ORIGINAL ARTICLE

Decompressive craniectomy: A salvage treatment for patients with central nervous system tumors

Craniectomía descompresiva: un tratamiento de rescate para pacientes con tumores del sistema nervioso central

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Abstract

Background: *Decompressive craniectomy (DC) has been used for the treatment of refractory increased intracranial pressure (ICP) in patients with brain trauma and stroke; its beneficial role is still a matter of debate. Little has been written on the role of DC in the setting of patients with intracranial tumors.* **Methods:** *We retrospectively reviewed our institutional tumor registry for all adult patients treated with a DC as an emergency treatment between January 2012 and June 2019.* **Results:** *A total of 61 patients were taken into surgery for a DC secondary to raised ICP related to a central nervous system tumor. The Kaplan-Meier curves in the study showed that 18.9 months was the mean survival time (MST) of the global population, 40 patients died (65.5%) during the follow-up period. Patients in the group of over 60 years had a worst survival time than younger patients (p = 0.01). Patients with intracerebral hemorrhage had the worst MST compared with the patients with other etiologies (p = 0.04).* **Conclusion:** *Our data show that in some selected cases DC is a viable option as a salvage treatment for patients with intracranial tumors.*

Key words: *Decompressive craniectomy. Meningioma. Glioblastoma. Low-grade glioma. Tumor.*

Resumen

Antecedentes: *la craniectomía Descompresiva (CD) se ha utilizado para el tratamiento del aumento de la presión intracraneal en pacientes con traumatismo cerebral y accidente cerebrovascular; su papel beneficioso sigue siendo un tema de debate. Poco se ha escrito sobre el papel de la CD en el contexto de pacientes con tumores intracraneales.* **Métodos:** *Revisamos retrospectivamente nuestro registro institucional de tumores para todos los pacientes adultos tratados con craniectomía descompresiva como tratamiento de emergencia entre enero de 2012 y junio de 2019.* **Resultados:** *Un total de 61 pacientes fueron llevados a cirugía por una CD secundaria a elevación de ICP secundario a un tumor del sistema nervioso central. Las curvas de Kaplan-Meyer mostraron que 18.9 meses fue el tiempo medio de supervivencia de la población global, 40 pacientes murieron (65.5%) durante el período de seguimiento. Los pacientes del grupo de más de 60 años tuvieron un peor tiempo de supervivencia que los pacientes menores (p = 0,01). Los pacientes con hemorragia intracerebral tuvieron la peor sobrevida en comparación con los pacientes con otras etiologías (p = 0,04).* **Conclusión:** *Nuestros datos muestran que en algunos casos seleccionados, la CD es una opción viable como tratamiento de rescate para pacientes con tumores intracraneales.*

Palabras clave: *Craniectomía descompresiva. Meningioma. Glioblastoma. Glioma de bajo grado. Tumor.*

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Introduction

Decompressive Craniectomy (DC) as a treatment for increased intracranial pressure (ICP) was introduced in the XIX century, and the first reports were made by Kocher in 1901 and by Harvey Cushing in 1905[1].

DC has been widely used for the treatment of abnormal ICP mostly for patients with traumatic brain injury (TBI) and stroke, nevertheless, DC has been used to manage intractable intracranial hypertension in other neurological conditions, but the evidence base is limited compared to that for TBI and stroke[2]. Little information exists regarding the role DC plays in patients with oncological pathologies.

This paper gathers a cohort of patients taken into surgery for DC to treat raised ICP related to an intracranial tumor and attempts to give an analysis to help better understand the role of this technique for patients with central nervous system (CNS) tumors.

Methods

An institutional database was reviewed for intracranial tumor cases treated in the period from January 2012 to June 2019. The diagnosis of the intracranial tumor was verified via pathology report generated by our institution. A retrospective chart review was performed to identify patients who were taken into surgery for a DC related to their intracranial tumor diagnosis.

We reviewed the clinical records of the patients and collected clinical and epidemiological data (age, sex, presenting symptoms, and functional status), tumor data (tumor location, and histologic characteristics), and treatment data. The Karnofsky Performance Status (KPS) score was used to assess a patient's functional status at different time points. The KPS score was either stated by the provider or retrospectively assigned by one of the authors based on the medical records.

The statistical analysis was performed using the SPSS software program, version 25 (IBM, Illinois, USA) measuring the mean, standard deviation (SD), median, and range of the discrete and continuous variables. We performed the KolmogorovSmirnov test to determine the normality of data distribution. For the analysis of parametric and non-parametric continuous variables, we used t-test and Wilcoxon test. For categorical variables, we used Chi-square test and fisher test. ANOVA test was used to compare the means among the different groups. The KaplanMeier curves and log-rank test was performed to determine the different variables until de outcome death occurs, examining if there was an independent risk factor on mortality. $p < 0.05$ was considered to have statistical significance.

Illustrative case

A 54-year-old woman developed progressive left-side hemiparesis and headaches of progressive intensity.

After magnetic resonance imaging (MRI) studies the diagnosis of an insular right side glioma was made. The patient was hospitalized and surgery was scheduled. On the night before the day of the surgery, the patient became drowsy and the left-side hemiparesis became worse. A computed tomography (CT) scan was made that showed progressive brain edema as well as progression of the cystic component of the lesion compared with the previous MRI image (Fig. 1A).

The patient was taken for an emergency surgery that consists of a subtotal resection and a DC. In the postoperative period the patient received medical treatment and had a good recovery over the next few days, a postoperative MRI was made to determine the extent of resection (Fig. 1B), and the following week was taken again into surgery to complete the resection (Fig. 1C).

After a 6 month follow-up period, the patient had a good recovery, although the hemiparesis persisted, she had a fair KPS and received adjuvant treatment with standard chemoradiation for a Grade II Oligodendroglioma.

She is still on follow-up appointments.

Results

A total of 6665 surgeries for the resection of intracranial tumors were performed between January 2012 and June 2019, out of these, 61 patients were taken into surgery for a DC secondary to raised ICP related to a CNS tumor, demographic and tumor-related characteristics are summarized in table 1. Table 2 shows the different clinical and demographic variables by tumor.

The distribution according to sex was fairly even, with a total of 34 patients being of female sex and 27 male patients, the mean age of the patient

population was 48.8 ±14.4 years, ranging from 17 years to 73 years. Glial tumors were the most frequent diagnosis; out of the 61 patients, 33 (54.1%) had some type of glial tumor, followed by meningioma in 21 cases (34.4%). Other tumors found were metastases in 3 cases (4.9%), lymphoma, esthesioneuroblastoma, paraganglioma, and finally, one tumor previously classified as a primitive neuroectodermal tumor.

The mean KPS before the DC was 82, (SD 13.8) showing that most of the patients had a good status prior to the complication leading to the emergency surgical event. The postoperative mean KPS was 49 (SD 25.4). To compare the difference between the KPS score we used the Wilcoxon test with a $p < 0.001$.

The main reason by far, that the DC was performed was cerebral edema that did not respond to medical management in 56 patients (86.8%), the remaining patients developed postoperative intracerebral hemorrhage and were taken into surgery for a DC.

In 21 cases the DC was performed at the time of the initial surgery (33%); the decision to perform a DC during the initial surgery was made by the inability to achieve dural closure due to raised ICP. Another 26 patients were taken to surgery in the first 72 h of the postoperative period (42%) due to the inability to control raised ICP in the postoperative period. The remaining patients required the DC later than 72 h (25%).

The Kaplan-Meier curves in the study showed that 18.9 months was the mean survival time (MST) of the global population (0-56 months), 40 patients died (65.5%) during the follow-up period.

We stratified the patients in different categories: tumoral grade and diagnosis, two age groups (< 60 and > 60), preoperative KPS (< 60 and > 60), indication for the DC (intracerebral hemorrhage, intraoperative and postoperative edema,), tumor localization (frontal, parietal, temporal, insular and skull base), and time of DC (initial surgery, early surgery < 72 h and late surgery > 72 h).

The patients having low-grade gliomas (LGG) (grade I-II) and meningiomas grade II-III had a MST of 22.9 and 32.7 months, respectively, with a better outcome than patients with high-grade gliomas (HGG) (III-IV), Metastasis, and other tumors ($p = 0.2$).

Patients in the group of over 60 years, had a worst survival time than the patients younger than 60, MST was 6.4 months and 22.7 months, respectively ($p = 0.01$) (Fig. 2).

Regarding the preoperative KPS, patients with a KPS of under 60 had an MST of 3.3 months compared with 19.7 months in the group with a KPS of > 60 ($p = 0.15$).

Table 1. Clinical and demographic variables of the study population

	n = 61
Age	48 ± 14.4 (17-74)
Sex F/M	34 (55.7%)/27 (44.3%)
Diagnosis	
Meningioma	21 (34.4%)
LGG	10 (16.4)
HGG	23 (37.7%)
Metastases	3 (4.9%)
Other	4 (6.6%)
Tumoral Grade	
Grade I	17 (27.9%)
Grade II	15 (24.6%)
Grade III	7 (11.5%)
Grade IV	18 (29.5%)
Metastasis	4 (6.6%)
Tumor Localization	
Frontal	14 (23%)
Temporal	13 (21.3%)
Parietal	8 (13.1%)
Insular	11 (18%)
Skull Base	15 (24.6%)
Side	
Left	28 (45.9%)
Right	31 (50.8%)
Bilateral	2 (3.3%)
Time to DC	
Initial surgery	21 (34.4%)
Early surgery < 72 h	25 (41%)
Late surgery > 72 h	15 (24.6%)
DC indication	
IOP brain edema	6 (9.8%)
POP brain edema	47 (77 %)
ICH	8 (13.1%)
Death	
Yes	40 (65.6%)
No	21 (34.4%)
Chemotherapy	
Yes	10 (16.4%)
No	51 (83.6%)
Radiotherapy	
Yes	15 (24.6%)
No	46 (75.4%)
Cranioplasty	
Yes	7 (11.5%)
No	54 (88.5%)
Preop KPS 82.7	82.7
Percentile 25	80
Percentile 50	90
Percentile 75	90
Postop KPS	49.8
Percentile 25	30
Percentile 50	50
Percentile 75	70

DC: Decompressive craniectomy, KPS: Karnofsky Performance Score, IOP: intraoperative, POP: postoperative, Intracerebral hemorrhage
Mean Values are presented as ±SD

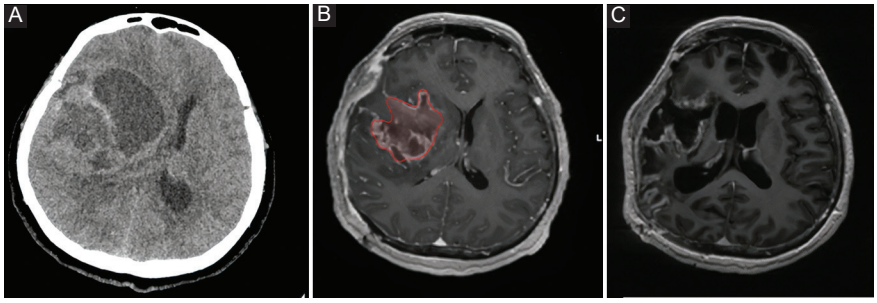

Figura 1. *CT scan taken prior to performing an emergency DC.* **A:** *immediate postoperative MRI with residual tumor.* **B:** *Postoperative MRI showing a GTR of the tumor C.*

Table 2. Clinical and demographic characteristics by tumor

Characteristic	LGG I-II (n = 10)	HGG III-IV (n = 23)	Meningioma I (n = 17)	Meningioma II-III (n = 4)	Metastases (n = 3)	Other (n = 4)	p value
Age years (SD)	39 ± 16.0	50 ± 13.0	51 ± 13.0	47 ± 13.3	62 ± 12.8	36 ± 13.6	p = 0.043
Sex							
Female	5	13	10	2	3	1	p = 0.6
Male	5	10	7	2	0	3	
Preop KPS	82±15.4	80±13.6	87±9.1	85±17.3	80±10.0	80±27.0	p = 0.75
Postop KPS	59±26.8	51±20.2	47±25.1	57±42.7	16±5.7	47±32.0	p = 0.21
Localization:							
Frontal	3	8	1	1	0	1	p = 0.001
Temporal	3	6	0	1	1	2	
Parietal	1	2	4	0	1	0	
Insular	3	7	0	2	1	0	
Skull Base	0	0	12	4	0	1	
Age group							
> 60	1	5	5	0	2	0	p = 0.29
< 60	9	18	12	4	1	4	
Time to DC							
Initial surgery	6	9	3	2	0	1	p = 0.16
Early surgery< 72 h	2	11	7	1	1	3	
Late surgery > 72 h	2	3	7	1	2	0	
Death							
Yes	6	16	11	1	3	3	p = 0.51
No	4	7	6	3	0	1	
Indication of DC							
IOP brain edema	1	3	1	1	0	0	p = 0.74
POP brain edema	9	15	14	3	3	3	
ICH	0	5	2	0	0	1	

Mean values are presented as ± SD
ǂInferential analysis: ANOVA test comparing the different mean values of the continuous variables. We performed the fisher test for the categoric variables.

When assessing the indication for the DC, patients with intracerebral hemorrhage had the worst MST compared with the patients with intraoperative and postoperative edema, 5 months versus. 24.6 and 21.2 months, respectively (p = 0.04) (Fig. 3).

When the DC was performed as the initial surgery, the MST was 22.6 months compared with an early surgery < 72 h, 9.1 months, and late surgery 16.4 months (p = 0.02) (Fig. 4).

Tumor location had no influence on the MST for the patients in this study.

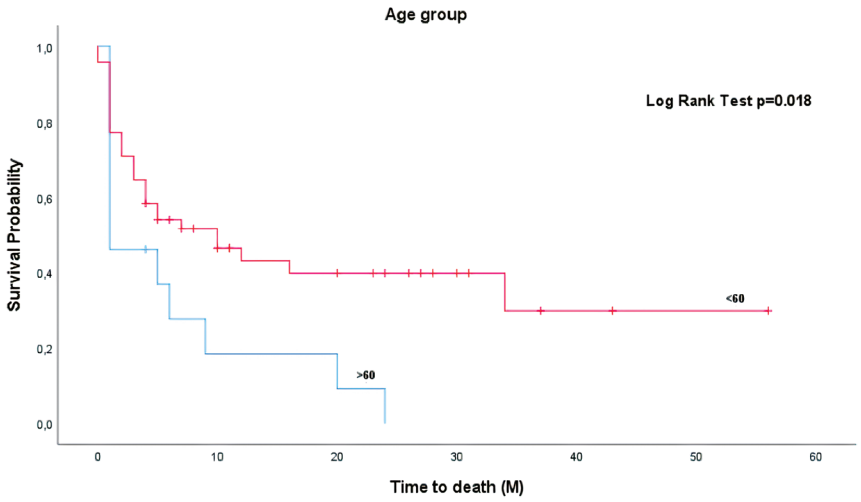

Figura 2. *Kaplan-Meyer curve that illustrates the survival probability between patients over and under 60 years old after a decompressive craniectomy for an intracranial tumor.*

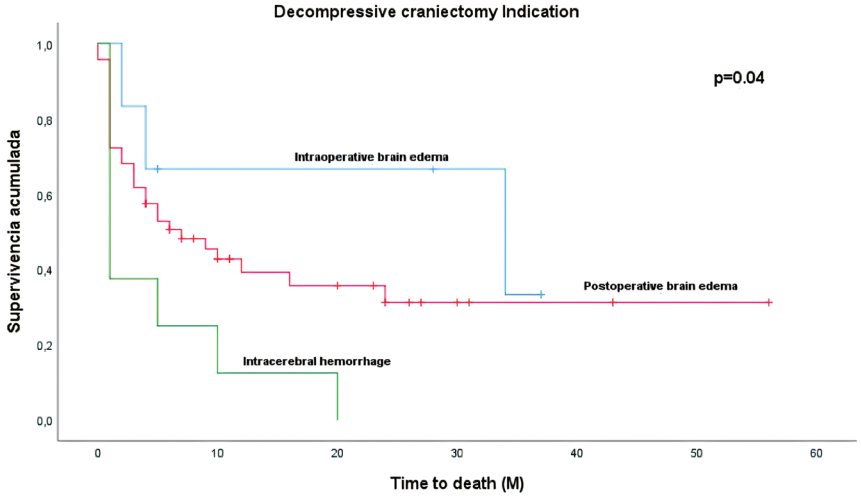

Figura 3. *Kaplan-Meyer curve that illustrates the survival probability after a decompressive craniectomy for different surgical indications.*

Discussion

Adequate control of ICP is of great importance for the outcome of patients with various neurological pathologies. This has been studied largely for patients with TBI and stroke[3,4].

It has been proven that DC has a positive effect on ICP, although its effects on the end results are still controversial[5,6].

Despite great advances in our knowledge of ICP and DC, there is little information regarding the role of DC in patients with oncological pathologies.

Among all neurosurgical procedures, craniotomy for the resection of an intracranial tumor has the second-highest rate for reoperation[7], which indicates the complexity of this surgery. Dasenbrock et al. stated the reasons and type of surgery for unplanned reoperation after craniotomy for tumor resection[8], in their article they established that DC was performed after the initial surgery for resection in 6.1% of a total 462 patients, although it was not established what lead to the decision to make the DC. It is worth noting that it was mentioned that meningiomas were more likely to be taken into surgery for reoperation than other types of tumors.

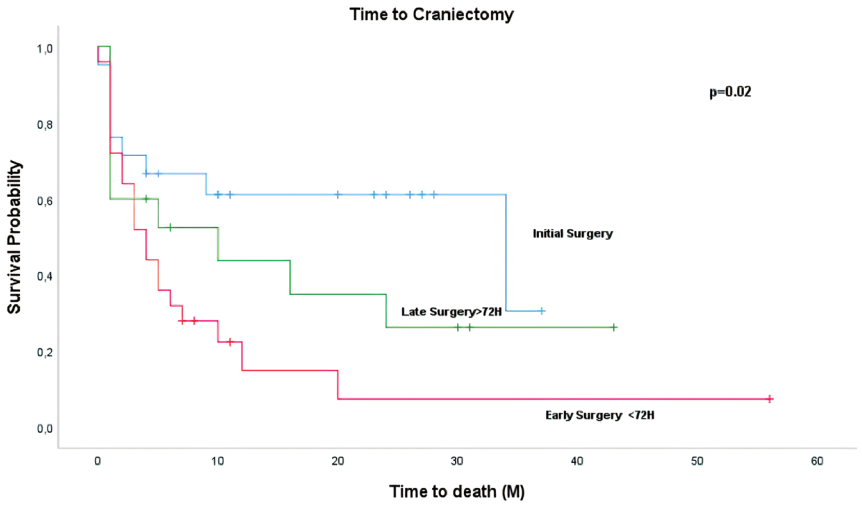

Figura 4. *Kaplan-Meyer curve that illustrates the survival probability after a decompressive craniectomy according to the different time periods the surgery was performed.*

In our series, the rate of DC performed for intracranial tumors was 0.9%, but it was performed more frequently in HGG than in meningiomas.

Regarding meningiomas specifically, Missori et al. reported six cases of emergency DC after removal of supratentorial convexity meningiomas[9], increased brain edema lead to further midline shift, which leads the authors to perform the DC. In this case series, 4 out of the 6 patients had a good or fair outcome, while one patient had a severe disability and another one died after 8 months.

In our series of patients, we present 21 cases of meningiomas that required a DC following the initial surgery for resection. The majority of cases were skull base meningiomas in 14 of the 21 patients, six patients had convexity meningiomas and one patient had an intraventricular meningioma.

After emergency DC craniectomy the survival rate for meningioma patients was 45% with a mean postoperative KPS of 70.

These results show that in patients with meningiomas that develop refractory postoperative edema, DC is an alternative that is worth considering as a salvage method, since it could be life saving and the functional outcome in survivors is good.

We could not find a case series that reports DC for glial tumors, specifically as the treatment for intraoperative and postoperative edema.

We present 33 patients with glial tumors that required DC as the result for refractory raised ICP.

The survival rate for patients with glial tumors that required an emergent DC is lower than what is seen for patients with meningiomas, although it could be argued that this is secondary to the natural history of the tumor itself. Out of all the patients with glial tumors, 36% of patients survived after the surgical treatment and the mean KPS was 64, although the overall survival did not differ between HGG and LGG, it is worth mentioning that the functional status was worse in HGG when compared to LGG. This is important, as most of LGG patients that survived after DC, went on to receive adjuvant treatment with radiation therapy and chemotherapy.

So in this pathology, the role of the DC is to achieve stabilization of the patient while the cause of the increased ICP is corrected, so that the patient is in a well enough state to receive and tolerate adjuvant treatment, given that the strongest factor that impacts survival is the oncological disease itself.

It was expected that low-grade tumors such as meningiomas and LGGs would have a better prognosis, as the role of the DC craniectomy is to relieve the temporary raised ICP and give a chance for these patients to continue the complementary treatment, and so, the natural course of the disease is expected to be better than the more malignant counterpart.

There are several case reports of intracerebral hemorrhages secondary to a brain tumor that was treated with DC, the pathologies and results vary.

DC for the treatment of spontaneous intracerebral hemorrhage has also been studied, a recent

meta-analysis that included eight studies[10], showed that DC as part of the treatment for this entity was related to a better outcome for the patients, compared to those in which DC was not performed. It is important to note that the articles in which spontaneous intracerebral hemorrhage was secondary to a brain tumor were excluded from the study, as they have been in most studies regarding this subject.

Iaconis et al. reported a case of a neuroblastoma in a 5-year-old girl with a hemorrhagic presentation that was initially treated with DC[11], in this case, the patient died after 6 months. On the other side of the spectrum, a case of a 34-year-old patient with a hemorrhagic brain metastasis was taken into surgery for a DC as part of the treatment; the patient had initially a good recovery after surgery, although the tumor had a late re-bleeding that caused the patient's death[12].

In our case series, seven patients were taken into surgery for a DC after developing an intracranial hemorrhage following the first surgery for tumor resection. Out of these seven patients, five patients had a HGG as the diagnosis. Despite being treated aggressively with medical and surgical treatment, none of these patients had a good outcome. The end result for these patients was not favorable, as all the patients ultimately died after a mean 3-month follow-up.

These results may suggest that refractory ICP secondary to intracerebral hemorrhage may represent a factor for poor prognosis in patients that require a DC following resection of an intracranial tumor.

Regarding intracerebral hemorrhages, it has been described that the presence of systemic cancer is an independent factor for poor prognosis in these patients[13], and should be taken into account when deciding if a patient may benefit from surgery, especially a DC.

None of the patients in our series that required a DC secondary to intracerebral hemorrhage had brain metastasis, although the analysis for histological diagnosis showed that patients with brain metastasis bared worst after DC that other tumors, again, most likely due to the nature of this specific pathology.

The value of a DC without addressing the main cause of the increased ICP has been questioned. In the case of raised ICP secondary to intracerebral hemorrhage, it has been shown that it is feasible to improve the patient's outcome by performing a DC without resecting the intracerebral clot at the moment of the initial surgery[14]. We believe that in selected cases this might also be the case for brain tumors that present with an intracerebral hemorrhage, and DC may be performed as a salvage treatment initially, this may include partial resection of the lesion and hemostasis control, and once the patient is stable, it may be taken into surgery with oncological intent.

It has been reported that DC as the initial treatment for raised ICP in brain tumors may cause intratumoral bleeding, so this approach must be taken with the necessary precautions[15].

Brain edema secondary to many pathologies is one of the main causes of raised ICP. Many tumoral pathologies cause a great deal of edema, and some patients may develop herniation syndromes secondary to brain edema caused by a tumor, requiring emergency procedures.

Zhu et al. reported a case of a 10-year-old girl that developed severe brain edema following the administration of chemotherapy for a glioblastoma requiring emergency DC, the patient in this case died some days later[16].

Most of the cases that required DC in our series were secondary to refractory brain edema, the average survival time for these patients was nearly 2 years, and faired better than those that required DC secondary to cerebral hemorrhage. We propose that DC should be considered in these patients because it is a life-saving procedure, and after recovery, most patients develop a good functional status and this allows the patients to go on and receive the definitive oncological treatment with a relatively good outcome.

As it is the case with other causes of raised ICP, early DC in our case series appears to be a factor that positively influences the outcome for patients in need of a DC. In the literature regarding TBI and DC, there is a tendency that indicates that early DC may be more helpful to improve the long-term outcome of patients with refractory raised ICP[17]. We believe that our results support this notion in patients with intracranial tumors as well.

It is worth mentioning that this study has many limitations; the retrospective nature of the study, as well as the inclusion of different tumoral pathologies in the final data, is something that has to be taken into account when analyzing the results.

Nevertheless, we hope that it is encouraging enough so that further and better studies are designed and better information is obtained regarding this issue.

Conclusions

Our data show that in some selected cases DC is a viable option as a salvage treatment for patients with

intracranial tumors, this procedure improves survival for patients with brain tumors and in some cases, allows the patients to recover just well enough to receive adjuvant treatment with radiation therapy and chemotherapy.

Older patients and patients with postoperative hemorrhage had the worst outcomes after DC. Further studies are needed to validate these results.

Conflicts of interests

The authors have no conflicts of interests

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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