Outcomes of decompressive surgery for patients with severe cerebral venous thrombosis: DECOMPRESS2 observational study

Sanjit Aaron[1] MD, Jorge M Ferreira [2] MD, Jonathan M Coutinho [3] MD, PhD, Patrícia Canhão [4,5] MD, PhD, Adriana Conforto[6] MD, Antonio Arauz[7], Marta Carvalho[8] MD, Jaime Masjuan[9] MD, Vijay K Sharma[10] MD, Jukka Putaala [11] MD, PhD, Maarten Uyttenboogaart[12] MD, David J Werring[13] MD, Rodrigo Bazan[14] MD, Sandeep Mohindra[15] MD, Jochen Weber[16] MD, Bert A Coert[17] MD, Prabhu Kirubakaran[1] MD, Mayte Sanchez van Kammen [3] MD, PhD, Pankaj Singh[1] MD, Diana Aguiar de Sousa [5,18] MD, PhD, José M Ferro[5] MD, PhD and the DECOMPRESS2 study group

Affiliations

[1] Neurology Unit, Department of Neurological Sciences, Christian Medical College & Hospital, Vellore, Tamil Nadu, India. ORCID 0000-0002-5151-150 sanjith@cmcvellore.ac.in

[2] Serviço de Neurologia, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal

ORCID 0000-0001-7138-7597

[3] Department of Neurology, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands

[4] Serviço de Neurologia, Departamento de Neurociências e Saúde Mental, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal. ORCID 0000-0003-3816-0416

[5] Centro de Estudos Egas Moniz, Faculdade de Medicina, Universidade de Lisboa, Portugal

ORCID 0000-0002-2343-9097

[6] Hospital das Clínicas, Universidade de São Paulo, São Paulo, Brazil ORCID 0000-0001-7869-3490

[7] Stroke Clinic, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico. ORCID: 0000-0002-3340-4138

[8] Serviço de Neurologia, Unidade Local de Saúde São João; Departamento de Neurociências Clínicas e Saúde Mental, Faculdade de Medicina da Universidade do Porto, Porto, Portugal. ORCID 0000-0001-6972-9287

[9] Servicio de Neurología, Hospital Universitario Ramón y Cajal, IRYCIS, Departamento de Medicina, Universidad de Alcalá. Red RICORS, Madrid, Spain. ORCID 0000-0003-1329-0943[10] Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

[11] Department of Neurology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

[12] Department of Neurology and Medical Imaging Center University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. ORCID 0000-0002-6934-4456

[13] Stroke Research Centre, UCL Queen Square Institute of Neurology, London, UK. ORCID 0000-0003-2074-1861

[14] Faculdade de Medicina Campus de Botucatu, Universidade Estadual Paulista Julio de Mesquita Filho, Botucatu, São Paulo, Brazil.

[15] Department of Neurosurgery, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India

[16] Department of Neurosurgery, Steinenberg Clinic, Reutlingen, Germany

[17] Department of Neurosurgery, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands

[18] Stroke Center, Lisbon Central University Hospital, Lisbon, Portugal

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Corresponding author

Prof. José M Ferro

Faculdade de Medicina, Universidade de Lisboa

Hospital Santa Maria, Centro de Estudos Egas Moniz, 6th floor

Avenida Professor Egas Moniz s/n 1649-035 Lisboa, Portugal

Phone/Fax: 00 351 217957474

Mail: jmferro@fm.ul.pt

Twitter: Diana Aguiar de Sousa, Diana_A_Sousa

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Abstract

Background

Decompressive neurosurgery is recommended for patients with cerebral venous thrombosis (CVT) who have large parenchymal lesions and impending brain herniation. This recommendation is based on limited evidence. We report long-term outcomes of CVT patients treated by decompressive neurosurgery in an international cohort.

Methods

DECOMPRESS2 was a prospective, international cohort study. Consecutive patients with CVT treated by decompressive neurosurgery were evaluated at admission, discharge, 6 and 12 months. Primary outcome was death or severe disability (modified Rankin Scale [mRS] 5-6) at 12 months. Secondary outcomes included patient and caregiver opinion on the benefit of surgery. The association between baseline variables before surgery and the primary outcome was assessed by multivariable logistic regression.

Results

118 patients (80 women, median age 38 years) were included from 15 centers in 10 countries from 12/2011 to 12/2019. Surgery (115 craniectomies, 37 hematoma evacuations) was performed within a median of 1 day after diagnosis. At last assessment before surgery, 68 (57.6%) patients were comatose, fixed dilated pupils were found unilaterally in 27 (22.9%) and bilaterally in 9 (7.6%). Twelve-month follow-up data were available for 113 (95.8%) patients. Forty-six (39%) patients were dead or severely disabled (mRS 5-6), of whom 40 (33.9%) patients had died. Forty-two patients (35.6%) were independent (mRS 0-2). Coma (OR 2.39, 95% CI 1.03-5.56) and fixed dilated pupil (OR 2.22, 95% CI 0.90-4.92) were predictors of death or severe disability. Of the survivors, 56 (78.9%) patients and 61 (87.1%) caregivers expressed a positive opinion on surgery.

Conclusions

Two thirds of patients with severe CVT were alive and more than one third were independent one year after decompressive surgery. Among survivors, surgery was judged as worthwhile by 4 out of 5 patients and caregivers. These results support the recommendation to perform decompressive neurosurgery in patients with CVT with impending brain herniation.

Non-standard Abbreviations and Acronyms

CT	computed tomography
CVT	cerebral venous thrombosis
DECOMPRESS2	DECOMPRESSIVE SURGERY FOR PATIENTS WITH CEREBRAL VENOUS THROMBOSIS, PART 2
MR	magnetic resonance
mRS	Modified Rankin Scale

Background

Cerebral venous thrombosis (CVT) is a less common but potentially life-threatening type of stroke that mostly affects young adults. Although around 75% of patients with CVT have a favorable outcome [1-2], a minority (around 4%) [3] dies in the acute phase. Brain herniation due to unilateral mass effect produced by large venous infarctions or parenchymal hemorrhages is the major cause of early death in CVT[3]. In ischemic stroke, randomized trials have shown that decompressive hemicraniectomy can be lifesaving in patients with malignant middle cerebral artery infarction, without increasing the proportion of patients who become severely dependent[4,5].

Decompressive hemicraniectomy may be also life-saving and is recommended for CVT patients with large lesions producing mass effect and impending brain herniation[6,7]. However, this recommendation is based on low quality evidence, consisting of case reports, retrospective case-series and a few prospective small series from referral centers [8-18], which are difficult to generalize and prone to bias. In many studies the outcome was measured only at discharge. Moreover, the characteristics of CVT patients who most benefit most with decompressive surgery and long-term patient-reported outcomes are not known.

To address these knowledge gaps, we conducted an international prospective cohort study of patients with CVT treated by decompressive surgery, aiming to report their vital and functional outcome and patient-reported outcomes, and to analyze predictors of poor outcome one year after surgery.

Methods

Design

Decompressive Surgery for CVT Study 2 (DECOMPRESS 2) was a prospective, observational multinational cohort study of patients with CVT treated by decompressive surgery, which followed the STROBE[19] guidelines (Supplemental Material).

Objectives

We aimed to report at discharge, 6 and 12 months 1) vital and functional outcomes 2) patient and caregiver satisfaction with surgery and 3) to analyze predictors of poor outcome.

Data availability statement

Anonymized data will be made available upon reasonable request by qualified researchers approved by the Steering Committee.

Inclusion and exclusion criteria

Investigators were required to include consecutive patients with CVT admitted to their institution meeting the following inclusion criteria: 1. Diagnosis of CVT by MR and MR Venography, CT Venography or intra-arterial venography; 2. Treated by decompressive craniectomy and/or hematoma evacuation; 3. Written informed consent, according to local laws and regulations. Patients with CVT diagnosed at exploratory neurosurgery or autopsy were excluded, as were those with CVT associated with head trauma or other intracranial disease (e.g., subdural hematoma, ruptured arteriovenous malformation, dural arteriovenous

fistula or development venous anomaly) with an additional potential underlying indication for neurosurgery.

Baseline information

Data on demographic information, dates of onset of symptoms, CVT diagnosis and surgery, presenting symptoms and signs, sinuses and veins involved, results of admission CT/MR, risk factors/associated conditions, clinical course, and treatments were collected (Table S1). The investigation of risk factors/associated conditions, further investigations and repeated neuroimaging and treatments were left to the discretion of the local investigators, who were advised to follow current CVT guidelines [6,7]. A detailed glossary with operational definitions was distributed to the participants.

Neurosurgery

We collected information on the last neurological examination and CT or MR performed before surgery, whenever available. The timing, type and technical details of the neurosurgical intervention and admission to intensive care were at the discretion of the local investigators and neurosurgeons. We systematically collected information on events and complications after surgery. We recommended to repeat CT or MR imaging after surgery.

Neuroimaging

To evaluate the degree of midline shift in each patient, investigators were requested to provide at least one anonymized slice of the CT/MR scan performed immediately before surgery. In cases where such examination was not available, the admission CT/MR was used. These slices were assessed by two independent investigators (JF and JMF at Universidade de Lisboa to measure midline shift. Disagreements between the investigators were solved by consensus. Midline shift was defined as the largest shift of the falx or septum pellucidum measured at the level of either the pineal or of the lateral ventricles.

Follow-up

Followup assessments were conducted at 6 (+/- 1) months and 12 (+/- 1) months after surgery (Table S1, flow-chart of the study). Whenever possible, patients were invited to attend outpatient clinic visits for a direct interview. If an in-person visit was not feasible, an alternative means of follow-up, such as phone interview, virtual visit, or contact with primary care doctor, was arranged. At each visit, the research team collected information on vital status and cause of death, if applicable, thrombotic complications, visual loss (decreased visual acuity or visual field abnormality), seizures, complications of surgery, new neurosurgical interventions, treatments and hospital admissions. Disability was assessed using the modified Rankin Scale (mRS)[20]. For telephone and virtual interviews, we used the mRS 3 questions interview[21]. mRS was evaluated by a trained investigator not directly involved in the surgical procedure. The opinions of both the patient and main caregiver concerning the outcome of surgery were also recorded[22].

Outcomes

Similar to the previous retrospective registry[11], the primary outcome was the mRS dichotomized between favorable (mRS 0-4) and unfavorable outcome (mRS 5 or death) at 12 months. Secondary outcomes were complete functional recovery (mRS 0-1), functional

independence (mRS 0-2), severe dependence (mRS 4-5) and death at discharge, 6 and 12 months. Causes and predictors of death will be reported in another publication.

Patient reported outcomes

To assess patient and caregiver satisfaction with the outcome of surgery at 6 and 12 months after surgery, patients and caregivers were asked to indicate, in retrospect and considering their current outcome status, whether they would again agree (yes, no, don't know) to undergo surgical treatment[22].

Prognostic variables

We a priori selected the following variables as potential predictors of outcome, based on data from a retrospective registry[11] and literature review: age (dichotomized by the median of the sample), sex, interval from diagnosis and worsening to surgery (dichotomized <24h), Glasgow Coma Scale (<9 (coma) vs ≥9) fixed pupils (none vs unilateral or bilateral), type of lesion (hemorrhagic vs. non-hemorrhagic), lesion size (dichotomized by the median of the sample), transtentorial herniation imaging signs, midline shift (>10mm), type (craniectomy, hematoma evacuation) and side of surgery. The last information available before surgery, either the admission clinical and imaging data, or the last observation and imaging before surgery, if available, was used for the analysis.

Sample size

To determine the sample size of the study we balanced the need of statistical power with feasibility. In the 20 centers participating in the previous retrospective registry[11], 34 patients were operated from 2005 to 2009. Assuming that the frequency of decompressive surgery remained stable, we estimated that 100 patients could be recruited within 5 years across 60 centers. With a sample size of 100 operated patients, the study had a power (1-β) of 0.81, 1-α 0.95, to detect a risk ratio of 2.0, assuming a risk of unfavorable outcome of 30% and of 60% on patients without and with a given prognostic factor, respectively.

Statistical analysis

We used descriptive statistics to summarize baseline and pre- and post-surgery variables and outcomes. No imputations for missing values were made. Bivariate associations between prognostic variables and outcomes were calculated using Chi2 statistics, with continuity correction when needed. For missing outcome data during follow-up, we used the "last observation carried forward" procedure.

To determine associations between prognostic variables and outcomes we used multivariable logistic regression (backward), entering as predictors a priori selected variables of interest (see above) with a $p<0.10$ in bivariate analysis. Variables with more than 10% missing values were not included. Prognostic variables were checked for collinearity. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated. Multivariable analyses were performed only for the primary outcome (mRS 5-6) and for dependence (mRS >2) at 12 months.

Subgroup analysis

The following subgroup descriptions were defined a priori: posterior fossa hemicraniectomy, bilateral hemicraniectomy, hemicraniectomy in patients older than 60 years, in patients with cerebral edema but no brain lesions, only hematoma evacuation, hemicraniectomy combined with endovascular thrombectomy/thrombolysis and repeated decompressive surgery. Because

of expected small numbers, only descriptive statistics (mRS at 12months) were reported for these subgroups.

The following sensitivity analysis were conducted: high-income vs middle-income countries, number of included patients per center, centers including more than 25% of all included patients and inclusion in the first and second halves of the duration of the study. Sensitivity analysis was performed only for the primary outcome (mRS 5-6) and for independence (mRS 0-2) at 12 months.

For the analysis of patient reported outcomes, we explored if patient and caregiver opinion (yes vs. no/don´t know) on the benefit of surgery at 12 months was associated with age, sex, country income or functional outcome.

Results

Of the hospitals and investigators contacted, 70 manifested interest to participate, but ultimately only 15 included at least one patient in the registry. Inclusion started in December/2011 and ended in December/2019. In this period, 118 patients were enrolled from 15 centers in 10 countries in Europe, Asia and America (Table S2). The flow of patients is described in Figure 1.

Baseline characteristics

Patient characteristics at CVT diagnosis are described in Table 1 and Table S3. Patients were predominantly female and young, with a severe presenting clinical picture: 31% were comatose, and 18% had unilateral or bilateral fixed pupils indicative of transtentorial herniation. Admission neuroimaging showed parenchymal lesions in 87%, which were generally large (median largest diameter 6.5 cm) and produced a midline shift in 70% of the patients and imaging signs of herniation in 37%.

Surgery and evolution during admission

Prior to surgery, neurological worsening was observed in 82 (70%) of the patients (Supplemental material, Figure S1), with the proportion of comatose patients increasing from 31 to 59%. CT or MR was repeated before surgery in 105 subjects (89%), showing new brain hemorrhages in 15 patients, enlargement of the index parenchymal lesion in 34 patients and increase in the proportion of patients showing midline shift >10 mm (17 to 33%) or imaging signs of herniation (37 to 61%). The majority of the patients (103, 87%) were admitted to an Intensive Care Unit. Of note, 84 (71%) received mechanical ventilation prior to surgery (Table S4).

Surgery was performed a median of 1 day after admission and of 1 day after diagnosis (IQR (0-2). Hemicraniectomy was done in 115 (98%) and hematoma evacuation in 37 (31%). Craniectomy was bilateral in 8 (7%) patients and of the posterior fossa in 2 cases (2%). Craniectomies were large, with a median size of 13 cm (IQR 11.5-15).

Medical and surgical complications during hospital admission were common after surgery (Table S5). Most common complications were seizures (12 patients, 10%), new intracerebral bleeding (16, 14%), pulmonary infections (27, 23%) and pulmonary embolism (6, 5%). Paradoxical brain herniation and external brain tamponade occurred in one patient each.

Eighteen (15%) of patients were reoperated, mainly to relieve persistent increased intracranial pressure.

Patients were discharged from the hospital where they had been operated a median of 23 days after admission. At discharge, 52 (44%) of patients had an unfavorable outcome (mRS 5-6), of whom 24% had died. The proportion of severely disabled (mRS 4-5) was high (49%, 58 patients). Only 9 patients (8%) were independent (mRS 0-2) at discharge (Figure 2).

Follow-up

6 months (Figures 1 and 2)

Of the 90 survivors from the acute phase, 10 died after discharge and two missed the 6-months follow-up. Follow-up was performed by clinic interview in 65 (86%) patients. Overall, 38 patients were dead (cumulative 32%) while 42 (36%) patients had an unfavorable outcome (mRS 5-6). The proportion of severely disabled (mRS 4-5) decreased to 14% (13 patients), the proportion of independent survivors rose to 32% (33 patients), and 13 (12 %) patients had fully functionally recovered (mRS 0-1).

Seizures occurred in 11 (13%) patients between discharge and 6 months. All other complications were infrequent (Table S5). Fourteen patients (16%) underwent a new neurosurgery, mainly cranioplasty (13 patients).

12 months

At 12 months follow-up 2 additional patients had died and three missed the 12 months follow-up. Follow-up was performed by clinic interview in 55 patients (85%). The cumulative number of deaths was 40 (34%). Forty-six patients (39%) patients had an unfavorable outcome (mRS 5-6). The proportion of severely disabled (mRS 4-5) further decreased to 9% (9 patients) (Figure 1 and 2). Forty-one patients (34 %) were independent (mRS 0-2) and the proportion of fully functionally recovered patients (mRS 0-1) rose to 16.1% (18 patients).

Seizures occurred in 12 (16%) patients between 6 and 12 months. All other complications were rare (Table S5). Ten patients (13%) underwent further neurosurgery, mainly cranioplasty (9 patients).

Subgroup analysis

Outcome for the prespecified subgroups is described on Supplemental material, table S6. All subgroups had few patients. None of the operated patients older than 60, neither those who underwent bilateral craniectomy nor those who had only cerebral oedema regained independence (Table S6)).

Sensitivity analysis

Sensitivity analysis did not show statistically significant differences in the primary outcome and independence at 12 months when comparing high-income vs middle income countries, number of included patients per center (1-2 vs >2), centers including more than 25% of the patients in the study or between inclusion in 2011-2015 and 2016-2019 (Table S7).

Prognostic factors

The bivariate analysis of the a priori selected prognostic variables per outcome is shown in Table 2. The distribution of the full mRS scores at 12 months by predefined prognostic factors

and surgery subgroups in displayed on Table S8. Unfavorable outcome (mRS 5-6) was significantly more frequent in patients in coma (Glasgow Coma Scale score <9) or with at least one fixed dilated pupil before surgery. Dependence (mRS >2) was more frequent in older patients, while complete functional recovery (mRS 0-1) was significantly less common among older subjects, patients who were treated with hemicraniectomy plus hematoma evacuation (vs. hemicraniectomy alone) and in patients who had left hemicraniectomy (vs. right).

Prognostic factors with p<0.10 in the bivariate analysis (Table 2) were entered in backwards logistic regression analysis to predict poor outcome and dependence. Final best model for unfavorable outcome retained coma (OR=2.39; 95% CI 1.03 – 5.56; p=0.04), and fixed dilated pupil (OR= 2.22; 95% CI 0.90-4.92; p= 0.26). For dependence, the retained variable was age>37 years (OR= 2.61; 95% CI 1.20 – 5.70; p=0.02)

Patient and caregiver satisfaction with surgery

Responses of surviving patients and caregivers in relation to their satisfaction with the results of surgery at 6 and 12 months follow-up visits are depicted in Figure 3. Only a few patients (2 at 6 and 12 months follow-up) and caregivers (5 at 6 months and 3 at 12 months follow-up) did not participate in the survey. Decompressive neurosurgery was judged as worthwhile by 4 out of 5 patients and caregivers. Caregiver satisfaction increased by 7% from month 6 to month 12 follow-up. Weighted kappa agreement between patients and caregivers' opinions was 0.85 at 6 months and 0.62 at 12 months. Satisfaction was not associated with patient age, sex or country income, but was more frequent among patients who were independent at 12 months as judged by the patients (52/59 (88%) vs. 4/11 (36%), p<0.01), but not when responded by the caregivers, as 9 out of 11 (82%) with mRS >2 judged surgery as worthwhile.

Discussion

In this large global cohort, two thirds of CVT patients treated by decompressive surgery were alive and more than one third were functionally independent one year after surgery. Coma, fixed dilated pupils and age were predictors of poorer outcomes. Decompressive surgery was judged as worthwhile by 4 out of 5 patients and caregivers. Operated patients had an impressive improvement from discharge to 12-months evaluation. In fact, the proportion of severely disabled patients decreased from 49% at discharge to only 9% at 12 months, while the proportion of those with complete functional recovery rose from to 2 to 16% from discharge to 12 months respectively.

Operated patients had a severe clinical picture before surgery, as more than half were comatose and 1/3 had unilateral or bilateral fixed dilated pupils. Coma was caused mainly by large unilateral hemorrhagic lesions, which produced a midline shift of more than 10 mm in a 1/3 of patients and other neuroradiological signs of vertical brain herniation in 60% of the patients. Patients who were not immediately operated upon hospital admission rapidly deteriorated, as shown by the near doubling of the proportions of participants in coma or with neuroimaging evidence of herniation. Although we cannot completely exclude additional causes contributing to depressed consciousness (e.g., seizures), the clinical severity and neuroradiological findings before surgery suggest that surgery was performed accordingly to current guidelines[6,7], i.e., to prevent death by brain herniation. However, we cannot exclude a

potential selection bias related to subjects who refused surgery and those who received only palliative care.

Previous information on decompressive surgery in CVT consist of case reports, retrospective case-series and a few prospective small series from referral centers [8-18] which are prone to bias. Retrospective studies have lower internal validity than cohort studies and tend to overestimate outcomes. This probably explains why the outcomes in DECOMPRESS2 are numerically less favorable than those of a systematic review of previously published series[7], showing higher mortality (34 vs. 19%), lower proportion of independent patients (34 vs 68%) and of those achieving complete recovery (16 vs. 31%). The proportion of patients with a good outcome (mRS ≤3) at one year after decompressive surgery (53%) in the current study was substantially higher than that reported for malignant middle cerebral artery infarcts (37%)[5]. Mortality was similar (34 vs. 29%), but the proportion with severe disability was much lower (9 vs 34%).

There are no randomized controlled trials of decompressive surgery in CVT. In two single-center case-series of malignant CVT, all patients who were not operated on died [10,16]. On the other hand, a recent systematic review which compared 56 CVT cases with surgery and 125 CVT cases that were medically managed concluded from a sensitivity analysis that surgery significantly decreased the odds of poor outcome, defined as mRS 3-6 (OR 0.03), but not mortality [18]. Unfortunately, operated and non-operated patients could not be matched for severity in that study, and indication bias could not be prevented.

A systematic review of decompressive surgery in CVT which compared the outcome of 116 patients operated within 48 h to 34 who were operated on after 48h, reported a decrease of mortality but not of poor outcome with earlier surgery[18]. Patients enrolled in DECOMPRESS2 were operated quite early (median 1 day after diagnosis) and we did not find differences in outcome associated with timing of surgery, suggesting that decompressive surgery should not be denied on the basis of a prolonged time interval from diagnosis or neurological worsening.

In ischemic stroke, hemicraniectomy increases survival among patients older than 60 years of age, although the majority of the survivors require assistance for daily living activities [23]. Although the numbers are very small, none of the DECOMPRESS2 patients aged more than 60 regained independence. The numbers were also too small to investigate the other prespecified subgroups (e.g., bilateral surgery, endovascular treatment plus surgery, posterior fossa surgery). Better evidence to inform the outcome of these patients could come from a systematic review of individual patient data of similar published and unpublished cases.

We found that coma and at least one fixed pupil were predictors of poor outcome in multivariable analysis, increasing the robustness of similar evidence from previous retrospective registry[11]. Nonetheless, 30% of patients in coma or with fixed dilated pupils before surgery were independent at 12 months, including 16% who had a complete functional recovery, signaling that surgery should not be denied to these patients.

We described for the first-time patient and caregiver views on the outcome of decompressive surgery in CVT, by reporting patients and caregivers' satisfaction with surgery at 6 and 12 months. Decompressive neurosurgery was judged as worthwhile by the vast majority of patients and caregivers. Satisfaction was not associated with patient age, sex or country income, but was more frequent among patients who were independent at 12 months. These results are rather similar to those reported after hemicraniectomy for ischemic stroke[24,25]. Patient and caregiver satisfaction despite incomplete recovery illustrate the "disability

paradox", as the majority of patients and caregivers give more value to retained capacities than to physical disability[26]. This positive appreciation of the results of surgery might be useful and ease the process of shared decision to perform decompressive surgery in malignant CVT.

The current study has several other innovative features. It is a large global cohort, including patients from high- and middle-income countries and with diverse health care systems. The 12-month follow-up was conducted primarily through direct interviews, resulting in a very low attrition rate. Moreover, pre- and post-surgery patient condition and outcomes were collected prospectively by local investigators not directly involved in the surgical procedure and were described in detail. Central reading of admission and of periprocedural neuroimaging was performed to quantify brain herniation.

Because of the observational design of our study, we cannot prove efficacy of decompressive surgery in CVT. DECOMPRESS2 had a long inclusion period, lasting for 8 years, with multiples centers from different countries. However, we did not find differences in outcome over time, by country income and by volume of included patients per center.

Conclusion

From the high survival and independence rates at 12 months, the very small proportion of patients who were alive but severely disabled, and the favorable patient and carer reported views on the outcome of surgery, we conclude that decompressive surgery is a valuable option for these patients. Results of DECOMPRESS 2 provide evidence-based support to the ESO-EAN CVT guidelines[7] recommendation of performing decompressive surgery in CVT patients with impending brain herniation.

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Supplemental Material

STROBE checklist

Tables S1-S8

Figure S1

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Figure legends

Figure 1. DECOMPRESS 2 Flow of patients

Figure 2. Distribution of Modified Rankin Scale (mRS) Scores at discharge, 6 and 12 months.

Bars represent % of patients for each score, except for score 6 (death) where it represents cumulative % of deaths

Figure 3. Patient and caregiver opinion on surgery outcome at 6 and 12 months follow-up

Table 1. Patient characteristics at the diagnosis of cerebral venous thrombosis

Number of included patients	118	
Female	80	67.8%
Age median (IQ Range)	38	(26-46)
Symptoms and signs		
Headache	104	88.1%
Aphasia	28	23.7%
Paresis	74	62.7%
Seizures	58	49.2%
Glasgow Coma Scale		
15	20	16.9%
9-14	60	50.8%
<9	36	30.5%
Dilated fixed pupil		
Unilateral	18	15.3%
Bilateral	3	2.5%
Major risk factors & associated conditions		
Oral contraceptives	26	22.0%
Pregnancy/puerperium	22	18.7%
Infection	10	8.5%
Malignancy	5	4.2%
Genetic thrombophilia	23	19.5%
No risk factor	18	15.3%
Sinus/vein thrombosed		
Superior sagittal sinus	70	59.3%
Left lateral sinus	54	45.8%
Right lateral sinus	38	32.2%
Deep venous system	9	7.6%
Cortical veins	56	47.6%
> 1 sinus	91	77.1%
Admission neuroimaging (CT in 106 and MR in 48)		

Parenchymal lesions	104	87.3%
Non-hemorrhagic	22	18.6%
Hemorrhagic	97	82.2%
Multiple lesions	36	30.5%
Lesion size (cm) Median (IQR)	6.5	(4.6-8.1)
Midline shift >10 mm	20	24.1%
Herniation signs	44	37.3%

Table 2. Outcome at 12 months by predefined prognostic factors and surgery subgroups

		Outcome (mRS), n (%)			
	N	0-1	0-2	4-6	5-6
Age (years)					
>37	60	4 (6.7)*	15 (25.0)**	31 (51.7)	27 (45.0)
≤37	58	15 (25.9)	27 (46.6)	21 (36.2)	19 (32.8)
Sex					
Women	80	14 (17.5)	30 (37.5)	35 (51.7)	31 (38.3)
Men	38	5 (13.2)	12 (31.6)	17 (36.2)	15 (39.5)
GCS score+					
<9	70	9 (12.9)	21 (30.0)	38 (54.3)	34 (48.6)
9-15	48	10 (40.8)	21 (43.8)	14 (29.2)*	12(25)¶
Fixed dilated pupils+					
Bilateral	9	0 (0)	2 (22.2)	6 (66.7)	6 (66.7)
Unilateral	27	5 (18.5)	9 (33.3)	14 (51.9)	14 (51.9)
None	79	14 (17.7)	30 (38.0)	30 (38.0)	25 (31.5)**
Neuroimaging+					
Hemorrhagic lesion	107	16 (15.0)	38 (35.5)	46 (43.0)	40 (37.4)
No hemorrhagic lesion	9	3 (33.3)	3 (33.3)	5 (55.6)	5 (55.6)
Lesion size ≥ 6.5 cm	78	9 (11.5)°	24 (30.8)	35 (44.9)	32 (41.0)
Lesion size < 6.5 cm	36	9 (25.0)	16 (44.8)	15 (41.7)	12 (33.3)
Midline shift >10 mm	39	3 (7.7)	12 (30.8)	19 (48.7)	17 (35.6)
Midline shift ≤10 mm	76	16 (21.1)	29 (38.2)	31 (40.8)	27 (43.6)
Herniation signs	72	6 (14.6)	29 (40.3)	31 (43.1)	26 (36.1)
No herniation signs	41	13 (18.1)	12 (29.3)	19 (46.3)	18 (43.9)
Surgery					
Diagnosis-surgery<1 day	44	8 (18.2)	16 (36.4)	19 (43.2)	17 (38.6)
Diagnosis-surgery≥1 day	72	11 (15.3)	26 (36.1)	31 (43.1)	28 (38.9)
Worsening-surgery<1day	60	10 (16.7)	19 (31.7)	29 (48.3)	25 (41.7)
Worsening-surgery≥1 day	22	2 (9.1)	8 (36.4)	12 (54.5)	11 (50.0)
Craniectomy, only	81	18 (22.2)*	30 (37.5)	34 (42.0)	32 (39.5)

Craniectomy + evacuation	34	1 (2.9)	10 (29.4)	17 (50.0)	31 (38.2)
Left hemispheric	75	9 (12.0)¶¶	28 (37.3)	31 (41.3)	26 (34.7)
Right hemispheric	30	9 (30.0)	11 (36.7)	12 (40.0)	11 (36.7)

mRS indicates Modified Rankin Scale, GCS means Glasgow Coma Scale

N, number with variable condition; (%), number with outcome/number with variable condition

+Last observation and neuroimaging before surgery

* p<0.01; ** p=0.02; ¶p=0.01; ¶¶ p=0.03; ° p=0.10

Only p values =0.10 or lower are shown