Functional outcome and mortality prediction after decompressive craniectomy in patients with malignant middle cerebral artery infarction

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Abstract

Background Although it is well known that performing decompressive craniectomy (DC) in cases of swollen middle cerebral artery infarction (SMCAI) improves patient outcomes, limited evidence presently exists on the likelihood of mortality and achieving functional outcome following DC. The aim of the present study was to identify the predictors of early in-hospital mortality and functional status six months after performing DC in a cohort of patients with SMCAI.

Material and methods All patients that had suffered SMCAI and underwent DC were included in the study sample and their demographic information, along with clinical and radiological findings, and risk factors were recorded for further analyses, which were conducted using the commercial software STATA. Modified Rankin Scale score (mRS) served as an outcome measure at 6-month follow-up.

Results DC was performed on 50 patients with SMCAI (72% of whom had left hemisphere infractions) aged 45.2 ± 10.2 years (range 24–67 years), 32 (64%) of whom were female and 18 (36%) were male. While the initial median Glasgow Coma Scale (GCS) score was 8 (range 4–13), clinical deterioration mostly occurred within the first five days, whereby DC was performed within 9 ± 7.2 h (range 2–36 h). Following surgery, 16 (32%) patients died while in hospital, whereas the remaining 34 were discharged after 135 days on average, and attended the 6-month follow-up, when the median mRS score of 3 (range 2–6) was recorded for this subsample.

Conclusions Younger age, higher GCS score, presence of isochoric pupils, history of prior treatment (e.g., embolectomy or tissue plasminogen activator), and shorter interval between clinical deterioration and surgery are associated with a lower likelihood of mortality and a greater odd of a favorable functional outcome.

Keywords Decompressive craniectomy, Malignant middle cerebral artery infarction, Functional outcome

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Introduction

Stroke is posited to be the second leading cause of death worldwide following Cerebrovascular disease [1] and is of ischemic type in 85% of cases, whereby 50% of these strokes occur along the middle cerebral artery (MCA). Approximately 10–15% of the patients that suffer MCA infarction (MCAI) will develop intracranial hypertension and malignant cerebral edema (MCE), leading to swollen middle cerebral artery infarction (SMCAI), which is associated with high mortality rates [2, 3]. In this type of stroke, the onset of Malignant cerebral edema (MCE) is usually occurs within 2–5 days [4, 5] and is fatal in about 80% of cases despite optimal intensive care treatment [6–8]. Empirical evidence, however, indicates that when decompressive craniectomy (DC) is performed as soon patients' condition starts to deteriorate, survival rates and functional outcomes can be improved. Theodor Kocher was the first to record surgical intervention aimed at relieving the intracranial pressure. While in 1901 Kocher recommended surgical trepanation in all cases of intracranial hypertension, this advice was related to traumatic brain injury (TBI), given that at the time ischemic stroke and the associated malignant edema were poorly understood. As a result, it took more than five decades for DC to be performed on a patient that had suffered ischemic stroke [9]. Since then, numerous studies on the effectiveness of DC in such cases have been conducted, including three European randomized controlled trials [10, 11] while the initial findings indicated that DC improves survival, a follow-up pooled analysis of the findings yielded by these trials revealed 22% mortality rate even with surgery [12]. As this procedure is now widely implemented, the factors that might contribute to post-DC mortality and different functional outcomes must be better understood, as this would facilitate the decision-making regarding treatment. For example, older age, and midline shift have been proposed as potential predictors of early mortality following SMCAI [13, 14]. Time from stroke onset to decompressive craniectomy and the degree of preoperative neurological impairment assessed using the National Institutes of Health Stroke Scale (NIHSS) [15] have also been shown to facilitate more accurate patient prognosis [10, 13, 16]. However, these results are based on individual investigations and cannot be generalized beyond the settings in which they were obtained [17]. Therefore, further research to evaluate the influence of vascular involvement, brain locality, or clinical neurological status prior to DC is warranted. The present study aims to contribute to this body of knowledge by examining the demographic, clinical, and radiological findings of patients with SMCAI that underwent DC as the potential determinants of early mortality and functional outcome at 6-month follow-up.

Materials and methods

This retrospective cohort study included 50 patients who were admitted to the neurology and/or neurosurgery department at Prince Mohammed Bin Abdulaziz Hospital, Kingdom Hospital, and Saudi German hospital at Riyadh, Saudi Arabia, between January 2017 and December 2020 due to SMCAI. The study sample was formed after excluding records of patients with GCS 3 and bilaterally dilated non-reactive pupils, patients with previous neurological deficits, and those with incomplete data. Upon admission, each of the 50 patients was treated with decompressive craniectomy (DC) while following the standard clinical pathway to ensure best medical treatment. To facilitate analyses, patients' medical charts were reviewed, and age, gender, clinical status, and brain CT scan findings were recorded. As each individual was subjected to GCS assessment on admission, the GCS score was employed to capture clinical status, whereas the modified Rankin Scale (mRS) score served as a measure of functional status at 6-month follow-up, with mRS ≤ 3 indicating favorable outcome [18, 19]. Clinical records review further indicated that surgery was performed early (within 24 h from the diagnosis) in all patients with GCS < 13, in whom midline shift > 7 mm or contralateral ventricular dilatation was noted, while delayed surgery (after 24 h from the diagnosis) was performed if patient's GCS declined by more than 2 points (when initial GCS at presentation was > 13) or when the midline shift increased above 10 mm. The time of stroke onset was obtained from the emergency medical services records while pre- and post-operative cerebral CT (performed using a multidetector scanner with coronal and sagittal reconstructions) was obtained from the department to which the patient was admitted. The images were assessed by a radiologist, neurologist and neurosurgeon to identify the size of infarction, contralateral ventriculomegaly, midline shift, and hemorrhagic infarction. As 16 patients died during the study period, only 34 were available for the follow-up, which was conducted on outpatient setting at the corresponding stroke clinic and neurosurgery departments at least six months after the DC. For all patents, age, gender, comorbidities (hypertension, heart disease, and diabetes mellitus), anisocoric pupils, and GCS before surgery, time from MCAI onset to DC, side of the lesion, contralateral ventriculomegaly, midline shift, and hemorrhagic infarction were recorded, along with previous treatment with tissue plasminogen activator and/or thrombectomy, and were considered as potential predictors of mortality.
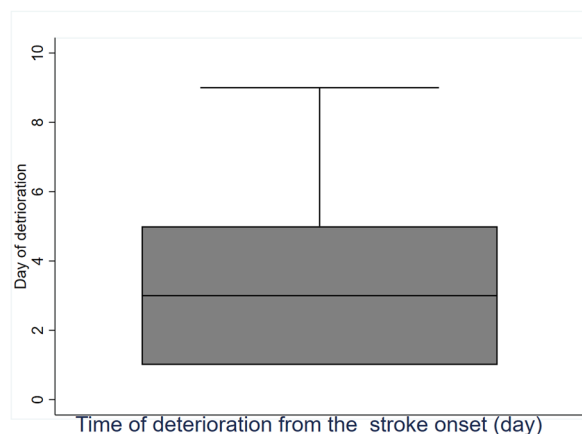
Fig. 1 Time of deterioration from the onset of stroke

Statistical analyses

The gathered patient data was subjected to statistical analyses utilizing the commercial software package STATA. Depending on the data type, mean ± standard deviation (SD) and/or median with interquartile ranges

and proportions were calculated as appropriate. In order to determine the outcome predictors, we compared the mean, median, or proportion between the two groups comprising of surviving and deceased patients using t-test, chi-squared, Wilcoxon test, and Kruskal–Wallis rank test. For the correlation between the treatment and outcome variables, univariate logistic regression was conducted, whereby stratification and multivariate regression analyses were performed in order to eliminate any cofounder effects (a 2-sided *p* value < 0.05 was considered statistically significant).

Results

Our sample comprised of 50 patients with SMCAI that underwent DC, aged 45.2 ± 10.2 years (range 24–67 years), 32 (64%) of whom were female and 18 (36%) were male. While clinical deterioration from the onset of stroke was observed from Day 1 until Day 9, in most cases it took place during the first 5 days, with a median value of 3, as shown in Fig. 1. Following the deterioration, patients were taken into surgery within 2–36 h (with the mean of 9 ± 7.2 h). While the speech-dominant

Table 1 Patients' characteristics

	N (%)	Mean ± SD	Median (range)
Age		45.2 ± 10.2	47 (24–67)
Gender			
Male	18 (36%)		
Female	32 (64%)		
Clinical findings			
GCS		7.5 ± 3	8 (4–13)
Isochoric pupils	10 (20%)		
Risk factors			
DM	9 (18%)		
Cardiac	6 (12%)		
Hypertension	22 (44%)		
Previous treatment	8 (16%)		
Radiological findings			
Contralateral ventriculomegaly	14 (28%)		
Midline shift		8.8 ± 3.4	9 (2–16)
Hemorrhagic infarction	4 (8%)		
Left side	36 (72%)		
Treatment			
Early surgery within	16 (32%)		
Delayed surgery	34 (68%)		
Time of deterioration (days)		3.2 ± 2.3	3 (1–9)
Deterioration to surgery time (hours)		9 ± 7.2	6 (2–36)
Outcome			
Mortality	16 (32%)		
MRS		4 ± 1.5	3 (2–6)

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Table 2 Univariate comparison of Predictors for mortality after decompressive craniectomy in malignant middle cerebral artery infarction

	Surviving 34 (68%) N (%), Mean ± SD (median)	Deceased 16 (32%), N (%), Mean ± SD (median)	p value
Age	42.9 ± 9.4	50.1 ± 10.4	0.018*
Gender			
Male	20 (58.8%)	12 (75%)	0.35
Female	14 (41.2%)	4 (25%)	
Clinical findings			
GCS	8.4 ± 2.9 (8)	5.6 ± 2.4 (4.5)	0.001*
Isochoric pupils	10 (29.45%)	0	0.02*
Risk factors			
DM	4 (11.8%)	5 (31.3%)	0.09
Cardiac	6 (17.7%)	0	0.07
Hypertension	16 (47%)	6 (37.5%)	0.5
Previous treatment	8 (23.5%)	0	0.03*
Radiological findings			
Contralateral ventriculo-megaly	12 (35.3%)	2 (12.5%)	0.09
Midline shift	8.3 ± 3.4	10 ± 3.3	0.09
Hemorrhagic infarction	2 (5.9%)	2 (12.5%)	0.5
Left side	24 (70.6%)	12 (75%)	0.7
Treatment			
Early surgery	10 (62.5%)	6 (37.5%)	0.7
Delayed surgery	24 (70.6%)	10 (29.4%)	
Time of deterioration (days)	3.4 ± 2.6 (3)	2.6 ± 1.6 (2.5)	0.25
Time lapse between deterioration and surgery time (h)	6.4 ± 3.7	14.6 ± 9.4	0.0001*

Table 3 Univariant correlation analysis between prognostic factors and functional outcome after decompressive craniectomy

| Prognostic factors	Correlation coefficient	p value
Age	0.047	0.008*
Gender	− 0.1	0.705
Clinical factors and radiological findings		
GCS	− 0.2	0.026*
Isochoric pupils	− 0.78	0.044*
Midline shift	− 0.03	0.566
Left side	0.21	0.539
Hemorrhagic infarction	0.008	0.094
Contralateral ventriculomegaly	0.65	0.036*
Risk factors		
Diabetes mellitus	0.66	0.03*
Cardiac	0.04	0.02*
Hypertension	0.48	0.17
Management		
Previous treatment (TPA or embolectomy)	0.26	0.13
Time lapse between stroke onset and surgery	− 0.13	0.2
Time lapse between deterioration and surgery	0.06	0.002*
Complications		
Redo	1.3	0.15
Postoperative infection	− 0.57	0.4
Sunken flap	− 0.98	0.002*
Hydrocephalus	0.35	0.35

*$p \leq 0.05$ indicates statistical significance

hemisphere (left side) was affected in 36 (72%) patients and in 20% of cases the pupils were isochoric, the most common vascular risk factors were hypertension (44%), diabetes mellitus (18%), and cardiac disease (12%). previous treatment with tissue-plasminogen activator was completed in (16%). The GCS at presentation ranged from 4 to 13 (with a median of 8), while the median mRS score was 3 (ranging from 2 to 6). As shown in Table 1, the most common surgery-related complications were sunken flap (18%), infection (16%), hydrocephalus (16%). Unfortunately, 16 (32%) patients died at the hospital 2.6 ± 1.6 days after decompressive craniectomy, leaving only 34 (68%) patients for the follow-up. When the surviving group's characteristics were compared to those of the deceased patients, statistically significant difference in their age was noted, as the former were younger

(42.9 ± 9.4 vs. 50.1 ± 10.4 years). Survival was also more likely if an individual had higher GCS, isochoric pupils, had received treatment previously, and was given surgical intervention within the first 24 h from the onset of clinical deterioration, as shown in Table 2. The correlations between prognostic factors and functional outcome after DC are reported in Table 3, indicating that older age, lower GCS, delayed intervention from deterioration, contralateral ventriculomegaly, diabetes mellitus, cardiac problems, postoperative sunken flap were the most reliable outcome predictors for poor functional outcome while younger age, higher GCS, and presence of isochoric pupils, were the most reliable outcome predictors for good functional status (Fig. 2), but multivariate logistic regression analysis of the statistically significant predictors in the univariate analysis led to fade out of this significance except for the GCS (Table 4). Over all favorable outcome was identified in 28 cases (56%), prognostic factors for prediction of favorable outcome are reported in Table 5 indicating that younger age, higher GCS, right

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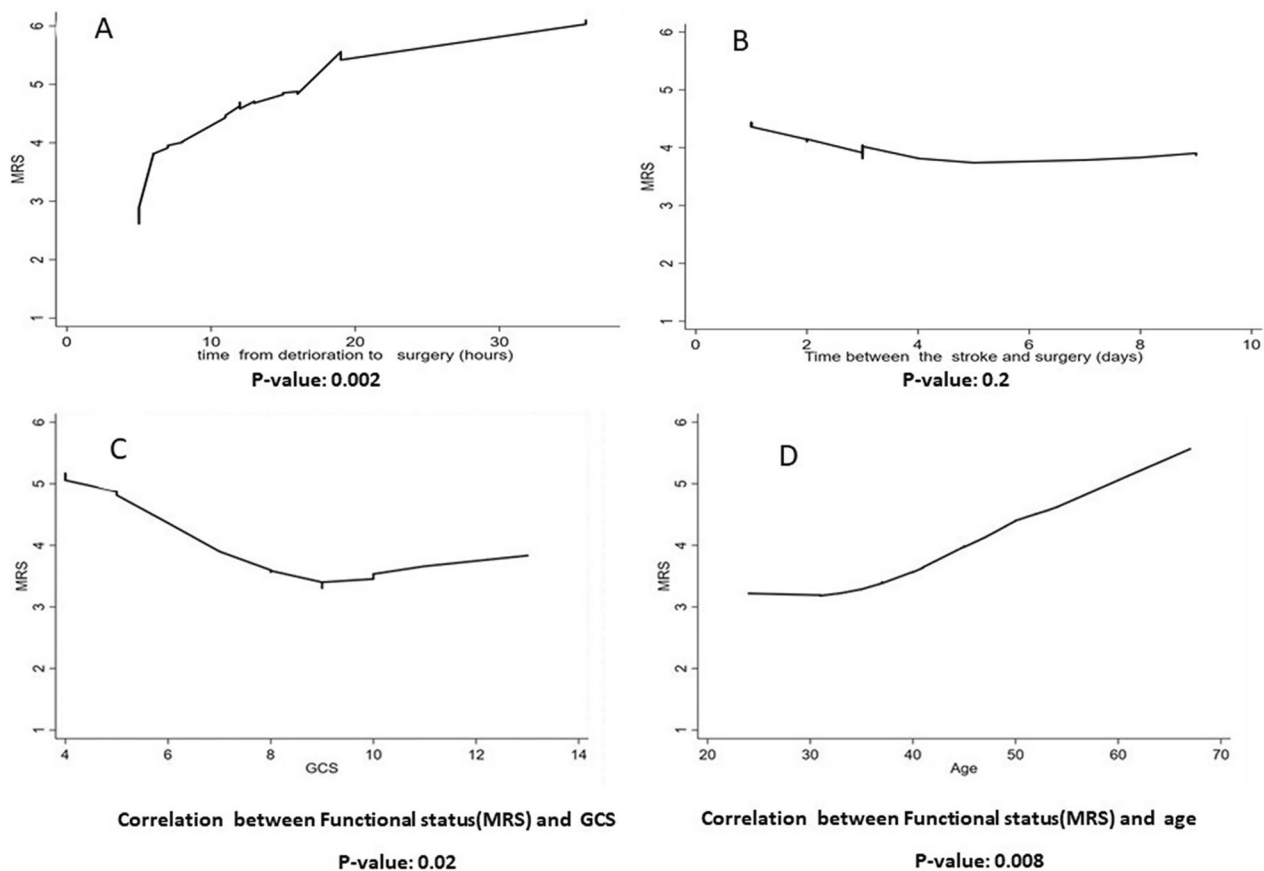
Fig. 2 Significant predictors for the functional outcome after decompressive craniectomy

Table 4 Multivariate model analysis for all significant predictor variables

	IRR	SE	z	p > z	95% CI
Age	1.01289	0.008	1.68	0.092	0.9979095–1.028095
GCS	0.934038	0.03	− 2.31	0.021*	0.8815424–0.9896597
Contralateral ventriculomegaly	1.149345	0.2	0.79	0.429	0.8138397–1.623162
Time of surgery from deterioration	1.013491	0.01	1.27	0.206	0.9926712–1.034748
DM risk	1.012116	0.2	0.06	0.955	0.6668062–1.536246
Cardiac risk	0.7226577	0.23	− 1.02	0.308	0.3871757–1.34883
Previous treatment	1.457637	0.7303067	0.75	0.452	0.5459835–3.891519

side DC, early detection of deterioration, earlier intervention and early cranioplasty are reliable predictors for favorable outcome while older Patient with DM and/or cardiac diseases and lower GCS with delayed intervention is usually associated with unfavorable outcome. Figures 3 and 4 show cases example for the criteria of the patient with favorable and unfavorable outcome respectively.

Discussion

Although DC surgery is frequently performed on patients with SMCAI, as it is believed that Decompressive craniectomy has an effective role in decreasing the mean intracranial pressure and may decrease mortality rates, and increase the favorable outcome [20] but the outcome is still uncertain, as many such individuals die within days following DC [12]. The benefits of DC with

Table 5 Significant predictors for favorable and unfavorable outcome after decompressive craniectomy in patients with middle cerebral artery infarction

	Number of patients	Favorable outcome	Unfavorable outcome	*p* value
N (%)	50	28 (56%)	22 (44%)	
Age	50	41.2	50.4	0.001*
Gender				
Male	18	12 (66.7%)	6 (33.33)	0.2
Female	32	16 (50%)	16 (50%)	
Clinical findings				
GCS	50	8	5	0.02*
Isochoric pupils	10	8 (80%)	2 (20%)	0.08
Risk factors				
DM	9	2 (22.2%)	7 (77.8%)	0.02*
Cardiac	6	0	6	0.02*
Hypertension	22	10 (45.5%)	12 (54.5%)	0.1
Previous treatment	8	6 (75%)	2 (25%)	0.2
Radiological findings				
Contralateral ventriculomegaly	14	8 (57.3%)	6 (42.7%)	0.9
Midline shift (mean)	50	8.5	9.3	0.4
Hemorrhagic infarction	4	0	4	0.01*
Left side	36	24 (66.7%)	12 (33.3%)	0.01*
Treatment				
Day of surgery from the onset (median)	50	2.5	3	0.6
Time lapse between deterioration and surgery time (h)	50	7	11.6	0.01*
Time of cranioplasty	26	84	240	0.001*

*Statistically significant value

respect to improving patients' functional status and quality of life (QoL) are also questionable, as there is limited information on the predictors of short-term mortality and functional status after DC Among other predicting factors, timing of surgery and preoperative clinical condition were evaluated where Early intervention and preoperative clinical condition, patients' age, site of infarct, and preoperative midline shift had been evaluated [21]. In accordance with our results, an association between age and early death after DC for patients with SMCAI has been reported by several authors [4, 9, 19] while others countered these findings [15, 21]. It is also worth noting that, in a European study conducted by Jüttler and his colleagues [22], about 22% of SMCAI patients (many of whom were aged below 60) were deceased within 30 days following DC [10, 23, 24]. Similar findings were obtained

in a North American setting by Frank Jeffrey and colleagues [25], who noted 21% mortality rate for their cohort (aged up to 75 years) while majority of our cases involved left side, we failed to establish a link between the impacted hemisphere [26] (dominant vs. non-dominant) and mortality or functional outcome. Our findings are in line with those yielded by several authors, including Gupta and colleagues [27]. They are also supported by the evidence yielded by the DESTINY [22], DECIMAL [11, 24], and HAMLET [10, 23, 24] trials, and also the Swedish malignant middle cerebral artery infarction study [28], indicating that the QoL and outcome are independent of hemisphere involvement.

Ample body of evidence indicates that preoperative GCS score is a reliable QoL predictor. Thus, as expected, in our study, the GCS score on admission was negatively

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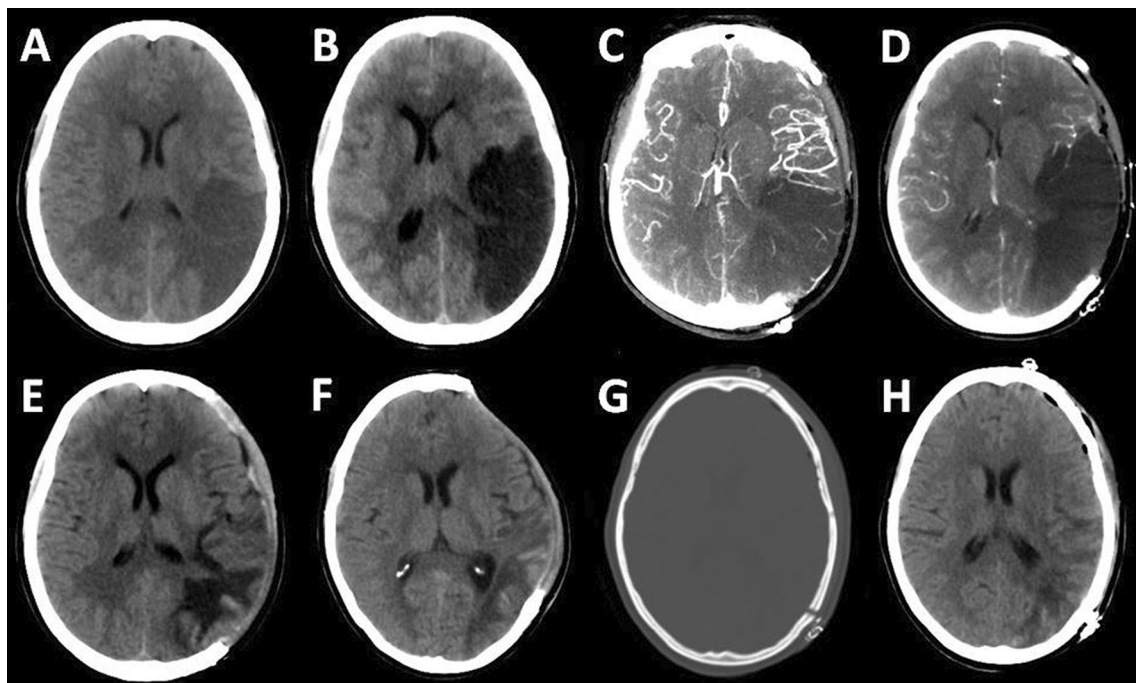
Fig. 3 Case 1: favourable outcome GOS 5 41 years old female patient known hypertensive on medications, came to the Emergency department with acute onset right side body weakness, headache and dizziness, on arrival to the hospital she was conscious with sensory dysphasia, the initial CT brain **A** revealed left T/P acute ischemic stroke with lower trunk left MCA territory distribution without midline shift, admitted under observation, on the 3rd day of her admission her GCS dropped to GCS 10, an urgent CT brain **B** revealed evolutional change at the infarction core with midline shift of about 5 mm, underwent emergency surgical decompressive craniectomy and duroplasty that was performed within 5 h from the time of deterioration and the patient was sent to ICU, on the second postoperative day patient weaned from ventilator, GCS 14, FU CTA brain was done (**C**, **D**) and revealed nice decompression. On the third POD, patient improved more and discharged from ICU and FU CT brain revealed lax brain at both one, two weeks PO (**E**, **F**), then Cranioplasty was performed after 19 days from DC, and post-cranioplasty follow up CT brain (**G**, **H**) showed no adverse effects and satisfactory reconstruction

correlated with functional impairment and was a significant predictor of early mortality. Other authors also suggested using the NIHSS score [10], whereby Kim and colleagues identified an NIHSS score > 18 on admission as an independent predictor of life-threatening brain swelling [29]. As isochoric pupils were also identified in our study as a significant survival predictor, we attribute this link to a more rapid intervention in such cases. However, we have failed to establish a link between the degree of midline shift at the time of DC and early mortality, even though this relationship was reported by Puetz and colleagues, who also noted that a postoperative midline shift of < 5 mm was associated with a favorable outcome [19]. Thus, given these discordant findings, it appears that the management plan needs to be determined for each individual SMCAI patient [18]. Nonetheless, a shorter interval between SMCAI onset and DC tends to improve survival as well as QoL [4, 6], as confirmed in our study. In accordance with this finding Refaat and Abdallah [21] had proven the role of early decompressive craniectomy in reduction of the mortality rate and improving functional outcome [21, 30].
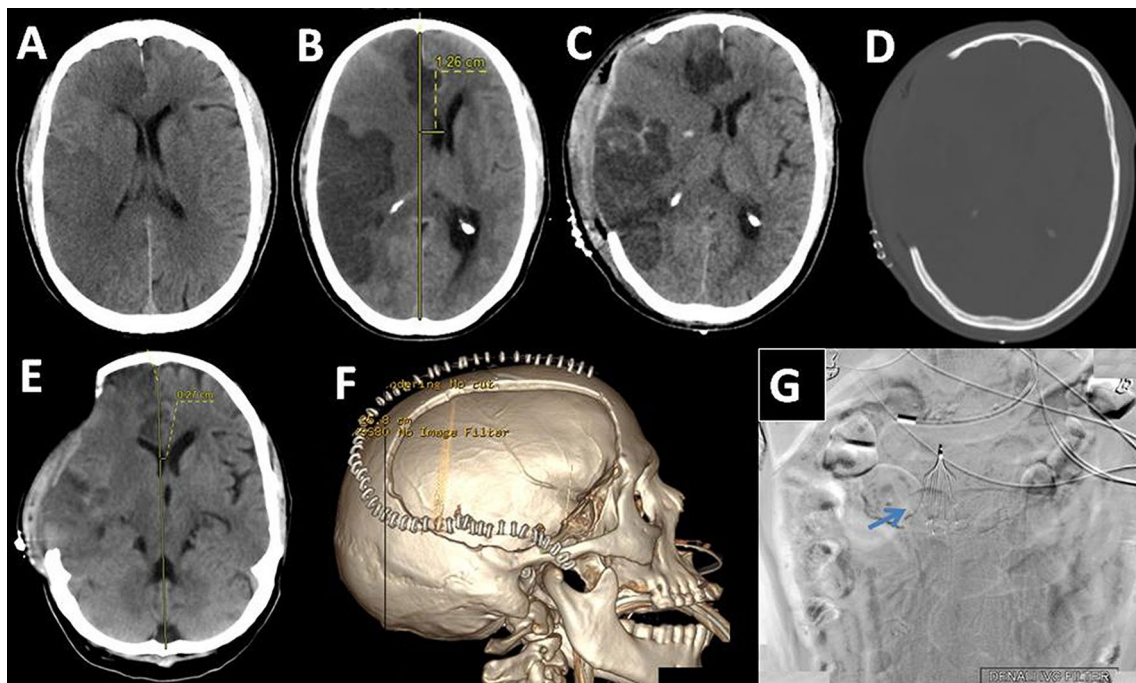
Fig. 4 Case 2: 55 years old female patient came to the Emergency department with acute onset left side body weakness, confused, the initial CT brain **A** revealed right acute ischemic stroke with lower trunk right MCA as well as small ACA territory distribution without midline shift, admitted under observation, on the 2nd day of her admission her GCS dropped to GCS 11, with unequal pupils an urgent CT brain **B** revealed evolutional change at the infarction core with midline shift of about 12 mm, underwent emergency surgical decompressive craniectomy and duroplasty that was performed within 2 h from the time of deterioration and the patient was sent to ICU, on the 2nd postoperative day he GCS 8t, FU CT brain was done (**C**, **D**, **F**) and revealed satisfactory decompression. After extubation her GCS was 11. FU CT brain revealed lax brain at two weeks PO (**E**), after two weeks patient developed left LL swelling and Doppler US revealed DVT, IVC filter **G** was inserted and started on anticoagulants, unfortunate she developed massive pulmonary embolism and passed away 18 days postoperatively

Study limitations

The relatively small sample size precludes firm conclusions.

Conclusions

According to our retrospective study of 50 SMCAI patients that underwent DC, younger age, higher GCS, presence of isochoric pupils, and history of previous treatment (embolectomy or tissue plasminogen activator), as well as shorter interval between clinical deterioration and surgery, can be considered as predictive factors for greater survival and more favorable functional outcomes in this population.

Abbreviations

DC   Decompressive craniectomy
SMCAI   Swollen middle cerebral artery infarction
mRS   Modified Rankin Scale score
GCS   Glasgow Coma Scale score
h   Hours
MCA   Middle cerebral artery
MCE   Malignant cerebral edema
TBI   Traumatic brain injury
MCAI   Middle cerebral artery infarction
NIHSS   National Institutes of Health Stroke Scale
CT   Computerized tomography scan
SD   Standard deviation
QoL   Quality of life
IRR   Incidence rate ratio

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (Kingdom hospital ethical committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication
For this type of study formal consent is not required.

Competing interests
The authors declare that they have no competing interests.

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