats) in which an MSI had been artificially induced. Twenty-four hours after treatment with surgery or osmotherapy, the brain tissue of the rats was analyzed. This showed greater benefit from the combination of surgery and osmotherapy versus surgery alone or osmotherapy alone [23]. Some suggest offering osmotherapy while awaiting surgery, once the surgical indication has been selected [19]. In our study, 34.78% of patients received combined surgery and osmotherapy. The death rate in this group was 43.8%. This could be explained by the fact that osmotherapy was offered in case of persistent clinical signs of ICHT despite surgery.

Currently, surgical treatment remains the most effective treatment in reducing mortality and functional disability, in the event of failure of the initial therapies (thrombolysis, thrombectomy). However, the time between the start of the MSI and the surgery should be as short as possible. In our study, the mean time to DHC was 48.1 hours, and 30/46 patients (65.2%) were operated within the first 48 hours. Some studies suggest that the 48 hour time limit be observed because after this time, the cerebral edema is sufficiently established and the pressure it exerts on the surrounding brain tissue has caused extensive irreversible ischemic necrosis. Craniectomy therefore has no beneficial effect on reducing the rate of severe functional disability (mRS at 5) [9]. However, there could be exceptions to the rule, in particular concerning infarctions which are constituted in several stages, or recurrences of cerebral infarction in the acute phase so that patients without initially presenting any criteria of malignancy, are found after more than 48 hours from onset of signs with an MSI. In our study population, two similar cases were recorded, with delays of 168 hours (7 days) and 120 hours (5 days).

Considering all the patients in our cohort, 45.7% of patients had an mRS ≤ 3 at 12 months and the mortality rate (mRS= 6) at 12 months was 30.4%. In the meta-analysis of the three large European studies, this score was noted in 43.1% of patients and the mortality rate was lower at 21.6% [2]. Without using a statistical comparison test, we find that there was a slight difference between the results of our cohort and those of the meta-analysis. This difference can be explained by several observations. Our cohort included patients over 60 years of age, patients with a delay of DHC> 48 hours. All these variables negatively influenced the vital or functional prognosis of our patients. In addition, the patients included in our study, although autonomous before CI, sometimes had associated comorbidities (heart disease, anemia) which decompensated during hospitalization, complicating management and possibly worsening the vital and functional prognosis. These results nonetheless attest to the constant effectiveness of surgery as an early treatment for cerebral edema in the MSI on better functional outcome.

Complications associated with craniectomy and cranioplasty were found in more than half of the patients (52.9%). The most represented were infections, cerebral hemorrhages, significant blood loss during surgery, and narrow craniectomy flaps in some cases. These complications can impact the vital and functional prognosis of patients [14]. In the literature, the complications found are represented by an insufficient decompression component, infection of the craniectomy site at the time of DHC or cranioplasty, hemorrhagic complications, headaches related to the difference in gradient between the pressure atmospheric and intracranial pressure [24,25]. Complications associated with MSI can also have a negative impact on the outcome of patients. These complications were represented in our study mainly by pneumonia, swallowing disorders sometimes leading to tracheostomy, hemorrhagic changes, epileptic seizures, painful shoulders.

Conclusion

DHC for MSI was performed in 0.3% of patients at the Besançon RUHC, within an average of and included 34.8% of patients aged> 60 years. The age of the patients ≤ 60 years, the delay of the DHC in the first 48 hours after the MSI are important factors to be taken into account for the decision of the DHC, because they correlate with a better functional prognosis (mRS ≤ 3). Age> 60 years is not on its own a contraindication to DHC for an MSI, although it correlated with a poorer prognosis both vital and functional at one year in our study. The NIHSS score <20 is correlated with a good functional prognosis (mRS ≤ 3). A high NIHSS score correlates

with a poorer functional prognosis but does not influence mortality. The lesion volume <145 cm^3 correlates with a good functional prognosis. The time to DHC> 48 hours correlates with a poorer functional prognosis. Mortality in the first year after DHC for an MSI correlated positively with age> 60 years, but not with NIHSS score> 20, lesion volume> 145 cm^3, or time to DHC> 48 hours.

Our study confirms the results of the meta-analysis of large European studies and attests that patients aged> 60 years and whose DHC times are> 48 hours, continue to benefit, albeit to a lesser extent, from the benefits of surgery.

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