Malignant Cerebral Venous Infarction: Decompressive Craniectomy versus Medical Treatment

Humain Baharvahdat[1,2], Sina Ahmadi[1], Babak Ganjeifar[1], Hamid Etemadrezaie[1], Samira Zabyhian[1], Payam Sasannejad[2], Gholamreza Bahadorkhan[1], Ashkan Mowla[3]

BACKGROUND: Cerebral venous thrombosis (CVT) is a common type of stroke in young adults and associated with 8% mortality. High intracranial pressure (ICP) and brain herniation are the most common causes of death in these patients. In contrast with malignant arterial middle cerebral infarction, there are few studies reporting the efficacy of decompressive craniectomy (DC) for treatment of high ICP in patients with CVT. In this study, we assess the clinical outcome of patients with CVT with impending brain herniation treated with DC versus medical management.

METHODS: In this retrospective study, medical records of all patients with CVT admitted to our hospital were reviewed. Patients with the following inclusion criteria were entered into the study: 1) CVT proven by contrast-enhanced magnetic resonance venogram and/or computed tomography venogram, 2) malignant CVT (impending brain herniation according to imaging and clinical finding), and 3) age between 16 and 80 years. Patients with deep venous system thrombosis, Glasgow Coma Scale (GCS) score of 3, and bilateral nonreactive midposition pupils or mydriasis on admission were excluded. Patients were classified into 2 groups: surgical group (DC group) including patients who received medical treatment and DC and medical group (MG) including patients who received only medical treatment. Outcomes and complications were assessed and compared between the 2 groups.

RESULTS: Of 357 patients with CVT hospitalized in our center, 48 patients entered into the study. Twenty-three patients were managed medically, and 25 patients were managed surgically. There was no significant difference between the groups concerning age, sex, presenting symptoms, transient and permanent risk factors of CVT, GCS score on admission, and pupils' reactivity on admission. All patients in the MG died during hospitalization in comparison with 8 patients in the DC group (100% vs. 32%, $P < 0.001$). Favorable outcome (modified Rankin scale score 0–2) was achieved in 52% of the DC group and 0% of the MG group ($P < 0.001$).

CONCLUSIONS: The results of our study confirmed that in contrast with DC, medical treatment could not prevent transtentorial herniation. DC is not only lifesaving for patients with CVT with impending brain herniation but also results in favorable outcome in most patients.

INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon type of stroke, and it mostly happens in young adults. It is associated with poor outcome in about 15% of cases, with approximately 8% rate of death.[1] High intracranial pressure (ICP), brain herniation because of hemorrhagic lesions, and diffuse edema were shown to be the most common causes of death in patients with CVT.[2] Decompressive craniectomy (DC) is a standard approach for malignant middle cerebral artery infarction to save lives.[3,4] For CVT, several studies have shown that DC might prevent death in many patients and result in good

Key words
- Cerebral venous infarction
- Decompressive craniectomy
- Medical treatment

Abbreviations and Acronyms
CT: Computed tomography
CVT: Cerebral venous thrombosis
DC: Decompressive craniectomy
GCS: Glasgow Coma Scale
ICP: Intracranial pressure
MG: Medical group
MRI: Magnetic resonance imaging
mRS: Modified Rankin scale

From the Departments of [1]Neurosurgery and [2]Neurology, Mashhad University of Medical Sciences, Mashhad, Iran; and [3]Department of Radiology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

To whom correspondence should be addressed: Ashkan Mowla, M.D. [E-mail: Mowla_a@yahoo.com]

Citation: World Neurosurg. (2019). https://doi.org/10.1016/j.wneu.2019.05.028

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

outcome in 30.7%; however, in contrast with ischemic stroke, a lower incidence of CVT accounts for a limited number of published case series, small controlled studies, and few systemic reviews to discuss the benefits of DC and/or hematoma evacuation in patients with CVT with suspected high ICP.[5-7] In our center, high ICP in patients with CVT is managed at the discretion of the treating physician medically or surgically or with both approaches. In this retrospective hospital-based study, we report the clinical outcome of patients with CVT with impending brain herniation treated with DC versus medical management.

METHODS

This study was approved by the ethical committee of Mashhad Medical Faculty, Mashhad, Iran. We reviewed the clinical records of patients with CVT who were treated in the neurologic and neurosurgical departments, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran, between March 2011 and March 2017. Patients with the following inclusion criteria were entered into the study: 1) CVT proven by contrast-enhanced magnetic resonance venogram and/or computed tomography venogram, 2) malignant CVT, and 3) age between 16 and 80 years. Malignant CVT was defined as supratentorial cortical stroke (ischemic or hemorrhagic) along with severe brain edema because of CVT associated with clinical (decline or loss of consciousness and unilateral or bilateral pupil dilation) or imaging signs of transtentorial herniation either at onset or after worsening. Patients with the following criteria were excluded: 1) patients with deep venous system thrombosis involving deep structures such as the midbrain, thalamus, and basal ganglia; and 2) patients with Glasgow Coma Scale (GCS) score of 3 and bilateral nonreactive midposition pupils or mydriasis on admission that did not improve after bolus dose of mannitol.

The following steps were performed to enter the patients into the study. First, we reviewed the medical records of all patients diagnosed with CVT (N = 357). We included patients with any reports of decline or loss of consciousness in clinical records or severe edema including midline shift or space-occupying lesions in imaging (head computed tomography [CT] scan or magnetic resonance imaging [MRI]). Then we excluded patients with deep vein system thrombosis or bilateral nonreactive pupils on admission that did not respond to bolus dose of mannitol.

In our center, on diagnosis of CVT, patients are admitted to the neuro intensive care unit and managed according to the guidelines of the American Heart Association/American Stroke Association on management of CVT, including anticoagulation (heparin or low-molecular-weight heparin). At the discretion of the treating physician, patients with malignant CVT were treated medically or surgically. For medical treatment, conventional medical therapy was done for lowering ICP using sedation and mannitol. In case of a surgical approach, anticoagulation was held for 6 hours and DC was carried out using a large frontotemporoparietal flap on the side of brain swelling, opposite to the midline shift, or a bifrontal craniectomy for generalized edema without touching the brain or any present hematoma. The dura mater was expanded with the periosteum, and the flap was preserved in abdominal subcutaneous tissue. Anticoagulation was restarted 1–14 days after the operation based on postoperative CT scans. If mannitol was started before the operation, it was discontinued gradually within 1–2 days after the operation. Other conventional medical therapy was continued for patients in the neurosurgical intensive care unit.

Clinical and radiologic data of patients were reviewed and the following parameters were collected: demographic data, risk factors for CVT, clinical findings on admission, GCS score on admission and before surgery, brain CT scan and MRI findings, cerebral dural sinus involved, interval timing between admission and operation, largest diameter of craniectomy flap, and complications of operation. Patients were assessed at time of discharge and at 6 months after discharge using the modified Rankin scale (mRS). The patients were classified into 2 groups: surgical group (DC group) including patients who received medical treatment and DC and medical group (MG) including patients who received only medical treatment. The risk factors of CVT were divided into 2 categories: 1) permanent risk factors when CVT was secondary to inherited thrombophilia or cancer, and 2) transient risk factors such as pregnancy, dehydration, or puerperium. Patient outcome was classified into favorable outcome when mRS score was 0–2 and poor outcome when mRS score was $\geq$3.

Continuous data were presented as mean $\pm$ SD, and categorical data were presented as count (%). Between the 2 groups, we compared continuous data using Student *t* test and categorical data using χ^2 and Fisher exact tests. Statistical analysis was performed using SPSS 16 (IBM Corp., Armonk, New York, USA), and $P < 0.05$ was considered significant.

RESULTS

Basic Characteristics

Of the 357 patients with CVT hospitalized in our center during the aforementioned time period, 48 patients met the criteria and were entered into the study. The mean age of the patients was 39.2 $\pm$ 11.8 years, with a range from 17 to 68 years. Twenty-eight patients (56%) were women. Twenty-three patients were managed medically and 25 patients were managed surgically. Table 1 shows the basic characteristics of the patients. Headache was the most common presentation among all patients (56%). Eighteen patients (38%) presented with loss of consciousness. Seventeen patients (35%) deteriorated clinically (GCS score lowered at least 2 points) during the first 48 hours of admission and required aggressive treatment, including sedation, intubation, and high-dose mannitol. There was no significant difference between the DC group and MG concerning age, sex, presenting symptoms, transient and permanent risk factors of CVT, GCS score on admission, and pupils' reactivity on admission (Table 1).

Radiologically, most patients (79%) had hemorrhagic infarction, and 89% of this group showed midline shift >5 mm. In 24 patients (50%) the lesion (ischemic and/or hemorrhagic lesions) was predominantly left-sided, and in 6 patients it was bilateral. Superior sagittal sinus was the most common involved sinus (63%), and multiple sinuses were involved in 17 patients (46%). There were no significant differences between the DC group and MG in terms of hemorrhagic lesion frequency, midline shift, and dural sinus involvement (Table 1).

Management and Outcome

Twenty-three patients were treated medically. All these patients received full sedation, intubation, and osmotic therapy for

Table 1. Basic Characteristic of Patients (N = 48)

Characteristic	All Patients	Medical Group (n = 23)	Surgical Group (n = 25)	*P* Value
Age (years)	39.2 ± 11.8	39 ± 12.7	39.4 ± 11.2	0.917
Female	28 (58)	14 (61)	14 (56)	0.732
Presenting symptoms				
Headache	27 (56)	14 (61)	13 (52)	0.372
Seizure	14 (29)	9 (39)	5 (20)	0.145
Loss of consciousness	18 (38)	6 (26)	12 (48)	0.117
Neurologic deficit	10 (21)	6 (26)	4 (16)	0.132
Transient risk factors	17 (35)	12 (52)	5 (20)	0.094
Permanent risk factors	2 (4)	1 (4)	1 (4)	0.367
GCS score on admission	11.6 ± 2.1	11.3 ± 2.2	11.8 ± 2.1	0.427
Unilateral fixed dilated pupil on admission	2 (4)	0 (0)	2 (8)	0.490
Midline shift >0.5 mm	41 (85)	19 (83)	22 (88)	0.564
Hemorrhagic infarction	38 (79)	16 (70)	22 (88)	0.116
Superior sinus	30 (63)	15 (65)	15 (60)	0.709
Lateral sinus	24 (50)	12 (52)	12 (48)	0.773
Multiple sinus	17 (46)	8 (35)	9 (36)	0.630
Acute deterioration*	17 (35)	8 (35)	9 (36)	0.930
Preoperative GCS score	N/A	N/A	8.8 ± 3	N/A

Values are mean ± SD, number of patients (%), or as otherwise indicated.
GCS, Glasgow Coma Scale; N/A, not available.
*Deterioration during the first 48 hours of admission.

decreasing ICP. Twenty-five patients were treated by DC without hematoma evacuation in the other group. Mean preoperative GCS score was 8.8 ± 3. Twenty patients had DC within 48 hours of admission and 5 patients had it after 48 hours (at 52, 72, 130, 144, and 219 hours of admission). The mean largest diameter of the flap was 14.1 ± 1.5 cm (range, 11.4–17.3 cm). The mean shortest diameter of the flap was 11 ± 2.2 cm (range, 9.2–17.3 cm). Two patients needed reoperation: one had subdural empyema and underwent reoperation for debridement and the other one was reoperated for enlarging the flap because the first flap was too small. Anticoagulation was restarted within 48 hours of operation in 11 patients (44%), in 2 patients on the third day, in 1 patient on the fourth day, in 5 patients on the fifth day, in 2 patients on the seventh day, and in 4 patients on the tenth day or later. One patient for whom anticoagulation was restarted on day 3 of postoperation showed increasing size of previous hematoma, and he died of brain herniation.

Outcomes of patients are shown in Table 2. On discharge, only 9 of 48 patients (19%) had favorable outcome. All patients in the MG died before discharge. This was significantly higher than the DC group (100% vs. 32%, respectively; $P < 0.001$). The cause of death in the MG was brain herniation. In the DC group, 5 patients died of brain herniation, 1 died of infection, and 2 died from pulmonary embolization. Nine patients (36%) in the DC group were discharged with mRS score ≤2. In other words, there was a significant difference between the 2 groups in terms of favorable outcome (36% in DC group vs. 0% in MG, $P < 0.001$). The mean time of follow-up was 31.4 ± 25.3 months (range, 6–66 months) after discharge. At the last visit, favorable outcome was seen in 13 patients in the surgical group (52%).

Overall, hemorrhagic infarction was associated neither with poor prognosis nor with death ($P < 0.001$ for both). Out of 15 patients with hemorrhagic infarction who were alive, 11 (73.3%) experienced favorable outcome without any significant deficit.

DISCUSSION

To our knowledge, this study is the largest study that compares outcome of DC and medical treatment in patients with malignant CVT. All patients who were managed with medical treatment died before discharge; however, most patients who underwent DC not only survived but also had an independent life at 6-month follow-up. The results of our study confirm the efficacy of DC in comparison with medical treatment in patients with malignant CVT and support the results of other relevant studies.[5-13]

In general, most patients with CVT have a favorable outcome, and only a small portion experience poor outcome or death (4%–16%).[1,14-17] Death is usually caused by transtentorial herniation from severe brain edema or large parenchymal lesion.[2] Patients

Table 2. Patient Outcome Comparison Between the Surgical Group and Medical Group (N = 48)

	All Patients	Medical Group (n = 23)	Surgical Group (n = 25)	*P* Value
Discharge mRS score				
1	2 (4.2)	0 (0.0)	2 (8)	<0.001
2	7 (14.5)	0 (0.0)	7 (28)	
3	5 (10.4)	0 (0.0)	5 (20)	
4	2 (4.2)	0 (0.0)	2 (8)	
5	1 (2.1)	0 (0.0)	1 (4)	
Death	31 (64.6)	23 (100)	8 (32)	
Favorable outcome at discharge	9 (19)	0 (0.0)	9 (36)	0.001
Follow-up mRS score				
0–1	9 (19.0)	0 (0.0)	9 (36)	<0.001
2	4 (8.3)	0 (0.0)	4 (16)	
3	2 (4.2)	0 (0.0)	2 (8)	
4	1 (2.1)	0 (0.0)	1 (4)	
5	1 (2.1)	0 (0.0)	1 (4)	
Death	31 (64.6)	23 (100)	8 (32)	
Favorable outcome at last follow-up	13 (27.1)	0 (0.0)	13 (52)	<0.001

Values are number of patients (%) or as otherwise indicated.
mRS, modified Rankin scale.

with impending herniation and large infarcts do not benefit from endovascular treatment or medical treatment.[18] The indication to proceed with DC in patients with CVT was different in different studies but usually included patients with progressive consciousness deterioration despite maximal medical treatment or any clinical/imaging sign of impending herniation.[6-8] Deep CVT could damage significant structures, such as the thalamus, basal ganglia, and brainstem, and result in loss of consciousness without any significant high ICP, which may explain poor outcome and poor response to DC.[19] Therefore, in this study, we excluded patients with significant deep cerebral venous involvement.

DC immediately brings down ICP by giving more space to the edematous brain and may prevent and reverse transtentorial herniation. It may decrease the pressure on the cerebral venous system, may reopen collapsed cortical veins, may improve venous drainage, and may reverse venous cerebral infarction.[8,20]

Diffusion-weighted images of MRI confirmed that most nonhemorrhagic lesions in CVT are because of vasogenic edema that usually resolved in follow-up MRI.[21-23] Also the nonhemorrhagic lesions because of toxic edema mostly include viable cells in contrast with arterial ischemia and could reverse in follow-up MRI.[21-23] Hemorrhagic lesions usually are nonhomogeneous in diffusion-weighted images,[22] and they may include variant part of hematoma, viable parenchyma, vasogenic edema, and cytotoxic edema.[20] This is confirmed by the high rate of favorable outcomes without any significant sequela in our hemorrhagic cases (73%) and also after DC.[6,7] In other words, we prefer not to evacuate the hemorrhagic lesions in CVT cases to prevent damage to viable parenchyma within hemorrhagic lesions. In our study, DC decreased 80% death associated with transtentorial herniation, and it confirmed that DC with sufficient dural expansion might be enough to decrease ICP and transtentorial herniation and to preclude the necessity of hematoma evacuation.

About 15% of our patients did not have the significant midline shift (>5 mm) that is reported in other series.[6] This could be explained by generalized edema because of sagittal sinus involvement resulting in edema of both hemispheres without any prominence. Therefore, decision-making for DC should include other components of edema in addition to midline shift, including compression of basal cisterns, and patient symptoms.

Anticoagulants were started in 84% of our patients in the first week of DC, including 44% in the first 48 hours. There was one incidence of hematoma progression (5%) leading to the patient's death. Although the data showed the safety of early onset of anticoagulants after DC, it required close monitoring of patients, especially with intracranial hemorrhage, including symptoms and imaging to find out any hematoma size change.

Our study has limitations. The study retrospectively reviewed the patients' medical records and the patients were not randomized. There is a possibility that we were not able to retrieve all the patients in MG that could have benefit from DC. The sample size was limited, and this could affect the results of the study.

CONCLUSIONS

The result of our study confirmed that medical treatment could not prevent transtentorial herniation. In contrast, DC is not only lifesaving for patients with CVT with impending brain herniation but also results in favorable outcome in most patients. Also, DC is a safe procedure, and anticoagulants could be restarted early with caution.

REFERENCES

1. Shakibajahromi B, Haghighi AB, Salehi A, et al. Clinical and radiological characteristics of and predictors of outcome of cerebral venous sinus thrombosis, a hospital-based study [e-pub ahead of print]. *Acta Neurol Belg*. 2018. https://doi.org/10.1007/s13760-018-1009-6.

2. Canhao P, Ferro JM, Lindgren AG, et al. Causes and predictors of death in cerebral venous thrombosis. *Stroke*. 2005;36:1720-1725.

3. Juttler E, Schwab S, Schmiedek P, et al. Decompressive surgery for the treatment of malignant infarction of the middle cerebral artery (DESTINY): a randomized, controlled trial. *Stroke*. 2007;38:2518-2525.

4. Vahedi K, Vicaut E, Mateo J, et al. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). *Stroke*. 2007;38:2506-2517.

5. Zuurbier SM, Coutinho JM, Majoie CB, Coert BA, van den Munckhof P, Stam J. Decompressive hemicraniectomy in severe cerebral venous thrombosis: a prospective case series. *J Neurol*. 2012;259:1099-1105.

6. Aaron S, Alexander M, Moorthy RK, et al. Decompressive craniectomy in cerebral venous thrombosis: a single centre experience. *J Neurol Neurosurg Psychiatry*. 2013;84:995-1000.

7. Zhang S, Zhao H, Li H, You C, Hui X. Decompressive craniectomy in hemorrhagic cerebral venous thrombosis: clinicoradiological features and risk factors. *J Neurosurg*. 2017;127:709-715.

8. Theaudin M, Crassard I, Bresson D, et al. Should decompressive surgery be performed in malignant cerebral venous thrombosis?: a series of 12 patients. *Stroke*. 2010;41:727-731.

9. Ebke M, Jurgens KU, Tomandl B, Merten U, Kastrup A. Surgical treatment of space occupying edema and hemorrhage due to cerebral venous thrombosis during pregnancy. *Neurocrit Care*. 2011;15:166-169.

10. Ferro JM, Crassard I, Coutinho JM, et al. Decompressive surgery in cerebrovenous thrombosis: a multicenter registry and a systematic review of individual patient data. *Stroke*. 2011;42:2825-2831.

11. Mohindra S, Umredkar A, Singla N, Bal A, Gupta SK. Decompressive craniectomy for malignant cerebral oedema of cortical venous thrombosis: an analysis of 13 patients. *Br J Neurosurg*. 2011;25:422-429.

12. Rajan Vivakaran TT, Srinivas D, Kulkarni GB, Somanna S. The role of decompressive craniectomy in cerebral venous sinus thrombosis. *J Neurosurg*. 2012;117:738-744.

13. Raza E, Shamim MS, Wadiwala MF, Ahmed B, Kamal AK. Decompressive surgery for malignant cerebral venous sinus thrombosis: a retrospective case series from Pakistan and comparative literature review. *J Stroke Cerebrovasc Dis*. 2014;23:e13-e22.

14. Cantu C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium. Review of 67 cases. *Stroke*. 1993;24:1880-1884.

15. de Bruijn SF, Stam J. Randomized, placebo-controlled trial of anticoagulant treatment with low-molecular-weight heparin for cerebral sinus thrombosis. *Stroke*. 1999;30:484-488.

16. Breteau G, Mounier-Vehier F, Godefroy O, et al. Cerebral venous thrombosis 3-year clinical outcome in 55 consecutive patients. *J Neurol*. 2003;250:29-35.

17. Mehraein S, Schmidtke K, Villringer A, Valdueza JM, Masuhr F. Heparin treatment in cerebral sinus and venous thrombosis: patients at risk of fatal outcome. *Cerebrovasc Dis*. 2003;15:17-21.

18. Stam J, Majoie CB, van Delden OM, van Lienden KP, Reekers JA. Endovascular thrombectomy and thrombolysis for severe cerebral sinus thrombosis: a prospective study. *Stroke*. 2008;39:1487-1490.

19. Namazi MR, Mowla A. Massive right-sided hemorrhagic pleural effusion due to pancreatitis; a case report. *BMC pulm Med*. 2004;4:1.

20. Weber J, Vida M, Greiner K. Sagittal sinus thrombosis with malignant brain oedema: pathophysiology of cortical veins after decompressive craniectomy. *Acta Neurochir (Wien)*. 2013;155:651-653.

21. Keller E, Flacke S, Urbach H, Schild HH. Diffusion- and perfusion-weighted magnetic resonance imaging in deep cerebral venous thrombosis. *Stroke*. 1999;30:1144-1146.

22. Chu K, Kang DW, Yoon BW, Roh JK. Diffusion-weighted magnetic resonance in cerebral venous thrombosis. *Arch Neurol*. 2001;58:1569-1576.

23. Ducreux D, Oppenheim C, Vandamme X, et al. Diffusion-weighted imaging patterns of brain damage associated with cerebral venous thrombosis. *AJNR Am J Neuroradiol*. 2001;22:261-268.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 15 February 2019; accepted 3 May 2019

Citation: World Neurosurg. (2019). https://doi.org/10.1016/j.wneu.2019.05.028

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***

1878-8750/$ - see front matter