

Decompressive craniectomy in massive cerebral infarction

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ABSTRACT

Twenty one patients were submitted to decompressive craniectomy for massive cerebral infarct. Ten patients (47.6%) presented a good outcome at the 6 months evaluation, eight had a poor outcome (38%) and three died (14.2%). There was no outcome statistical difference between surgery before and after 24 hours of ictus, dominant and non-dominant stroke groups. Patients older than 60 years and those who had a Glasgow Coma Scale (GCS) < 8 in the pre-surgical exam presented worst outcome at six months ($p < 0.05$). Decompressive craniectomy for space-occupying large hemispheric infarction increases the probability of survival. Age lower than 60 years, GCS ≥ 8 at pre-surgical exam and decompressive craniectomy before signs of brain herniation represent the main factors related to a better outcome. Dominant hemispheric infarction does not represent exclusion criteria. **Key words:** cerebral infarction, decompressive hemicraniectomy, surgical decompression.

Craniectomia descompressiva no infarto cerebral extenso

RESUMO

Vinte e um pacientes foram submetidos a craniectomia descompressiva para o tratamento de infarto cerebral extenso. Dez pacientes (47,6%) apresentaram boa evolução em avaliação após 6 meses, 8 apresentaram evolução desfavorável (38%) e 3 faleceram (14,2%). Durante o seguimento, não se evidenciou diferença estatística na evolução entre pacientes operados antes e após 24 horas do ictus, nem entre lesões envolvendo o hemisfério dominante versus não dominante. Pacientes com mais de 60 anos e aqueles com Escala de Coma de Glasgow (ECG) < 8 na avaliação pré-operatória apresentaram pior evolução após 6 meses ($p < 0,05$). A craniectomia descompressiva para infartos hemisféricos extensos aumentam a probabilidade de sobrevivência. Idade abaixo de 60 anos e ECG ≥ 8 no exame pré-operatório e craniectomia descompressiva antes de sinais de herniação cerebral representam os principais fatores relacionados a uma melhor evolução clínica. Infarto hemisférico envolvendo o hemisfério dominante não representa um critério de exclusão. **Palavras-chave:** infarto cerebral, hemicraniectomia descompressiva, descompressão cirúrgica.

Ischemic stroke is a medical emergency and the most common affection of the central nervous system (CNS). This is the second-leading cause of death worldwide and the first cause of morbidity¹. Ischemic stroke correspond to 85% of all strokes with a mortality of 10-50%. Large space-

occupying infarction accounts for 1-10% of all supratentorial infarction with signs of elevated intracranial pressure (ICP) and brain herniation usually in the second to the fifth day leading to a mortality rate of 53% to 89%²⁻⁵. The high mortality rate makes some authors call this stroke as

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“malignant” infarct and create the term malignant middle cerebral artery syndrome to describe the rapid development of fatal brain swelling⁶. Large space-occupying infarction is generally secondary to an occlusion of the carotid artery or the M1 segment of the middle cerebral artery (MCA), including or not the anterior cerebral artery (ACA) or the posterior cerebral artery (PCA). Neuroimaging criteria varies between the authors: infarct volume on diffusion-weighted magnetic resonance imaging (MRI) of more than 145 cm³; brain computed tomography (CT) ischemic changes affecting more than two-thirds of the MCA territory and including the basal ganglia; brain CT ischemic changes affecting at least two-thirds of the MCA territory with space-occupying edema; signs on CT of an infarct of at least 50% of the MCA territory, with or without additional infarction in the territory of the anterior or posterior cerebral artery on the same side^{5,7}.

Many studies have suggested that decompressive surgery, consisting of a hemicraniectomy and duraplasty, reduces mortality and improves outcome in patients with massive brain infarctions^{5,8}.

We report our series of 21 patients treated with decompressive craniectomy.

METHOD

Study design

In this retrospectively designed study, we describe the results of decompressive hemicraniectomy in 21 patients with large hemispheric infarctions at UNICAMP Medical School Hospital from March 2003 to September 2007. We have considered massive cerebral infarction as brain CT ischemic changes affecting at least two-thirds of the MCA territory with space-occupying edema or both MCA and ACA or PCA infarctions leading to a minimum of 50% hemispherical volume compromised. We analyzed gender, age, Glasgow Coma Scale (GCS) on admission and pre-surgical evaluation, clinical status on pre-surgical exam, time from initial symptoms to decompressive craniectomy, length of stay in the hospital and Glasgow Outcome Scale (GOS) 6 months after discharge. Data was subsequently analyzed for comparative study of patients with good to moderate outcome (GOS≥4) and patients with poor outcome (GOS≤3).

Patient selection

The decision to perform decompressive craniectomy was based on the presence of a space-occupying large

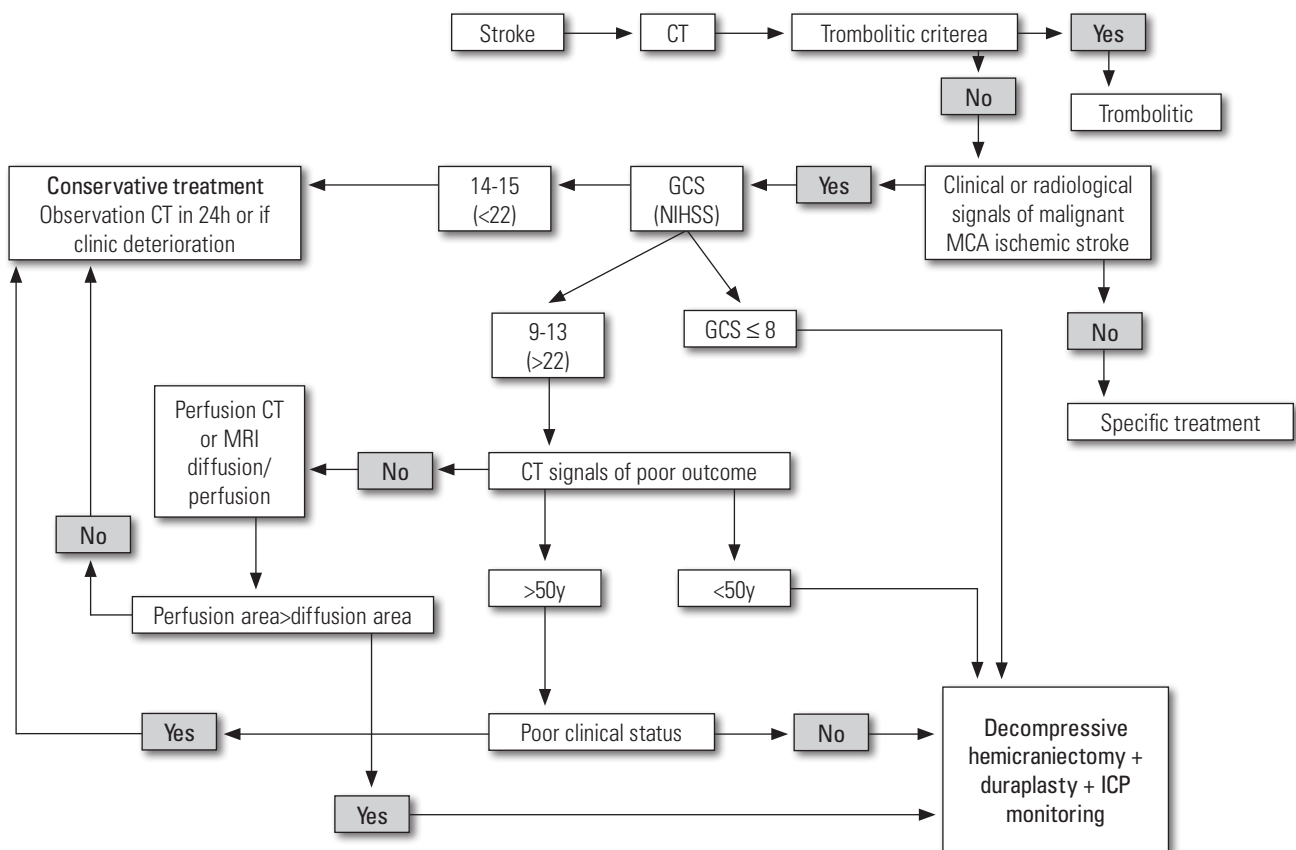


Fig 1. Approach to ischemic stroke.

Table 1. Analyze of outcome.

Grade	Characteristics (6)	Outcome
G1	Functionally independent - BI \geq 90; or mRS 0-1; or GOS 5	Good
G2	Mild to moderate disability - BI=60 to 89; or mRS 2-3; or GOS 4	Good
G3	Severely disabled - BI <60; or mRS 4-5; or GOS 2 to 3	Poor
G4	Death	Poor

G1-4: grade 1-4; BI: Barthel index; mRS: modified Rankin score; GOS: Glasgow Outcome Scale.

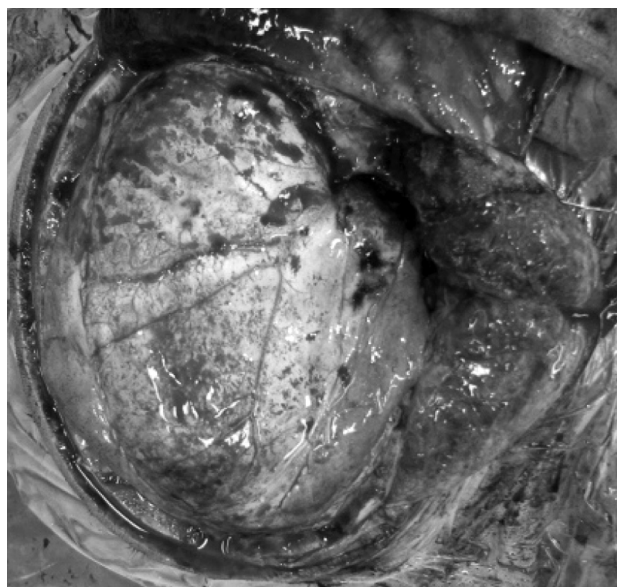


Fig 2. A right sided question mark incision. The skin flap and the temporal muscle were dissected on a separate manner to provide an increase in the exposure of the middle fossa. Then a dura-plasty using aponeurotic galeal flap after decompressive craniectomy for brain expansion.

hemispheric infarction on CT scan and the clinical status of the patients. Patients with GCS $>$ 13 and no midline shift or basal cistern compression at initial evaluation were managed in the intensive care unit. Neurological deterioration or development of brain herniation signs were indications to decompressive craniectomy as patients initially presented with GCS \leq 8 and cistern compression or midline shift at CT scan. Figure 1 shows our approach to ischemic stroke. The patients presented with GCS between 9 and 13 were individually managed.

Surgical technique

A question mark-shaped skin flap based on the ear and a wide craniotomy was performed on the affected side with partial removal of the frontal, temporal, and parietal bones, so that the floor of the middle fossa could be exposed and the bone flap have a minimum of 12 cm diameter. The dura was opened in a "C" shape all over and 1cm distant to the border of the craniotomy. Homologous

temporal fascia was placed into the incision for volume-enlarged dural repair (Fig 2). The bone flap was placed in a subcutaneous pocket overlying the abdomen for preservation until subsequent cranioplasty.

Data analysis

To make possible the comparison between the different studies, the outcomes were classified into 4 specific categories (Table 1): grade 1 (G1) functionally independent; grade 2 (G2) mild to moderate disability; grade 3 (G3) severely disabled; and grade 4 (G4) death⁸. Good outcomes were defined as functionally independent or mild to moderate disability. Poor outcomes were defined as severe disability or death. It was not necessary that the study fulfill all the criteria listed, for instance, a G1 outcome could be based only on a GOS of 5, or only on a Barthel index $>$ 90, or on a mRS 0-1, not been necessary all three classifications.

Statistical analysis

All data are expressed as mean \pm standard deviation (SD). Mann-Whitney U non-parametric tests, t tests and Fisher's exact test were used for analysis of statistical evidence, with $p < 0.05$ considered significant. Statistical software, SPSS 14.0 (SPSS Inc., Chicago, IL) was used for statistical analysis.

RESULTS

A total of 21 patients (16 males and 5 females) were submitted to decompressive craniectomy during the period analyzed by the study (Table 2). The mean age was 50.09 ± 14.29 years. On admission, the mean GCS was 12 ± 2.42 points (range from 6 to 14).

The mean GCS on immediate pre-surgical evaluation was 8 ± 2.19 points. Nine patients (42.85%) presented with pupillary changes on pre-surgical evaluation; afasia occurred in six cases (28.5%) and hemiplegia presented in all patients.

Seventeen patients (80.95%) had "malignant" MCA infarction and 4 (19.04%) had associated ACA territory infarction. The dominant hemisphere was affected in 6 cases (28.5%) and the non-dominant hemisphere in 15 cases (71.4%).

Table 2. Characteristics of 21 patients included in the study.

Pct	Gender	Age	Stroke side	Admission GCS	GCS before surgery	Pupils	Time to surgery	GCS after surgery	discharge (days)	GOS
1	Male	56	Right	14	8	Isocoria	<24h	15	14	4
2	Male	28	Left	13	8	Isocoria	<24h	15	33	3
3	Female	48	Right	13	7	Isocoria	<24h	15	42	4
4	Female	59	Left	9	6	Anisocoria	48-72h	11	24	3
5	Male	53	Right	14	8	Anisocoria	48-72h	15	34	4
6	Male	56	Right	11	11	Isocoria	24-48h	15	7	4
7	Male	35	Right	15	8	Isocoria	<24h	15	28	4
8	Male	42	Left	14	8	Anisocoria	24-48h	12	23	3
9	Male	21	Right	15	6	Anisocoria	48-72h	15	16	4
10	Male	30	Right	12	11	Anisocoria	24-48h	15	15	4
11	Female	39	Right	9	6	Anisocoria	72-96h	Die	13	1
12	Male	71	Left	10	7	Anisocoria	72-96h	Die	8	1
13	Male	56	Right	14	12	Isocoria	<24h	15	10	3
14	Female	47	Right	13	8	Isocoria	<24h	8	109	2
15	Male	63	Right	10	6	Anisocoria	<24h	6	65	2
16	Male	79	Right	15	5	Anisocoria	<24h	Die	10	1
17	Male	44	Left	10	10	Isocoria	<24h	11	15	4
18	Male	58	Right	13	13	Isocoria	<24h	15	13	4
19	Male	61	Right	6	6	Isocoria	24-48h	12	21	3
20	Female	48	Left	10	7	Isocoria	48-72h	11	16	3
21	Male	58	Right	12	7	Isocoria	24-48h	14	25	4

Pct: patient; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale.

Time between onset of symptoms and decompressive craniectomy was less than 24 hours in 10 (47.61%), 24-48 hours in 5 (23.8%), 48-72 hours in 4 (19%) and 72-96 hours in 2 cases (9.52%). We have considered that early surgery was a decompressive craniectomy in the absence of brain herniation signs and in patients with GCS >8 despite the length of hospital stay. It was carried out in 12 cases and late surgery in other 9 patients. Length of stay in the hospital was of 25.76 ± 23.3 days. Surgery improved significantly the GCS of patients comparing the immediate pre-operative scores (8.0 ± 2.19) and immediate post-operative GCS (11.62 ± 4.41), ($p < 0.05$). Occurrence of GCS <9 in the pre-surgical evaluation was associated to a higher length of hospital stay (30.06 ± 25.3 versus 12.0 ± 3.46 , $p < 0.05$).

There was no statistical significance in the outcome between men and women, surgery before and after 24 hours of ictus, left and right side stroke groups ($p > 0.05$). Patients older than 60 years presented worst outcome at six months (1.75 ± 0.957 versus 3.41 ± 0.87 points in GOS, $p < 0.05$). The presence of brain herniation signs represented a variable associated to poor prognosis, but statistical significance was not reached in this study (2.59 ± 1.33 versus 3.5 ± 0.67 points in GOS, in patients with and without pupillary changes, respectively; $p = 0.09$). According to the Mann-Whitney test, the group of patients who had a poor GCS in the pre-surgical evaluation presented a trend toward poor prognosis, however statistical significance was not demonstrated (2.88 ± 1.14 versus 3.8 ± 0.44

points in GOS, $p = 0.08$). However, when GCS ≤ 7 is used to predict poor prognosis, we reached statistical evidence ($2.72 \pm 1.27 \times 3.54 \pm 0.68$ points in GOS, $p < 0.05$).

Ten patients (47.61%) presented a good outcome at the 6 months evaluation. Eight patients who survived had a poor outcome (38%). Three patients of our series died (14.2%) after the surgical procedure, secondary to the presented brain lesion and hemodynamic failure.

DISCUSSION

Patients with massive space-occupying hemispheric infarction have a poor prognosis, as mass effect usually develops rapidly with occurrence of clinical deterioration in the first 2 to 4 days^{5,9,10}. Decompressive surgery has been studied as a way to relieve the intracranial hypertension and tissue shifts related to mass lesions. Bendszus et al. in a case report study, analyzing perfusion CT before and after decompressive craniectomy showed the value of this procedure to spare the ischemic but not infarcted area¹¹.

Non-randomized studies suggest that late and early decompressive surgery reduces mortality and increases the number of patients with a favorable functional outcome after massive hemispheric infarction compared to the conservative treatment^{4,5,8,10,12}. Indeed, early decompressive surgery with duraplasty is related with even a better outcome^{9,12}.

Several conservative measures have been proposed to limit brain tissue shifts and reduce intracranial pressure,

Table 3. Conservative treatment of massive cerebral infarction.

Paper	Study design	Patients	Mean age	Mortality	Survivors outcome
Rieke et al. ⁴	Open, nonrandomized, control trial	21/53	49	76%	G1:0%; G2:10%; G3:14%
Holtkamp et al. ²	Retrospective descriptive study	12/24	65	83%	G1:0%; G2:0%; G3:17%
Kuroki et al. ³	Retrospective/prospective descriptive study	7/15	79	85%	G1:0%; G2:0%; G3:15%
HAMLET ⁷	Multicenter prospective randomized open study	9/23	43	89%	G1:0%; G2:11%; G3:0%
DECIMAL ¹⁶	Multicenter prospective randomized open study	18/38	43	78%	G1:0%; G2:22%; G3:0%
DESTINY ¹⁵	Multicenter prospective randomized open study	15/32	46	53%	G1:0%; G2:27%; G3:20%
Vahedi et al. ⁵	Metanalysis of randomized trial	42/93	44	71%	G1:0%; G2: 21%; G3:7%
Total	–	82	51	75%	G1:0%; G2:13%; G3:11%

G1 (BI \geq 90; mRS 0 to 1; or GOS 5); G2 (BI 60 to 85; mRS 2 to 3; or GOS 4); G3 (BI $<$ 60; mRS 4 or 5; or GOS 2 to 3); G4 death.

Table 4. Surgical treatment of malignant middle cerebral artery infarction.

Paper	Study design	Pcts	Mean age	Treatment indication	Mort	Survivors outcome
Rieke et al. ⁴	Open, nonrandomized, control trial	32/53	49	Late surgery	34%	G1:0%; G2:18%; G3 47%
Holtkamp et al. ²	Retrospective descriptive study	12/24	65	Late surgery	33%	G1:0%; G2 + G3: 67%
Kuroki et al. ³	Retrospective/prospective descriptive study	8/15	72	Late surgery	12%	G1:0%; G2:44%; G3:44%
Uhl et al. ²⁴	Multicenter retrospective descriptive study	188	57	Late surgery	37%	G1:1,6%; G2:18%; G3:49%
Woertgen et al. ¹⁷	Retrospective descriptive study	48	48	Late surgery	26%	G1:7%; G2:18%; G3:50%
Kilincer et al. ⁹	Non-randomized prospective study	32	58	Late surgery	50%	G1:0%; G2:0%; G3: 50%
Gupta et al. ⁸	Metanalysis of non randomized trials and retrospective study	138	50	Review of 12 studies	24%	G1:7%; G2:35%; G3:34%
HAMLET ⁷	Multicenter prospective randomized open study	14/23	51	Randomized	21%	G1:0%; G2:29%; G3:50%
DECIMAL ¹⁶	Multicenter prospective randomized open study	20/38	43	Randomized	25%	G1:0%; G2:50%; G3:25%
DESTINY ¹⁵	Multicenter prospective randomized open study	17/32	43	Randomized	18%	G1:0%; G2:48%; G3:35%
Vahedi et al. ⁵	Metanalysis of 3 randomized trial	51/93	45	Review of 3 randomized studies	22%	G1:0%; G2:43%; G3:35%
Our institution	Retrospective descriptive study	21	50	Late surgery	14%	G1:0%; G2:47% ;G3:38%
Total	Non-randomized	435	54		31%	G1:3%; G2:24% ;G3:44%
Total	Randomized	51	45		22%	G1:0%; G2:43%; G3:35%
Total	–	486	53		30%	G1:3%; G2:25% ;G3:43%

Pcts: patients; Mort: mortality. G1 (BI \geq 90; mRS 0 to 1; or GOS 5); G2 (BI 60 to 85; mRS 2 to 3; or GOS 4); G3 (BI $<$ 60; mRS 4 or 5; or GOS 2 to 3); G4 death. Late surgery: signals of brain herniation; early surgery: before the firsts signals of brain herniation. The study of Rieke et al and Holtkamp et al. are already included in the study of Gupta et al. The HAMLET, DECIMAL and DESTINY are included in the metanalysis of Vahedi et al.

including intensive care therapy, mild bed elevation, sedation, hyperventilation, osmotic therapy, hypothermia and others. However, conservative treatment for massive brain infarction has been reported (Table 3) with a high mortality rate and poor outcome despite all those measures, suggesting that they are of limited value^{6,13,14}.

The three randomized trials, DECIMAL, DESTINY and HAMLET confirm these findings. DECIMAL and DESTINY were interrupted because of a significant difference

in mortality favoring decompressive surgery and HAMLET is still ongoing and aims to include 112 patients^{5,7,15,16}.

Several trials (Table 4) have described the effects of decompressive surgery on functional outcome after space-occupying infarction. As shown in Tables 3 and 4, the decompressive surgery increases the probability of survival from 25% to nearly 70% and the probability of a good outcome (G1 and G2) from 13% to 28%; however, the probability of surviving in a condition requiring as-

sistance and severe disability (G3) increases from 11% to 43%, probably due to the higher number of survivors. Therefore, information about quality of life of survivors is essential for guiding the therapeutic decision⁵. In spite of previous reports in the literature differ with respect to the functional outcome and quality of life after decompressive surgery for space-occupying infarction^{5,17}, even patients with aphasia may improve significantly¹⁸.

It is unclear which groups of patients benefit most from the procedure. Vahedi et al.⁵ demonstrated that surgery was beneficial ($p < 0.01$) independently of age (above and below 50 years), presence of aphasia, and time to randomization (above and below 24 h) when compared to conservative treatment. Kuroki et al.³ describe that the decompressive surgery outcome is better than the conservative treatment even in patient with more than 70 years old. Patients with the larger infarctions as found in the internal carotid artery (ICA) infarct were more likely to have a poorer prognosis as expected and according to Kilincer et al.⁹ surgery for an ICA infarction is not beneficial, unless exceptional cases as very young age, non-dominant hemisphere, and good clinical condition.

Identification of patients at high risk of malignant edema based on radiographic and clinical criteria might allow early hemicraniectomy, defined as a surgery performed before signs of brain stem herniation, as a mean of improving mortality and patient outcome^{6,9,10,12,19}. According to Schwab et al.¹⁰, early hemicraniectomy also reduces the time of critical care therapy from 13.3 to 7.4 days. Although no statistical significance was reached, we observed an important trend toward poor prognosis in the group of patients that had pupillary changes ($p = 0.09$).

Radiographic signs such as early hypodensity of $>50\%$ of the MCA territory and/or additional vascular territories (ACA or PCA)^{12,19-24}, ICA infarct 9, midline shift ≥ 10 mm^{9,19}, effacement of subarachnoid space^{19,20}, attenuation of corticomedullary differentiation^{19,20}, presence of hydrocephalus^{19,25} may predict which patients will develop malignant edema or bad outcome. Infarct volume of more than 200 cm³ has 91% accuracy to predict malignant hemispheric infarction¹² and the extent of infarct of more than two-thirds of MCA territory has a sensitivity of 93% and specificity of 95% and they are the two most sensitive and specific single explanatory variable for prediction of mortality¹⁹. On the other hand, brain edema is maximized after 24-72 hours¹⁹, so an early CT examination should not be considered sensitive enough to predict the final outcome^{19,20,25}.

Clinical signs such as early clinical deterioration⁹, early nausea or vomiting^{22,23}, and a National Institute of Health Stroke Scale (NIHSS) score ≥ 20 for left^{22,25} or ≥ 15 for right hemisphere infarction²², pre-operative GCS score ≤ 7 ⁹, hypertension or heart failure, and increased pe-

ripheral white blood cell count^{12,22}, also may predict which patients will develop malignant edema or have a poor outcome. Lam et al.¹⁹ indicate that a NIHSS >22 is predictive of high mortality. In our study, patients who presented GCS <8 in the pre-surgical exam demonstrated a tendency toward poor outcome, which in our view indicates that the surgical approach should not be delayed until neurological deteriorations occurs.

Although elevated ICP was correlated with higher mortality²⁶, ICP monitoring should not be the only parameter in the determination of surgical timing as clinical signs of deterioration or herniation can precede the increase in ICP²⁷.

Time from stroke to surgery has also been studied before. Non-randomized series have suggested that outcome is substantially improved if surgical treatment is initiated within 24 h of stroke onset as compared with longer time windows for treatment^{5,10,17}. Schwab et al.¹⁰ presented benefits of decompression before 24 hours after stroke. In a group of 31 patients, 26 (84%) had a BI >60 at follow up in their study. Gupta et al.⁸, however, did not show benefit to surgery <24 hours, probably due to a greater proportion of patients (64%) with signs of herniation before surgery in his group. Vahedi et al.⁵ in a systematic review, conclude that the timing of surgery did not affect outcome. We did not observe difference in outcome between patients submitted to surgery before or after 24 hours. We believe the reason for the no significant difference in timing of surgery was the poor general clinical status of patients who presented early to our department. In our view, timing between clinical deterioration and surgery and immediate pre-operative GCS are both more relevant factors than timing from stroke to surgery.

The age has been demonstrated to be an important predictor of outcome in decompressive hemicraniectomy. There are reports of poor functional outcomes and increased mortality in older patients compared to younger^{2,28}. The cut-off point age to predict a good outcome is uncertain. Wijdicks and Diringer²⁹ studied the natural history of 42 patients with MCA territory infarction, 3 of 11 patients (28%) <45 years died, whereas 20 of 22 patients >45 years, 90.9% died. Important studies suggest that the optimal recovery occurs in patients less than 50 years^{8,24,28,30}. However, Holtkamp et al.² use a cut-off point of 55 years and Kilincer et al.⁹, when selected 60 years as a cut-off point, provided one of the strongest predictors of outcome. In our series, there was no statistical difference when used a cut-off age of 50 years. However, patients older than 60 years presented worst outcome at six months follow up.

Offering life-saving treatment for large dominant hemisphere infarcts is controversial, mainly because surgery may leave patients with an unacceptable poor quali-

ty of life because of hemiplegia and aphasia²⁸. The side of the infarct did not have prognostic relevance in our study, as demonstrated by other series^{8,9,17,24}. In Gupta et al.⁸ review, the 27 patients who had decompression of the dominant hemisphere had functional outcome similar to the 111 patients who had non-dominant infarcts. In Kilincer et al.⁹, half of the patients had dominant hemispheric infarction with global aphasia preoperatively, 6/7 patients in the good outcome group had a dominant hemispheric infarction and most of the patients showed considerable improvements in their aphasia, a finding confirmed by other authors^{4,10,18,31}. Therefore, we believe infarction side should not be exclusion criteria for surgery. We agree with some authors that language deficits may be of small consequence in patients who are severely disabled by hemiplegia; also, non-dominant hemisphere strokes can lead to severe depressive, abulic, or neglect states that may interfere with rehabilitation efforts and are as disabling as aphasia^{8,32}. On the other side, global disability scales such as the BI, mRS, and GOS may emphasize mobility as opposed to language dysfunction^{8,9}.

It is not clear which patients may avoid severe disability after the procedure. A large number of patients or relatives (70%) stated that they would undergo the procedure again if faced to the same situation⁸. Even 79% of the patients and their family are satisfied with the surgical results³³.

In conclusion, decompressive craniectomy for space-occupying large hemispheric infarction increases the probability of survival that can yield good functional outcomes in some cases. Careful patient selection, made on an individual basis, and early operation may improve the functional outcome for large hemispheric infarction. Information about quality of life of survivors is essential for guiding such decisions because most patients require extensive rehabilitative therapy and lifelong assistance.

There are limitations in our study. Although we present important data about decompressive surgery, it is a non-randomized retrospective study with results that need confirmation by larger randomized trials. Although there is not a consensus for the surgical treatment of massive hemispheric infarction, we recommend: (1) in patients under 60 years old; (2) in patients with CT scan evidence of massive cerebral infarction with GCS ≥ 8 ; (3) decompressive craniectomy before signs of brain herniation if possible. Dominant hemispheric infarction does not represent an exclusion criteria.

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