The Efficacy of Strokectomy in the Treatment of Malignant Cerebral Infarction Patients

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Research

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Abstract

Introduction

Strokectomy refers to the resection of infarct brain tissue. Used alone, in combination with decompressive hemicraniectomy (DHC), or as a remedial surgery to DHC for malignant cerebral infarction (MCI) patients, strokectomy has reduced mortality rates and improved functional outcomes of patients with MCI. However, the role of strokectomy in the treatment of MCI patients is controversial. The aim of this retrospective study was to investigate the efficacy of strokectomy in MCI treatment in order to explore its beneficial effects on improving patient outcomes.

Methods

This retrospective study was carried out between January 2017 and September 2019 in the First Affiliated Hospital of Jinan University and Guangdong 999 Brain Hospital in Guangzhou, China. We reviewed patients with MCI who underwent DHC with or without strokectomy. We collected and analyzed the following data for all patients: demographics, Glasgow Coma Scale scores (GCS), National Institutes of Health Stroke Scale (NIHSS) scores, observational data in the intensive care unit (ICU), post-surgery intracranial pressure (ICP) monitoring, midline shift before and after surgery, and functional outcomes measured with the modified Rankin Scale (mRS) at 6 months.

Results

We recruited 95 patients (53 men; mean age, 59.71 ± 10.65 years; age range, 38 - 78 years). After surgery, patients who received DHC and strokectomy were associated with a lower ICP curve; decreased midline shift; and less mannitol, hypothermia, and hypertonic saline therapies than those who received DHC alone. No patient in the DHC+strokectomy group had malignant high ICP or needed remedial surgery; in contrast, 16 patients in the DHC group had malignant high ICP after DHC, and remedial surgery was recommended. Five patients received remedial surgery and survived, while the 11 who refused remedial surgery died. The mortality rate during ICU stay was 19.4% in the DHC group and 7.1% in the DHC+strokectomy group. While the rate of poor outcomes and mortality was significantly different between the two groups at 6 months after surgery, good outcomes did not differ significantly.

Conclusions

Strokectomy performed in combination with DHC can effectively decrease post-surgery ICP, reduce midline shift, and reduce mortality during the six months following surgery. Moreover, strokectomy performed as a remedial surgery could decrease malignant high ICP after DHC and reduce mortality.

Introduction

The introduction of decompressive hemicraniectomy (DHC) as a treatment for malignant cerebral infarction (MCI) has reduced the mortality rate of MCI from approximately 80% to 20-40% [1][2][3][4][5].

Although the decrease in mortality is a great advancement in the treatment of MCI patients, it is still high enough to warrant further study. The primary reason for the relatively high mortality after DHC may be that even undergoing maximal DHC, some patients with MCI experience progressive swelling of the affected hemisphere and inevitable herniation that could be fatal for MCI patients [6][7][8][9][10]. Strokectomy, resection of the infarct brain tissue, used alone or in combination with DHC or as remedial surgery to DHC, leads to lower mortality rates compared to patients treated with DHC only [8][10][11]. However, due to its intrinsic drawbacks, (e.g., more time needed to operate, higher blood loss, the possibility of removal of viable neural tissue), it remains a controversial option in the treatment of MCI patients [12].

Until now, there are no guidelines concerning the selection of treatment modalities for patients with MCI; patients suitable for surgery are treated differently according to the preference of neurosurgeons. Selecting appropriate treatment modalities for patients with MCI remains to be elucidated. Therefore, the aim of this study was to investigate the efficacy of strokectomy used in combination with DHC, or as a remedial surgery to DHC in order to explore its beneficial effects in MCI treatment to improve patient outcomes.

Methods

Patient selection

We performed a retrospective study of patients with MCI who underwent decompressive hemicraniectomy with or without strokectomy between January 2017 and September 2019 in The First Affiliated Hospital of Jinan University (52 patients) and Guangdong 999 Brain Hospital (43 patients) in Guangzhou, China. Inclusion criteria were as follow: patients diagnosed with middle cerebral artery (MCA) infarction with or without ipsilateral anterior cerebral artery (ACA) or posterior cerebral artery (PCA) infarction and who showed severe swelling with compression of the ipsilateral lateral ventricle or midline shift on CT scans. Exclusion criteria were any of the following: patients with bilateral dilated pupils, severe comorbidity, reduced life expectancy, or bilateral large territory infarction. A total of 95 patients were included in this study. All subjects had written informed consent given by their caregivers and the study protocol was approved by the corresponding institute committee on human research.

Procedure

The surgical removal of a large bone flap was conducted as described by Subramaniam [13]. During the operation, some patients with edematous brain bulging after durotomy then underwent strokectomy. The extent of resection included the anterior temporal lobe and a portion of the frontal lobe above the Sylvian fissure. The fissure vein was protected with caution during the procedure. Intracranial pressure (ICP) was monitored with the intraparenchymal insertion of an ICP probe (Sophysa, France).

Post-operative intensive care unit stay

Immediately after surgery, patients were transferred under anesthesia, intubation, and mechanical ventilation to the neurosurgery intensive care unit (ICU), where they received the following therapy: antihypertensive medication, dehydrating agents (mannitol or hypertonic saline) if necessary, sedation, low-molecular-weight heparin, intravenous fluids, and proton-pump inhibitors. Mannitol therapy was administered when ICP persistently exceeded 15 mm Hg. Hypothermia was considered as an alternative therapy to decrease high ICP if malignant brain edema could not be alleviated with mannitol or hypertonic saline. Brain computed tomography (CT) scans were performed as needed to evaluate the patient's intracranial condition, and treatment strategies were adjusted accordingly. In cases of refractory elevated ICP, therapy was further enhanced with the repeated administration of mannitol injections, hypertonic saline, and hypothermia therapy if necessary. The persistence of refractory increasing ICP and midline shift accompanied by decreasing Glasgow Coma Scores (GCS) and pupil mydriasis despite the comprehensive multimodality treatment indicated the remove of the infarct tissue with remedial surgery. Permission and signed written consent was requested of the patients' caregivers to perform remedial strokectomy to alleviate the deadly mass-effect and decrease the high ICP. Conservative management was continued in case of refusal.

The appropriate timing of mechanical ventilation discontinuation and extubation depended on consciousness recovery and the severity of complications. If patients remained comatose for more than 7 days, tracheotomies were performed. The mechanical ventilation time and intubation time were recorded. ICP was monitored continuously until the peak stage of brain swelling had passed, and ICP began to decrease.

Patients were transferred to rehabilitation wards after meeting the following conditions: stable vital signs, no signs of herniation, no fever, controlled pulmonary infection, extubation or tracheotomies performed, maintenance of oxyhemoglobin saturation at normal levels without mechanical ventilation.

Data Collection

Clinical data were collected for all patients, including age, sex, baseline medical comorbidities, presence of pupillary asymmetry, NIHSS score, and GCS. All preoperative and postoperative brain CT scans and magnetic resonance images were reviewed to measure the midline shift at the level of the *septum pellucidum* before and after surgery. Duration of stay in ICU and the time needed for mechanical ventilation were recorded. Hypertonic saline therapy and refractory hypernatremia were also recorded. Mortality in ICU stay was recorded. Mortality and modified Rankin Scale (mRS) scores at 6 months after surgery were used as outcome parameters.

Statistical analyses

Statistical analyses were performed with SPSS 13.0 for Windows (SPSS Inc., Chicago, IL). P-values of less than 0.05 were considered statistically significant. Two-tailed Student t-tests were used for normally distributed variables. Mann-Whitney U tests were used for ordinal variables. Dichotomous variables were compared with Pearson's χ^2 test or the Fisher's exact test when appropriate. ICP curves were generated with GraphPad Prism software (version 5.0).

Results

Overview of the included patients

The present retrospective study included 95 patients: 67 patients in the DHC group and 28 patients in the DHC+strokectomy (DHC+S) group (Fig. 1 A). All patients were transferred to the ICU after surgery and to rehabilitation wards when vital signs were stable. The overall death rate at six months after surgery was 20% (19/95): 14.7% (14/95) died during their ICU stay and 5.3% (5/95) in the rehabilitation stage.

In the DHC group, 51 of 67 patients had normal or moderately increased intracranial pressure (NICP). Of the 51 patients, 49 became stable after treatment and were transferred to the rehabilitation ward, and two died (one due to a pulmonary embolism and one due to severe post-surgery intracranial infection). Of the 67 patients, 16 suffered from malignant high intracranial pressure (MICP) accompanied by decreasing GCS scores, increased midline shift and pupil mydriasis. Of these 16 patients, five underwent remedial surgery and survived after prolonged stays in the ICU; however, 11 refused remedial surgery and died from complications related to severe brain herniation. Of the 54 patients transferred to rehabilitation wards in the DHC group, four died (two of severe pneumonia and two of pulmonary embolism) in the following 6 months.

No patients in the DHC+S group developed malignant ICP during their stay in the ICU. One death in the ICU was caused by acute heart failure. In the rehabilitation stage, one patient died due to severe lung infection caused by aspiration.

Preoperative data

The preoperative data obtained from all the patients are presented in Table 1. Site of infarction and the severity of swelling measured with preoperative head CT differed significantly between the two treatment groups. Sex, age, preoperative GCS, preoperative NIHSS score, time from ictus to operation, and etiology of ischemia did not differ significantly between the treatment groups.

Treatments in the ICU

There were significant differences in the variables of mannitol therapy, hypothermia therapy, hypertonic saline therapy, remedial surgery recommended, and time of ICU stay between the two groups. No statistical differences in the variables of tracheotomy, acute renal failure, duration of mechanical ventilation, and mortality in ICU were observed between the DHC and DHC+S groups (Table 2). Refractory high ICP and increasing midline shift accompanied by decreasing GCS scores and pupil mydriasis were observed after surgery in 16/67 patients in the DHC group (23.89%) and in none of the patients in the DHC+S group; hence, no patient in the latter group required further surgery.

Characteristics of patients in DHC group with or without malignant high ICP

We observed 16 patients with refractory elevated ICP accompanied by decreasing GCS scores and pupil mydriasis that could not be alleviated with repeated mannitol injections, hypertonic saline, or hypothermia therapy. Remedial surgery to remove infarct tissue was proposed. We divided these patients into two groups for analysis (Table 3). Large territory infarctions and mannitol therapy were significantly more common among the 16 patients who were recommended to receive remedial surgery (group 1) than among the remaining 51 patients in the DHC group without malignant high ICP (group 2).

Post-surgery ICP monitoring

All patients were implanted with ICP probe to allow for the monitoring of their ICP (Fig. 1 B). The calculation of ICP curves was based on the mean ICP of each patient per day in both groups. The data of five patients in the DHC group who underwent remedial surgery obtained on the day of the secondary surgery and afterwards were excluded from the calculation of ICP curves. Results are shown in Figure 1. The patients in the DHC+S group had lower ICP measurements.

Midline shift calculations before and after surgery

All patients were monitored with dynamic head CT scans following surgery. The midline shifts of these patients at the level of septum pellucidum were measured and compared. The results revealed that midline shifts decreased significantly after surgery in the DHC+S group, while those in the DHC group increased slightly, but not significantly, after surgery (Table 4).

Functional Outcomes at 6 months

The mRS was used as an outcome parameter to evaluate the quality of life of the patients at 6 months following surgery. The values of mRS obtained at 6 months were grouped and categorized as good outcomes (mRS 1–3), poor outcomes (mRS 4-5), and death (mRS 6). The distribution of mRS is shown in Figure 1C. While the rate of poor outcomes or death differed significantly between the two groups, rates of good outcomes did not. In the DHC group, 29.9% of the patients had good outcomes at 6 months, 44.8% had poor outcomes, and 25.4% died; in the DHC+S group, 21.4% of the patients had good outcomes, 71.4% had poor outcomes, and 7.1% died.

Discussion

Previous randomized controlled trials (RCTs) (DESTINY, DECIMAL and HAMLET) have shown that DHC reduces mortality and improves functional outcomes of patients with MCI [14][15][16]. However, the mortality rate following DHC ranges between 20 and 40% [4][17][18]. This high mortality is attributable to increasingly high ICP and herniation due to refractory brain swelling [7][19][20]. Patients with refractory increasing high ICP and midline shift accompanied by decreasing GCS scores and pupil mydriasis must elect to continue conservative treatment or receive remedial surgery. Concerning the latter option, the application of strokectomy as a remedial strategy has yielded favorable results [6][19][20].

Indicating that strokectomy used in combination with DHC or as remedial surgery to DHC can effectively reduce post-surgery ICP and decrease rates of mortality, our findings have the following implications: (1) as demonstrated by the decreased ICP, midline shift, and brain stem compression in the DHC+strokectomy group following surgery, strokectomy is effective in treating high post-surgery ICP; (2) strokectomy reduces mortality both when performed in combination with DHC or as a remedial surgery for patients with high ICP after DHC; (3) reduced mortality in DHCstrokectomy group resulted in an increased proportion of patients with poor outcomes; and (4) strokectomy is safe for and beneficial to MCI patients.

While the present and previous findings clearly indicate that strokectomy is a life-saving procedure for patients with malignant high ICP, strokectomy has remained controversial. For example, Wartenberg et al., Pandhi et al., and Cheung et al. have all advised against the resection of the infarction and strokectomy, as the margins between infarct and the penumbra are poorly defined, the procedure risks the removal of potentially viable neural tissue from the margins of the ischemic penumbra [21][22][23]. By contrast, Kostov et al. suggested that strokectomy alone may be equivalent to a DHC with or without brain resection. Since high ICP before or after DHC would further reduce perfusion of the remaining viable tissue, the removal of the anterior temporal lobe and uncus can directly relieve brainstem compression and rescue the penumbra, and the bone flap may be immediately replaced if sufficient strokectomy was achieved[11].

When strokectomy is indicated, the surgeon should ensure that sufficient infarct resection has been achieved. Insufficient strokectomy could prevent the attenuation of the high ICP and brain herniation. In contrast, viable tissue may most likely be removed with radical resection. While Kostov et al. suggested the use of indocyanine green-video angiography to guide the extent of resection, implementing this strategy during surgery would be excessively time-consuming[11]. We recommend the partial resection of the infarct: that of the anterior temporal lobe can prevent uncal herniation and brain stem compression, and the resection of a portion of the frontal lobe above the Sylvian fissure can avoid compression of the structure of the diencephalon.

Our research indicates that 14/16 (87.5%) patients with progressive swelling in the DHC group featured infarcts in regions beyond MCA territory that involved the ACA or PCA territories. This indicates that patients with large infarcts might develop malignant high ICP after DHC. ICP and midline shift could progressively deteriorate patient prognoses and elevate mortality rates up to 30-70%. The realization of a second surgery, including strokectomy, may help decrease mortality rates and achieve better outcomes, especially in cases of infarction that involve more than one vascular territory.

Conclusions

Resection of infarct brain tissue, performed in combination with DHC or as a remedial surgery after DHC, is an effective and safe treatment of MCI that can significantly decrease post-surgery ICP and reduce mortality. However, due to the retrospective nature of this study, the operative procedures and the treatment in ICU were not standardized; hence, randomized, prospective study is warranted to confirm our conclusions.

Abbreviations

ACA: anterior cerebral artery; CT: computed tomography; DHC: decompressive hemicraniectomy; GCS: Glasgow Coma Scale scores; ICP: intracranial pressure; ICU: intensive care unit; MCA: middle cerebral artery; MCI: malignant cerebral infarction; MICP: malignant high intracranial pressure; mRS: modified Rankin Scale; NICP: moderately increased intracranial pressure; NIHSS: National Institutes of Health Stroke Scale; PCA: posterior cerebral artery; RCTs: randomized controlled trials.

Declarations

Ethical Approval and Consent to participate

All subjects gave written informed consent by their caregivers and the study protocol was approved by the Jinan University Ethics committee. (No. KY-2020-043)

Consent for publication

Not applicable.

Availability of supporting data

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that there are no competing interests.

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Authors' contributions

Ning Li, Chunmei He, Shiyong Wang and Xiangyu Wang contributed to patients enrollment, literature search, study design, data analysis, data interpretation, and writing of the manuscript.

Dr. Wei Li and Yehai Li contributed to data analysis, data interpretation, and critical review of the manuscript.

Dr. Liu Zhang, Yongjian Feng, Weilong Ding, Min Guan contributed to patient enrollment, data collection, and critical review of the manuscript.

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Tables

Table 1. Pre-operative data of patients with MCI

	DHC n=67	DHC+S n=28	Total n=95	P-value
Sex				
Male	37(55.2%)	16(57.1%)	53(55.8%)	0.864
Female	30(44.8%)	12(42.9%)	42(44.2%)	
Age (mean ± SD)	60.64±10.68	57.46±10.43	59.71±10.65	0.186
Pre-op GCS (median)	9(5-13)	8(5-12)	9(5-13)	0.259
Pre-op NIHSS (median)	23(18-32)	25(20-36)	24(18-36)	0.147
Hours from ictus to operation (mean±SD)	17.41±5.60	18.23±5.95	17.65±5.68	0.524
Site of infarction				
MCA only	46 (68.7%)	11 (39.3%)	57 (60.0%)	0.008
MCA+ACA and/or PCA	21 (31.3%)	17 (60.7%)	38 (40.0%)	
Etiology of ischemia				
Large-vessel Atherosclerosis	22(32.8%)	9(32.1%)	31(32.6%)	0.714
Cardioembolic	26(38.8%)	8(28.6%)	34(35.8%)	
Coagulopathy	11(16.4%)	6(21.4%)	17(17.9%)	
Other/unknown	8(11.9%)	5(17.9%)	13(13.7%)	
Preop head CT				
Marginal swelling[1]	25(37.3%)	5(17.9%)	30(31.6%)	0.007
Pronounced swelling[2]	34(50.7%)	12(42.9%)	46(48.4%)	
Massive swelling[3]	8(11.9%)	11(39.3%)	19(20%)	

[1] Midline shift at the level of septum pellucidum < 5mm;

[2] Midline shift at the level of septum pellucidum ≥ 5mm and < 10mm;

[3] Midline shift at the level of septum pellucidum ≥ 10mm

Abbreviations: MCI, malignant cerebral infarction; DHC, decompressive hemicraniectomy; DHC+S, DHC+strokectomy; SD, standard deviation; Pre-op, pre-operative; GCS, Glasgow Coma Score; NIHSS, National Institutes of Health Stroke Scale; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; CT, computed tomography.

Table 2. Observational data in ICU.

	DHC(n=67)	DHC+S(n=28)	P
Mannitol therapy	50(74.6%)	10(35.7%)	0.000
Hypothermia	31(46.3%)	4(14.3%)	0.003
Hypertonic saline	31(46.3%)	3(10.7%)	0.001
Tracheotomy	50(74.6%)	22(78.6%)	0.682
Acute renal failure	6(9.0%)	1(3.6%)	0.670
Remedial surgery recommended	16(23.9%)	0	0.002
ICU stay (days)	11.64±4.12	9.82±2.54	0.033
Mechanical ventilation (days)	8.12±3.72	6.75±2.63	0.077
Mortality in ICU	13(19.4%)	2(7.1%)	0.217

Abbreviations: ICU, intensive care unit; DHC, decompressive hemicraniectomy, DHC+S, DHC+strokectomy.

Table 3. Characteristics of patients in the DHC group with or without malignant high ICP

	Group 1(16)	Group 2(51)	P-value
Sex（M/F）	7/9	32/19	0.179
Age (mean±SD)	61.25±11.68	60.49±10.47	0.837
Pre-op GCS (median)	7.5（5-12）	9(5-13)	0.174
Pre-op NIHSS (median)	26(19-32)	22(18-32)	0.063
Hours from ictus to operation (Mean ± SD)	17.06±5.24	17.52±5.75	0.778
Site of infarction			0.004
MCA only	6(37.5%)	39(76.5%)	
MCA+ACA and/or PCA	10(62.5%)	12(23.5%)	
Preop head CT			0.601
Marginal swelling	6(37.5%)	19(37.3%)	
Pronounced swelling	7(43.8%)	27(52.9%)	
Massive swelling	3(18.8%)	5(9.80%)	
Mannitol therapy	16(100%)	35(68.6%)	0.008
Hypothermia	11(68.8%)	20(39.2%)	0.039
Hypertonic saline	10(62.5%)	21(41.2%)	0.136
Acute renal failure	4(25.0%)	2(3.9%)	0.026

Abbreviations: DHC, decompressive hemicraniectomy; ICP, intracranial pressure; M, male, F, female; SD, standard deviation; Pre-op, pre-operative; GCS, Glasgow Coma Score; NIHSS, National Institutes of Health Stroke Scale; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; CT, computed tomography.

Table 4. Midline shift calculations before and 1 day after surgery

	DHC	DHC+S	P-value
Pre-op	6.48±2.22	8.07±2.14	0.002
Post-op	6.81±2.09	4.46±1.00	0.000

Abbreviations: DHC, decompressive hemicraniectomy; DHC+S, DHC+strokectomy; Pre-op, pre-operative; Post-op, post-operative.

Table 5. Functional outcomes and mortality at 6 months.

Outcome	DHC (67)	DHC+PS (28)	P-value
Good (mRS 0-3)	20(29.9%)	6(21.4%)	0.401
Poor (mRS 4-5)	30(44.8%)	20(71.4%)	0.018
Mortality (mRS=6)	17(25.4%)	2(7.1%)	0.043

Abbreviations: DHC, decompressive hemicraniectomy; DHC+S, DHC+strokectomy; mRS, modified Rankin Scale.

Figures

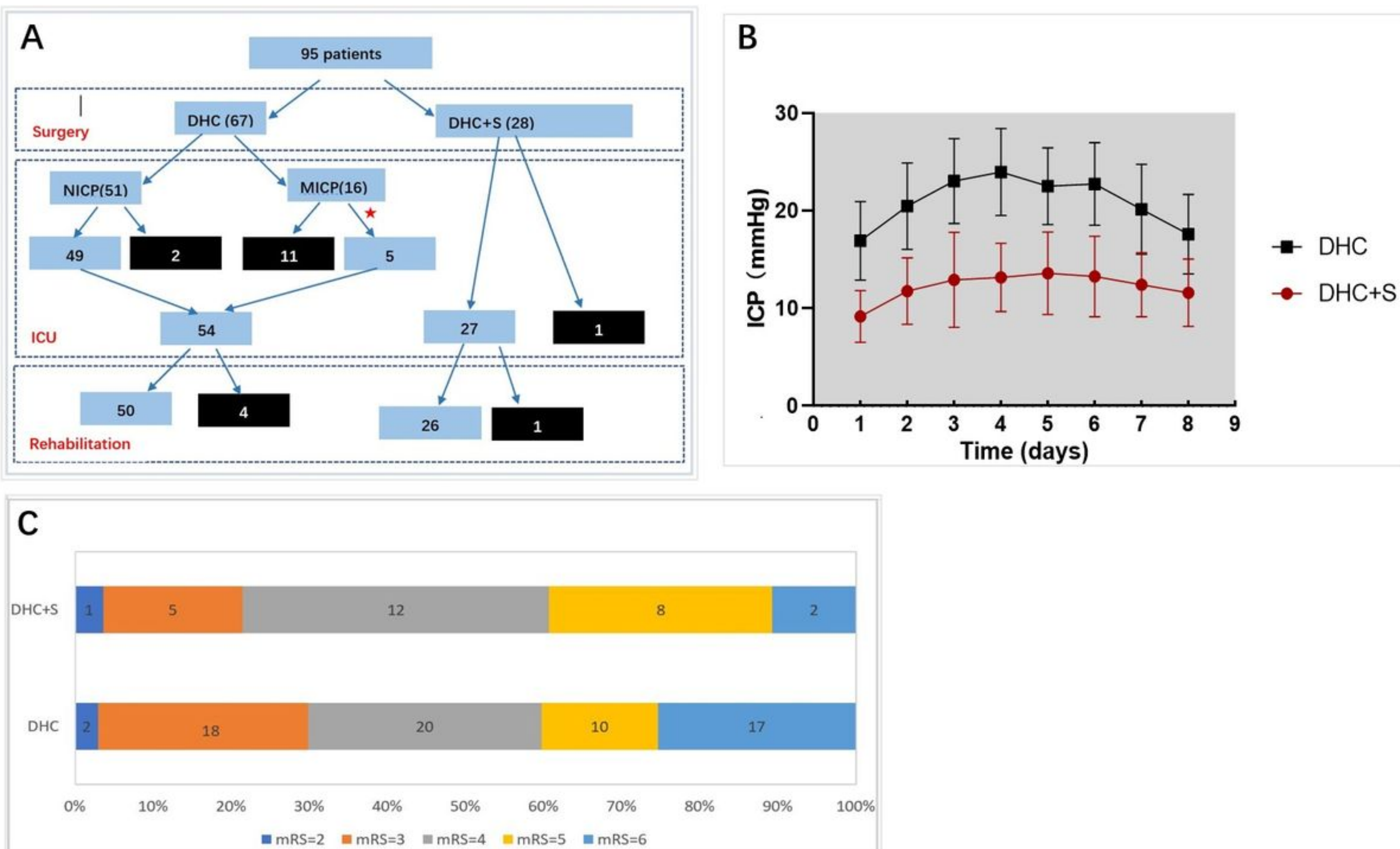

Figure 1

A: Overview of the included patients. B: The comparison of ICP curves in DHC group and DHC+S group. Note that DHC+S group had much lower ICP compared to DHC group after surgery. C: Bar graph showing the distribution of six-month patient functional outcomes as determined by mRS. The numbers within each box denote the number of patients.