

# Effects of timing to surgery on outcomes among adult patients with traumatic expansive intracranial hematomas in a sub-Saharan tertiary hospital: A prospective cohort study

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## Research Article

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# Abstract

## Background

Despite the fact that traumatic expansive intracranial hematomas (EIH) are frequent, it is debatable whether the timing of surgery affects the prognosis of patients. The study assessed the effect of timing to surgery on outcomes among adult patients with EIH at Mulago National Referral hospital (MNRH).

## Methods

A prospective study was conducted among adult TBI patients with intracranial hematoma during a period of 1 year and follow up for 6 months. Participants were grouped into two arms based on the early (within 24 hours) or late (over 24 hours) surgical evacuation of EIH. The Kaplan–Meier survival curve and log-rank test were used to test for differences in survival status among groups. The level of significance was determined at a p-value of  $< 0.05$ .

## Results

The analysis covered 324 individuals in all, and 10.2% of them died. Majority of patients (59.6%) had delayed surgery. Patients who underwent early surgery within 24 hours of accident had a median time to mortality of 2 days while those who underwent surgery more than 24 hours had a median time to mortality of 4 days ( $p=0.004$ ). Patients who underwent early surgery had a median LOS similar to those who had late surgery of 2 days ( $p=0.278$ ). The overall survival was 46.6%, 95% CI= (17.0 to 71.9). The survival was significantly influenced by QoLIBRI, GOS, SDH, SAH, contusion. Among the survivors, 73.8% were in good functional outcome at discharge. Surgical timing groups were different according to mortality, QoLIBRI at 180 days, which was on average lower in the late surgery group, and complications, which were higher in the same group. Delayed surgery was more associated with posttraumatic seizures (PTS), infection, bleeding, pneumonia, paralysis, nausea, vomiting and decompressive craniectomy.

## Conclusion

Early surgery was associated with early mortality, but was neither associated with shorter LOS nor with better survival. Late surgery was associated with lower long-term QoLIBRI, higher complication rate. This study demonstrates that there are still differences in outcome about when to operate. Further high-quality studies are needed to solve this disparity.

## Introduction

Expansive intracranial hematoma (EIH) due to traumatic brain injury (TBI), following road traffic accidents, assaults, and falls are a common problem worldwide. EIH refers to evidence of increased hematoma volume of over 33% or absolute hematoma growth over 6mL from initial scan with varying consequences (1). Prompt evacuation of an EIH in a patient with worsening consciousness is lifesaving. Though, numerous patients arrive with a stable low-level or high-level of consciousness. There is

uncertainty regarding the indications and timing of surgery, which is reflected in significant practice variances, particularly in patients with an acute subdural hematoma (ASDH) or a traumatic intracerebral hematoma (TICH) (2). Comparative-effectiveness reports have demonstrated that early evacuation of ASDH does not result in a better outcome as compared to a strategy favouring initial conservative therapy in situations where there is surgical equipoise (3).

For patients with an expanded TICH, a study by Maas et al. revealed no overall apparent benefit of early surgery. However, those with moderate TBI (GCS 9–12) or isolated TICH had improved outcomes after early surgery than with continued conservative therapy. Contrarily, conservative care was linked to better outcomes in patients with mild TBI and those with a smaller TICH (< 33 cc) (2). These findings concur with reports of the surgical trial in traumatic intracerebral haemorrhage (STITCH) trial (4). Therefore, surgery does not appear to have a consistent effect on ASDH and TICH. There is a need for deliberate efforts to build research capacity so that high quality and evidence-based results are generated. In addition, guidelines may be based on meta-analyses of data from the collaborative European Neurotrauma effectiveness research in TBI (CENTER-TBI), transforming research and clinical knowledge in TBI (TRACK-TBI), and STITCH(Trauma) studies (2).

The controversy remains about the use of decompressive craniectomy (DC) in patients who have sustained TBI. Patient selection, timing and many aspects of the procedure are continuing to be debated and to some extent there has been disagreement about the rationale of the procedure itself. It has been presumed that two studies i.e. RESCUEicp and DECRA would definitively guide on when and how DC should be utilized. Despite publication of the high-quality trials, DC remains a controversy (5). Choosing to perform a DC is still challenging and the overall benefits should be balanced against the outcomes and complications on a case by-case basis. Other trials are needed in order to consolidate current knowledge in the TBI management (6–9). In addition, several prospective RCT have not demonstrated evidence on the surgical timing in influencing the outcome (10). Whether EIH in TBI should be evacuated urgently or lately remains debatable and controversial. Furthermore, previous studies demonstrated that TBI sequels may persist or worsen over time with elevated blood pressure, pupil reactivity and Glasgow scale as independent predictors of mortality (11, 12). In addition, an observation study in TBI patients with an ASDH and AEDH conducted at Mulago National Referral Hospital (MNRH) showed that the overall proportion of favourable thirty-day outcome was 71.7%, with 42.3% and 81.7% for ASDH and AEDH with moderate, severe TBI as independent factors associated with unfavourable outcome (13). Globally, timely evacuation is frequently used as quality indicator for optimal trauma care(14). TBI patients typically present at MNRH emergency unit within 24 hours while others present beyond 24 hours. However, there is limited information on the effect of surgical evacuation (early or late) on outcomes in Uganda and other low middle-income countries (LMIC). This study assessed the effect of timing to surgical evacuation on outcomes among adult patients with EIH at MNRH, Kampala, Uganda.

## Methods

### Study design and setting

A prospective cohort study among TBI patients with expansive intracranial hematoma undergoing surgical evacuation was conducted at MNRH, Kampala, Uganda, between the 16th of June 2021 and the 17th of June 2022 and participants were followed up for 6 months. Ethics approval was obtained from School of Medicine (SOMREC) IRB (Mak\_SOMREC-2020-38).

## **Patient population**

### **Study population**

Patients aged 18 years and above, had two positive CT scan for brain expansive hematoma as defined as an increase in acute intracranial traumatic hematoma volume >33% or absolute hematoma growth >6ml from the initial scan within 72 hours of injury during the study period and who meet the inclusion criteria were recruited in the study.

### ***Inclusion criteria for patients***

Participants were TBI patients aged 18 years and above, post resuscitation GCS of 4 to14, with brain evidence of EIH on two CT scans (increase in hematoma volume >33% or absolute hematoma growth > 6ml from the initial scan) exclusively, eligible for cranial surgery and enrolled in the study within 24 hours of initial presentation to hospital. A written signed informed consent from the patient or their next of kin was obtained

### ***Exclusion criteria for patients***

Patients with (1) unknown time of injury, (2) penetrating trauma, (3) known pre-thrombocytopenia, (4) a history of coagulation disorders, and (5) used anticoagulants, (6) pregnancy, (7) and those with the inability to consent before surgical intervention were excluded from the study.

## **Sample Size & determinism**

The sample size calculated by using epitool tool where expected incidence in unexposed is 0.05; assumed relative risk is 3; confidence level is 0.95; power is 0.85; the formula for comparison between two groups (early and late surgical outcomes) with continuous variables with 10% of possible dropout, estimated at 324 patients (both groups). (<https://epitools.ausvet.com.au/samplesize>).

## **Study procedure**

Patients were recruited from their admission at the Accident and Emergency Department of the MNRH. The study protocol was explained by the research assistants to potential participants or their relatives. Prior to surgery, informed consent was gained from patients who were hemodynamically stable, and the research assistant then gave them an interviewer-guided questionnaire. For participants who were seriously ill, the informed consent was sought from the closer next of kin. Teams were asked to complete the data collection forms on Redcap, including the follow-up data and the authorship confirmation forms by 17 th December 2022.

## **Study variables**

### **Imaging assessment**

After the initial trauma assessment and resuscitation, a Brain CT scan was obtained. Hematoma CT findings and measurement were obtained from the neuro-radiologists. Follow-up scans were performed within 72 considering the time between the TBI and first CT hours and based on neurosurgeons' recommendations.

### **Outcomes data**

Patients were recruited from their admission at the Accident and Emergency Department, followed up in the operative theatres, postoperatively in the neurosurgery ward, and neurosurgical outpatient clinics up to 6 months for occurrence of complications and recording of Glasgow outcome scale (GOS) and quality of life (QoL). Outcomes data were obtained at enrollment (baseline) and then at 1day, 30, 90 and 180-days post discharge. Clinical outcomes were recorded during these outpatient visits. These data were used to fill specific data tool record forms, and outcomes were adjudicated centrally with the use of an outcomes document with case definitions as a guide.

The principal outcomes included death from any cause, length of hospital stay (LOS), complications (posttraumatic seizures, imaging evidence of expansive hematoma, spasticity, cerebrospinal fluid leakage, bleeding diastasis, laboratory apparent platelet dysfunction, clinical evidence of fever, infection source gastrointestinal tract (GIT), upper respiratory tract (URT) pneumonia, Urinary tract, perinephric, skin abscesses or wound complication). A five-category scale known as the GOS is frequently used to evaluate the functional outcome following an acute brain injury (15). The score is determined by a person's level of independence at home and in the community, as well as their capacity to work, engage in social and recreational activities, maintain personal connections, and resume their typical activities following an injury (16). The QOLIBRI scores were scored on a 0 up to 100 scale , where 100 was the best possible quality of life after sTBI and 0 was the worst possible quality of life after traumatic expansive hematomas (17).

### **Quality control**

#### ***Avoid duplicate entries***

A list of patients' baselines including the patient's IPN, names, gender, age, education level, occupation, place of residence, and telephone number combined with their Redcap ID was preserved by the research team and checked by the research assistants. Before assessing surgical evacuation intervention outcomes, each patient was contacted to check that the patient is alive, and confirm the patient's baselines.

#### ***Missing data***

To avoid loss of any information, the research team reported the overall outcomes alongside the individual outcomes for each surgical evacuation intervention outcomes. Annals with 5% of misplaced items were omitted from the final analysis. As well, research teams with 5% of lost archives were excepted from the partnership, and their data was discarded in this study.

### ***Data validation***

Data accuracy is important to strengthen the internal validity of the study design and the study results. Therefore, data validation was done by the primary data collection items.

### **Statistical analysis**

Categorical variables were tested for association using  $\chi^2$  test while for continuous variables, the t-test was used(18, 19). Only the evidence of expansive hematoma event was used to calculate the incidence of expansive hematoma; for individual types of events, the first occurrence of that event was used. Estimates of hazard ratios and 95% confidence intervals were derived from Cox regression models that compared outcome and rates of new-onset clinical-event rates according to radiological patterns; these regression models were stratified according to timing of surgery (early or delayed), quality of life (<75 or  $\geq$ 76), GOS( unfavorable or favorable), GCS(mild, moderate and severe), types of hematomas( EH or no EH, epidural, subdural, subarachnoid and contusion), Complication(CSF leak, fever, infection source, wound dehiscence, bleeding disorders and nutritional deficit). To assess for the effect of surgical evacuation (early or late) on time to mortality and length of hospital stay, Kaplan Meir survival curves were used to demonstrate this and log rank test was used to assess for statistical significance. The level of significance was determined at a p-value of < 0.05. Data was analyzed using R.

## **Results**

A total of 1500 participants were eligible to participate in the trial between June 16, 2021, and December 17, 2022. 324 (21.6%) of them were included in the study. One thousand one hundred and seventy-six patients were excluded because they did not fulfill the inclusion criteria or did not give consent or assent or parental permission. Out of 324 enrolled patients, the early surgical evacuation was performed for 112 (34.6%), 193(59.5%) underwent delayed surgery and 19(5.9%); analysis in this study is therefore limited to these 324 patients (figure 1).

### **Baseline outcomes of patients with intracranial hematomas**

In this study, majority of the participants were between 18 and 28 years 141 (43.5%), most of the patients were male 261 (80.6%) and majority 152 (48.0%) being boda riders. The results show that most of the patients 184 (56.8%) being from rural residence. Majority 172 (54.6%) had injuries due to traffic accidents (Table 1).

Table 1 : **Baseline demographic of patients with intracranial hematomas**

<b>Variables</b>	<b>No expansive hematoma No. (%)</b>	<b>Expansive hematoma No. (%)</b>	<b>Total No. (%)</b>	<b>P- Value</b>
<b>n, (%)</b>	<b>132 (40.7)</b>	<b>192 (59.3)</b>	<b>324 (100.0)</b>	
<b>Age n (%)</b>				
18-28	77 (58.3)	64 (33.3)	141 (43.5)	
29-38	29 (22.0)	24 (12.5)	53 (16.4)	
39-48	9 (6.8)	30 (15.7)	39 (12.0)	
>48	17 (12.9)	74 (38.5)	91 (28.1)	< 0.001
<b>Gender, n (%)</b>				
Female	24 (18.2)	39 (20.3)	63 (19.4)	
Male	108 (81.8)	153 (79.7)	261 (80.6)	0.634
<b>Patients' occupation, n (%)</b>				
Farming	11 (8.3)	26 (14.0)	37 (11.7)	
Family business	16 (12.1)	38 (20.4)	54 (17.0)	
Employed	9 (6.9)	13 (7.0)	22 (6.9)	
Boda rider	72 (54.5)	80 (43.0)	152 (48.0)	
Taxi driver	23 (17.4)	29 (15.6)	52 (16.4)	0.109
<b>Residence type / location, n (%)</b>				
Rural	78 (59.1)	106 (55.2)	184 (56.8)	
Urban	54 (40.9)	86 (44.8)	140 (43.2)	0.488
<b>Matrimonial state, n (%)</b>				
Unmarried	62 (47.0)	65 (33.9)	127 (39.2)	
Married	70 (53.0)	127 (66.1)	197 (60.8)	0.017

**Table 2 : Baseline outcomes of adult TBI patients with intracranial hematomas**

Intracranial hematomas were observed in all 324 patients and of these 10.2% died. Of the 324 patients, 193 (59.6%) had late surgical evacuation (defined by surgery of >24 hours), 112 (34.6) had early surgery (defined by surgery of <24 hours) and 19 (5.9%) were managed conservatively. However, 291 (89.8%) were alive until the end of the study. Among these patients, 239 (73.8%) were discharged with favourable condition (defined by GOS of >3), 85 (26.2%) were discharged with unfavourable condition (defined by GOS of <3).

The percentage of patients who experienced complications were 58% higher among delay surgery group (72.5% vs. 41.1%,  $p<0.0001$ ). Similarly, the proportion of patients who developed other complications was higher among delay group ( $p<0.0001$ ), respectively (Table2).

**Table 2 : Baseline outcomes of adult TBI patients with intracranial hematomas**



<b>Variables</b>	<b>Delay (&gt;24hrs)</b>	<b>Early (within 24hrs)</b>	<b>Conservative Management</b>	<b>Total</b>	<b>P-value</b>
n (%)	193 (59.6)	112 (34.6)	19 (5.9)	324 (100.0)	
Discharge Fate, n (%)					
Death	20 (10.4)	12 (10.7)	1 (5.3)	33 (10.2)	
Alive	173 (89.6)	100 (89.3)	18 (94.7)	291 (89.8)	0.762
Glasgow Outcome Scale (GOS) - outcome, n (%)					
Unfaourable	58 (30.1)	23 (20.5)	4 (21.1)	85 (26.2)	
Favourable	135 (69.9)	89 (79.5)	15 (78.9)	239 (73.8)	0.166
Complications, n (%)					
No	53 (27.5)	66 (58.9)	17 (89.5)	136 (42.0)	
Yes	140 (72.5)	46 (41.1)	2 (10.5)	188 (58.0)	0.000
Infection (Y), n (%)	11 (5.7)	5 (4.5)	0 (0.0)	16 (4.9)	0.000
Bleeding (Y), n (%)	68 (35.2)	25 (22.3)	1 (5.3)	94 (29.0)	0.000
Blood clots (Y), n (%)	2 (1.0)	1 (0.9)	0 (0.0)	3 (0.9)	0.000
Pneumonia (infection of the lungs) (Y), n (%)	10 (5.2)	0 (0.0)	1 (5.3)	11 (3.4)	0.000
Arterial hypertension (Y), n (%)	30 (15.5)	4 (3.6)	0 (0.0)	34 (10.5)	0.000
Tachycardia (Y), n (%)	59 (30.6)	15 (13.4)	1 (5.3)	75 (23.1)	0.000
Bradycardia (Y), n (%)	23 (11.9)	7 (6.3)	0 (0.0)	30 (9.3)	0.000
Desaturation (Y), n (%)	11 (5.7)	2 (1.8)	0 (0.0)	13 (4.0)	0.000
Seizures (Y), n (%)	42 (21.8)	8 (7.1)	1 (5.3)	51 (15.7)	0.000

Nausea/vomiting (Y), n (%)	22 (11.4)	8 (7.1)	0 (0.0)	30 (9.3)	0.000
Muscle weakness (Y), n (%)	10 (5.2)	3 (2.7)	0 (0.0)	13 (4.0)	0.000
Brain swelling (Y), n (%)	25 (13.0)	12 (10.7)	1 (5.3)	38 (11.7)	0.000
Leakage of cerebrospinal fluid (the fluid that surrounds and cushions the brain) (Y), n (%)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.3)	0.000
Risks associated with the use of general anesthesia (Y), n (%)	3 (1.6)	1 (0.9)	0 (0.0)	4 (1.2)	0.000
Amnesia (Y), n (%)	21 (10.9)	9 (8.0)	0 (0.0)	30 (9.3)	0.254
Aphasia (Y), n (%)	36 (18.7)	15 (13.4)	1 (5.3)	52 (16.0)	0.202
Paralysis (Y), n (%)	45 (23.3)	14 (12.5)	0 (0.0)	59 (18.2)	0.007
Abnormal balance or coordination (Y), n (%)	6 (3.1)	0 (0.0)	1 (5.3)	7 (2.2)	0.125
Coma (Y), n (%)	26 (13.5)	10 (8.9)	2 (10.5)	38 (11.7)	0.487
Fever (Y), n (%)	19 (9.8)	12 (10.7)	2 (10.5)	33 (10.2)	0.970
Spasticity (Y), n (%)	51 (26.4)	16 (14.3)	4 (21.1)	71 (21.9)	0.047
Bleeding diathesis (Y), n (%)	72 (37.3)	25 (22.3)	3 (15.8)	100 (30.9)	0.008
QOL at 1day, n (%)					
0 to 75	183 (94.8)	105 (93.8)	16 (84.2)	304 (93.8)	
76 to 100	10 (5.2)	7 (6.3)	3 (15.8)	20 (6.2)	0.186
QOL at 30days, n (%)					
0 to 75	154 (79.8)	87 (77.7)	15 (78.9)	256 (79.0)	
76 to 100	39 (20.2)	25 (22.3)	4 (21.1)	68 (21.0)	0.909
QOL at 90days, n (%)					
0 to 75	89	44 (39.3)	6 (31.6)	139	

	(46.1)			(42.9)	
76 to 100	104 (53.9)	68 (60.7)	13 (68.4)	185 (57.1)	0.300
QOL at 180days, n (%)					
0 to 75	64 (33.2)	26 (23.2)	2 (10.5)	92 (28.4)	
76 to 100	129 (66.8)	86 (76.8)	17 (89.5)	232 (71.6)	0.037
Type of surgery, n (%)					
Evacuation only	65 (33.7)	25 (22.3)	0 (0.0)	90 (27.8)	
Decompression only	2 (1.0)	1 (0.9)	0 (0.0)	3 (0.9)	
Both craniotomy	109 (56.5)	80 (71.4)	0 (0.0)	189 (58.3)	
Both craniectomy	15 (7.8)	5 (4.5)	0 (0.0)	20 (6.2)	
ND	2 (1.0)	1 (0.9)	19 (100.0)	22 (6.8)	0.000
Severity group of GCS, n (%)					
Mild	107 (55.4)	73 (65.2)	12 (63.2)	192 (59.3)	
Moderate	38 (19.7)	21 (18.8)	4 (21.1)	63 (19.4)	
Severe	48 (24.9)	18 (16.1)	3 (15.8)	69 (21.3)	0.391
Expansive Hematoma, n (%)					
No	75 (38.9)	48 (42.9)	9 (47.4)	132 (40.7)	
Yes	118 (61.1)	64 (57.1)	10 (52.6)	192 (59.3)	0.658

### Effect of early and late surgical evacuation on mortality

There was a statistically significant difference in mortality between individuals who had early surgical evacuation and those who had late surgical evacuation ( $p=0.004$ ). A patient's median time to death was 2 days for early surgical evacuation and 4 days for late surgical evacuation (figure 2).

### Effect of surgical evacuation on Length of hospital stay

When patients who had early surgical evacuation were compared to those who had late surgical evacuation, there was no difference in Length of hospital stay. Patients who had early surgical evacuation had a median length of hospital stay similar those who had late surgical evacuation of 2 days (Figure 3).

### **Survival trends of TBI patients with expansive intracranial hematomas after surgery.**

In this study, the overall survival was 46.6%, 95% CI= (17.0 to 71.9) based on Kaplan–Meier curve. The median survival time was 12.8 months, 95% CI= (11.1 to 13.0). The estimated cumulative survival was 97.38% (95% CI: 94.83–98.68) within the first month of follow-up, 94.35% (95% CI: 90.92–96.50) after 2 months of follow-up, 93.95% (95% CI:90.43–96.20) after 3months of follow-up,90.81% (95% CI: 86.32–93.87%) after 6 months of follow-up, 62.07% (95% CI: 40.35–77.83) after 12 months of follow-up, and 46.55 (95% CI: 16.96–71.93) after 15.9 months of follow-up. The probability of survival decreased as the follow-up time increased, especially within the first months of follow-up according to the Kaplan–Meier survival curve for time to death for TBI patients with intracranial hematomas after surgery (Figure 4).

### **Effect of surgical timing on survival**

Surgical timing was not associated with survival ( $p=0.486$ ) (Figure 5).

The overall survival (OS) of patients with EIH after surgery decreases over time( $p=0.184$ ) (Figure 6).

EIH Patients with mean arterial pressure (MAP) of 95 mmHg and above had significantly worse overall survival than patients with MAP less than 95 mmHg ( $p=0.025$ ) (Figure 7).

Subanalysis of EIH following each type of intracranial hematomas revealed that ASDH had worse OS than patients without ASDH( $p=0.0267$ ) (Figure 8).

Patients with contusions had worse OS than patients without contusions ( $p=0.001$ ) (Figure 9) Figure 9 : Survival of expansive hematoma patients with contusion

Patients with subarachnoid hemorrhage had worse OS than patients without subarachnoid ( $p=0.001$ ) (Figure 10)

Epidural hematoma was not associated with survival ( $p=0.979$ ) (Figure 11).

Intracerebral hematoma was not associated with survival ( $p=0.2546$ ) (Figure 12).

Patients with Glasgow outcome scale (GOS) less than 3 (unfavourable outcome) had worse OS than patient with favourable outcomes (defined by GOS of >3) ( $p<0.0001$ ) (Figure 13).

Patients with quality of life after TBI (QUOLIBRI) less than 75 % (poor QUOLIBRI) had worse OS than patient with good QUOLIBRI (defined by QUOLIBRI of >75%) ( $p<0.0001$ ) (Figure 14).

## Discussions

This study assessed the effect of surgery on outcomes among adult patients with EIH at Mulago National Referral hospital (MNRH), Kampala, Uganda. All 324 patients with intracranial hematomas had a mortality rate of 10.2%, which is lower than the 20% overall mortality rate seen in a prospective research in China on patients who underwent early versus late craniectomy after a traumatic brain injury (20). The mortality rate observed in this study agrees with the findings obtained in a study conducted in Uganda (9.6%)(21). In this study, majority of patients underwent delayed surgery more than 24 hours (59.6%), which concurred with previous observation in Uganda where the majority of patients take more than 4 hours to reach hospitals after trauma and several factors which prevent patients from receiving timely surgery including cost of repeat imaging and surgical utilities, limited theatre access, delayed decision making etc.(21, 22). However, 291 (89.8%) alive until the end of the study. Among these patients, 239 (73.8%) were discharged with favourable condition (defined by GOS of >3), 85 (26.2%) were discharged with unfavourable condition (defined by GOS of <3). These findings are slightly much better compared with a study conducted at MNRH (71.7%)(13).

When compared to the early evacuation group, the proportion of patients who experienced complications was 58% higher in the delay evacuation group (72.5% vs. 41.1%,  $p < 0.0001$ ). Similarly, the percentage of patients who developed complications such as posttraumatic seizures, infection, etc. was higher among delay evacuation group ( $p < 0.0001$ ), respectively (Table 1).

### Survival status

The overall survival was 46.6%, 95% CI= (17.0 to 71.9) based on Kaplan–Meier curve (Figure 4). This finding correlates with the severity and pathophysiology of intracranial hematomas (2). This result is consistent with research done in Ethiopia (47.53%) (12) and a systematic review (46%) (23). Brooks et al similarly showed a poor prognosis for TBI patients (24), which contrasts with a study done in England and Wales where a significant rise in survival rates for people with ASDH was seen from 59% to 73% over time (11). These differences may have been due to variations in the study settings (HIC versus LMIC) (2). In addition, LMIC can be challenging due to a lack of pre-hospital system, few intensive care unit beds and standardised guidelines in management of TBI patients with intracranial hematoma (25). These findings concur with a study that reported that survival of TBI patients was low (12). Furthermore, the mortality rate among severe TBI (GCS  $\leq 8$ ) patients with intracranial hematomas was 63.6%, which is higher compared with a study conducted in Ethiopia where the cumulative incidence of death was 49.71% (12), but slightly lower compared with a prospective study in Uganda where the mortality among severe TBI patients with hyperglycemia at MNRH was 68.8% (26). In addition, the present findings in the study differ from the Chinese retrospective study where the mortality rate observed among severe TBI patients was 21.8% (27). This mortality rate difference observation can be explained by the sample size, changes in the treatment protocols and accessibility in intensive care units.

### Effect of surgical evacuation on mortality and length of hospital stay

In this study, the median time to death for patients who underwent early surgical evacuation was 2 days, compared to 4 days for patients who underwent late surgical evacuation. A statistically significant difference in mortality ( $p=0.004$ ) was seen between individuals who underwent early surgical evacuation and those who underwent late surgical evacuation (Figure 2). This finding corroborates with previous studies where early surgery was not associated with better outcomes(3, 28). Thus, surgical timing appeared to be correlated with mortality but is not associated with length of hospital stay ( $p=0.278$ ) (Figure 3). The median hospital stay for patients who had early surgical evacuation was 2 days, the same as it was for those who had late surgical evacuation. This finding contradicts a study that found that fast surgery within four hours was strongly related with a shorter hospital stay (14).

### **Factors associated with survival**

The survival was significantly influenced by mean arterial pressure (MAP) of above 95 mmHg, SDH, SAH, contusion, QoLIBRI and GOS. Holding the rest of variables constant, increasing MAP by 1 unit from 95 mmHg would make the survival of become worse (Figure 7). Although some research, including this study, have correlated this observation with high mean arterial pressure (MAP) which was positively correlated to EIH and outcomes (29-31) and patients with post-admission SBP of more than 160 mmHg have a substantially higher risk of expansive hemorrhages thus worse survival (30, 32). The ongoing rupture and bleeding of small veins may help to explain this and managing blood pressure early could be one of the possible therapy goal. In addition, these findings concur with a study that reported that survival of TBI patients was low and elevated blood pressure, GSC, and non reactive pupils are predictors of mortality (12). Holding the rest of variables constant, given a patient has EIH, having SDH, SAH and contusion (Figures would make the overall survival become worse over time (33-36). Patients with EIH after TBI had a 30-fold higher risk of adverse outcomes and a 10-fold higher chance of dying (37). In addition, holding the rest of variables constant, given a EIH patient with QoLIBRI less than 75% has worse overall survival than EIH patient with QoLIBRI of over 75% ( $p<0.0001$ ) (Figure 14). Previous studies have shown a connection between the overall survival and mental health status, physical well-being, and psychological well-being(38). Finally, EIH patients with Glasgow outcome scale (GOS) less than 3 (unfavourable outcome) had worse OS than patient with favourable outcomes (defined by GOS of  $>3$ ) ( $p<0.0001$ ) (Figure 13).

## **Conclusion And Recommendations**

This study established that immediate surgery within 24 hours was linked to early mortality but not to shortened LOS or improved survival. Surgery postponed for longer than 24 hours is linked to higher complications. As a result, it is agreed that if surgery is delayed for longer than 24 hours, which is a strategy that favors initial conservative therapy when there is surgical equipoise, it will not produce a better outcome than early surgery within 24 hours. MAP of above 95 mmHg, SDH, SAH, contusion, QoLIBRI and GOS were factors associated with overall survival. Further studies should be conducted to identify predictors of mortality in adult patients with EIH following TBI at MNRH.

# Abbreviations

ASDH: acute subdural hematoma, DC: decompressive craniotomy, EDH: epidural hematoma, EIH: expansive intracranial hematoma, GCS: Glasgow coma scale, GOS: Glasgow outcome scale, ICH: Intracranial hemorrhage; LMIC: low middle-income countries, MNRH: Mulago National Referral Hospital, QOLIBRI: quality of life after brain injury; RCT: randomized clinical trials, SAH: subarachnoid hemorrhage, SDH: Subdural hematoma, STICH: Surgical Trial in Intracerebral Hemorrhage, TBI: Traumatic Brain Injury; TEH: Traumatic expansive hematoma.

# Declarations

## Ethical approval and consent to participate

The study was approved by the Makerere University School of Medicine Research Ethics Committee (SOMREC), recorded as Mak\_SOMREC-2020-38. All study methods were carried out in conformity with Ugandan laws and regulations, the Good Clinical Practice guidelines, and the Helsinki Declaration.

## Informed consent

Prior to surgery, informed consent was gained from patients with a stable high-level of consciousness and not in pain, and the research assistants then gave them an interviewer-guided questionnaire. For a critically ill patient, the informed consent was sought from the next of kin. A written signed informed consent from the patient or their next of kin was obtained from each participant.

## Consent for publication

Not applicable.

## Competing interests

All authors have declared no conflict of interest.

## Availability of data and material

Datasets used in the current study are available from the corresponding author on reasonable request.

## Funding

There is no funding to be declared.

## Authors' contributions

Larrey Kasereka Kamabu: involved in study design and conception. Godfrey S. Bbosa assisted in drafting the article. Louange Maha Kataka did data acquisition, statistical analysis and interpretation. Moses Galukande, Godfrey S. Bbosa, Joel Kiryabwire, Hervé Monka Lekuya, Juliet Nalwanga Sekabunga,

Louange Maha Kataka, Doomwin Oscar Deogratus Obiga involved in critical revising the article. All authors agreed on the final manuscript.

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## Figures

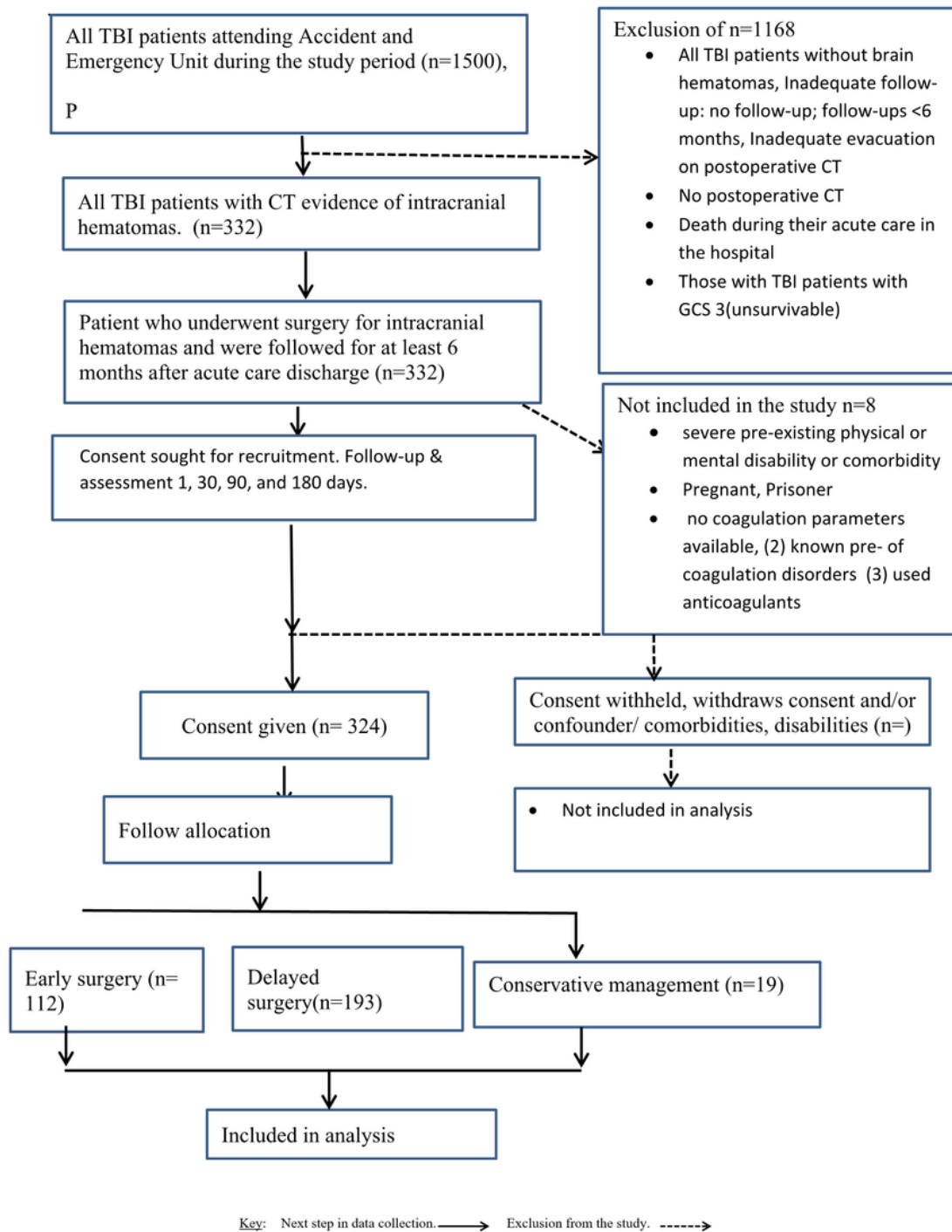
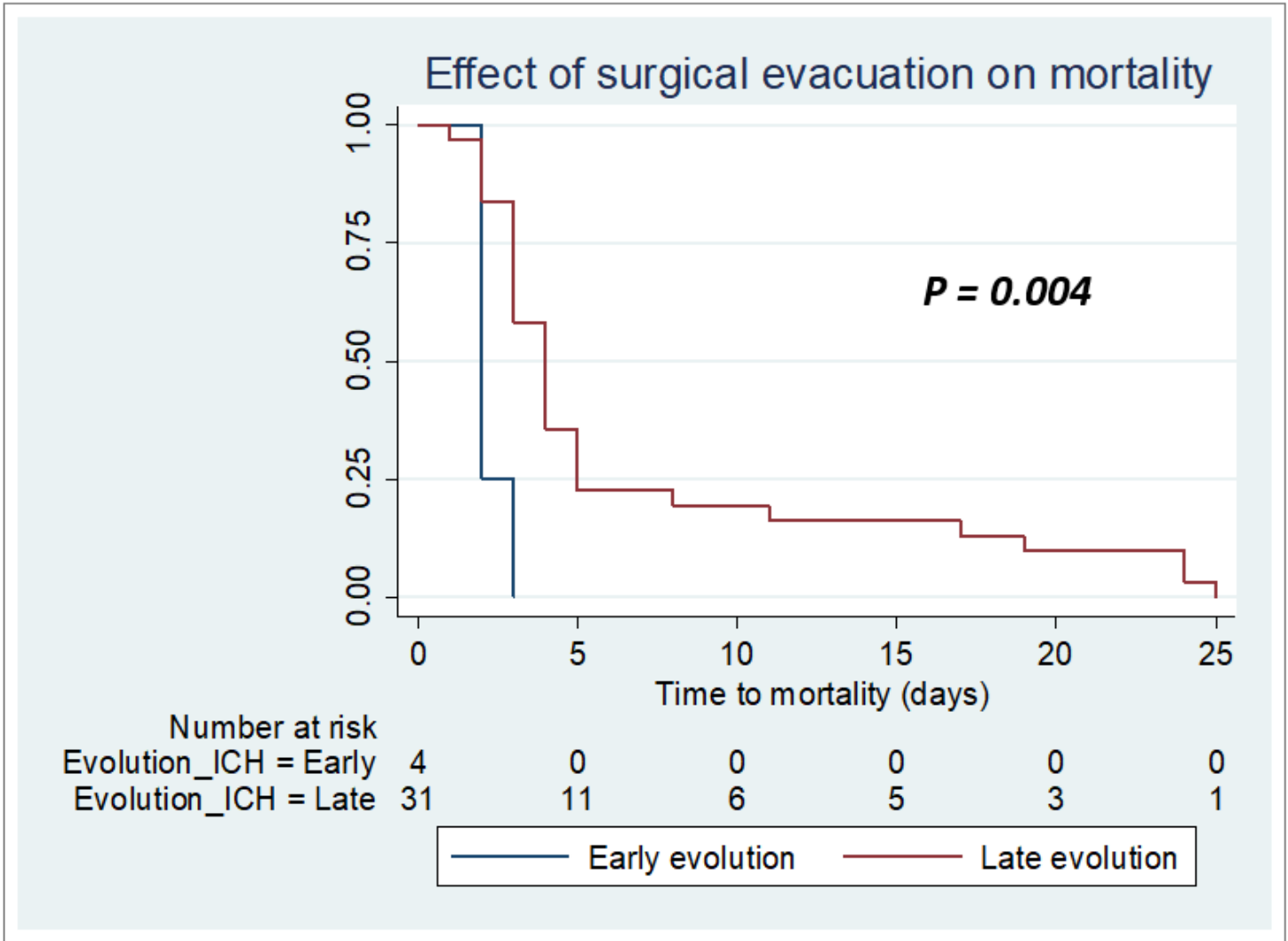


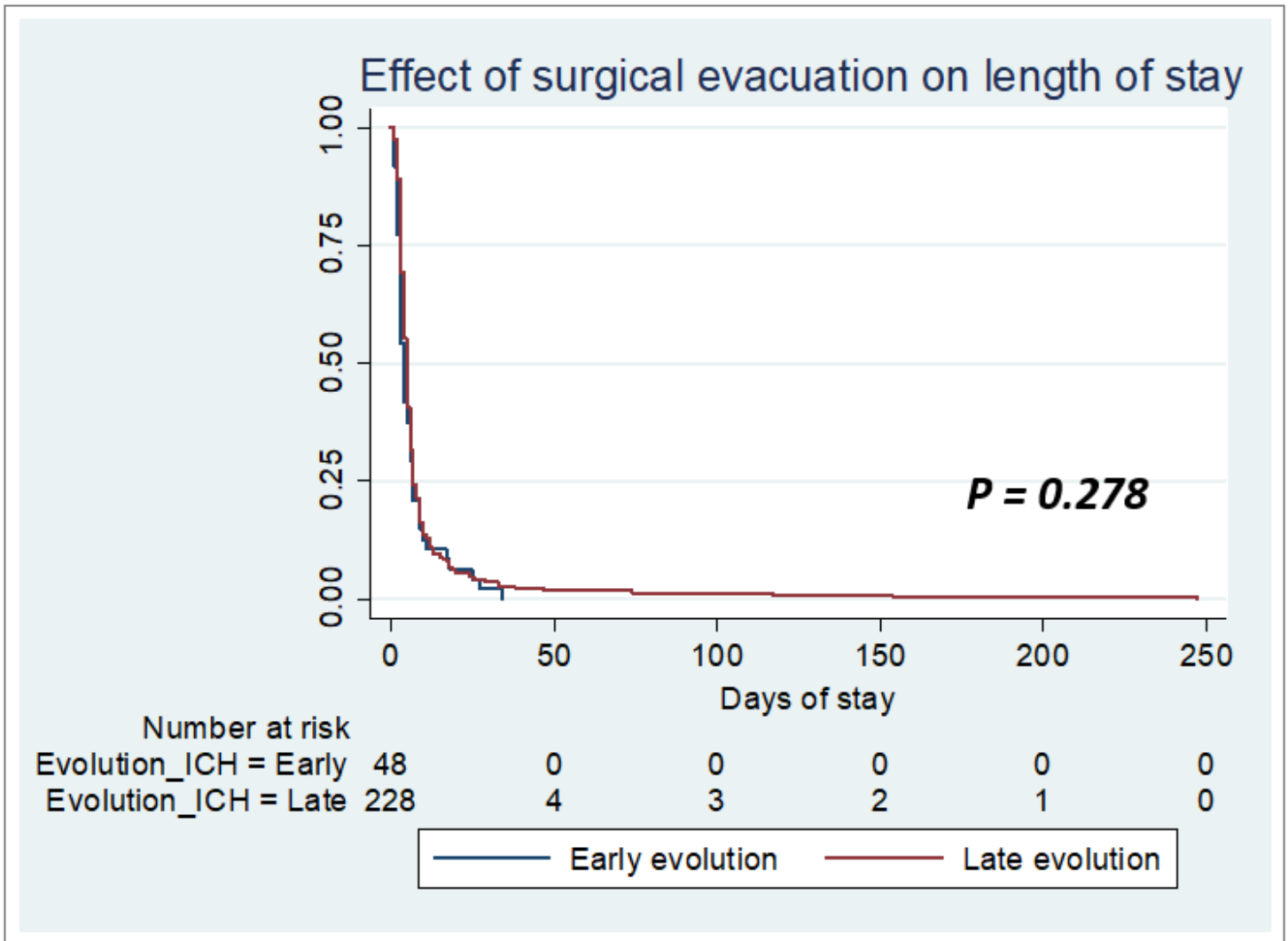
Figure 1

Flow chart of patient's recruitment



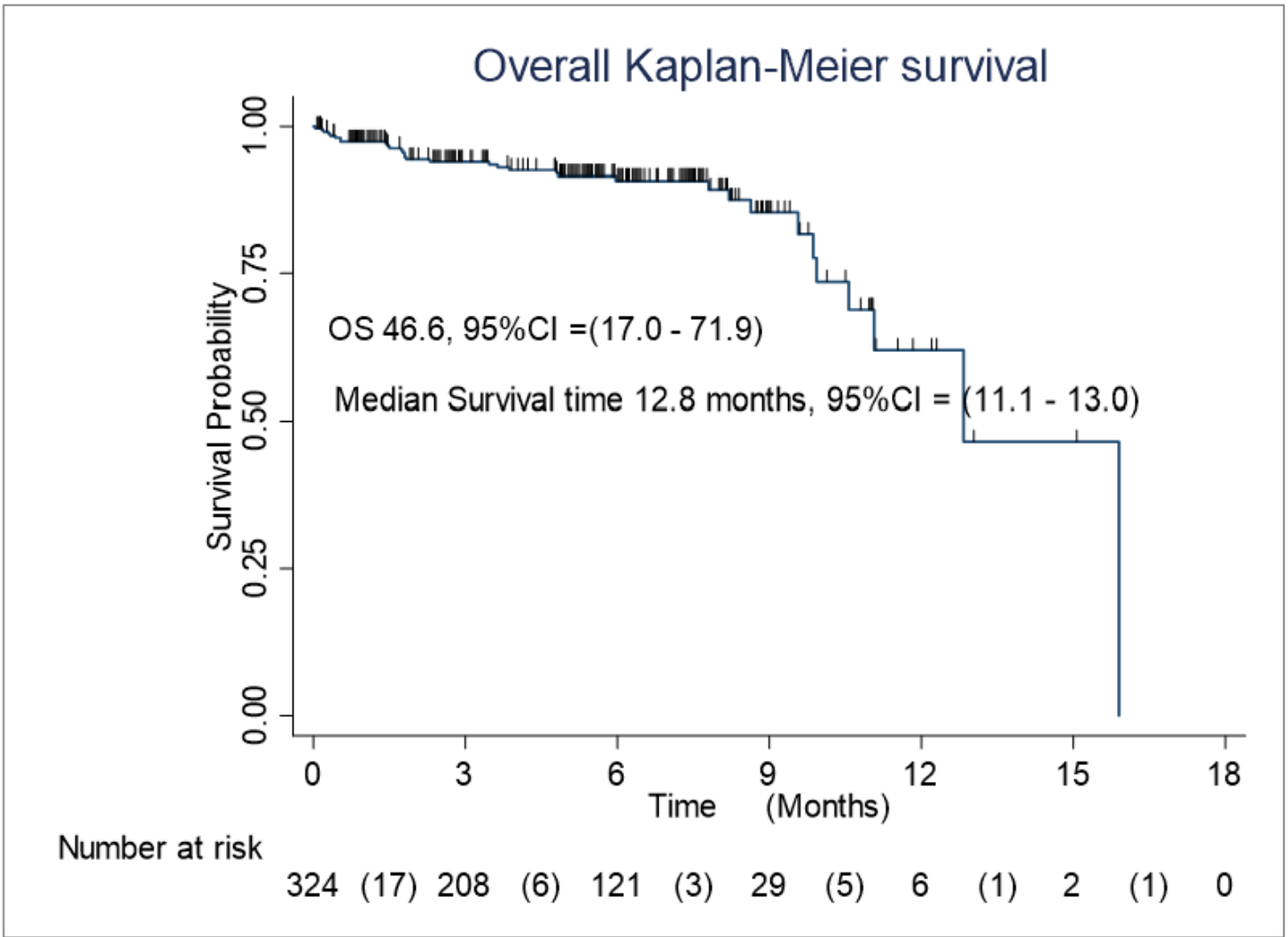
**Figure 2**

Effect of early and late surgical evacuation on mortality



**Figure 3**

Effect of surgical evacuation on Length of hospital stay



**Figure 4**

Overall Survival trends of TBI patients with expansive intracranial hematomas after surgery

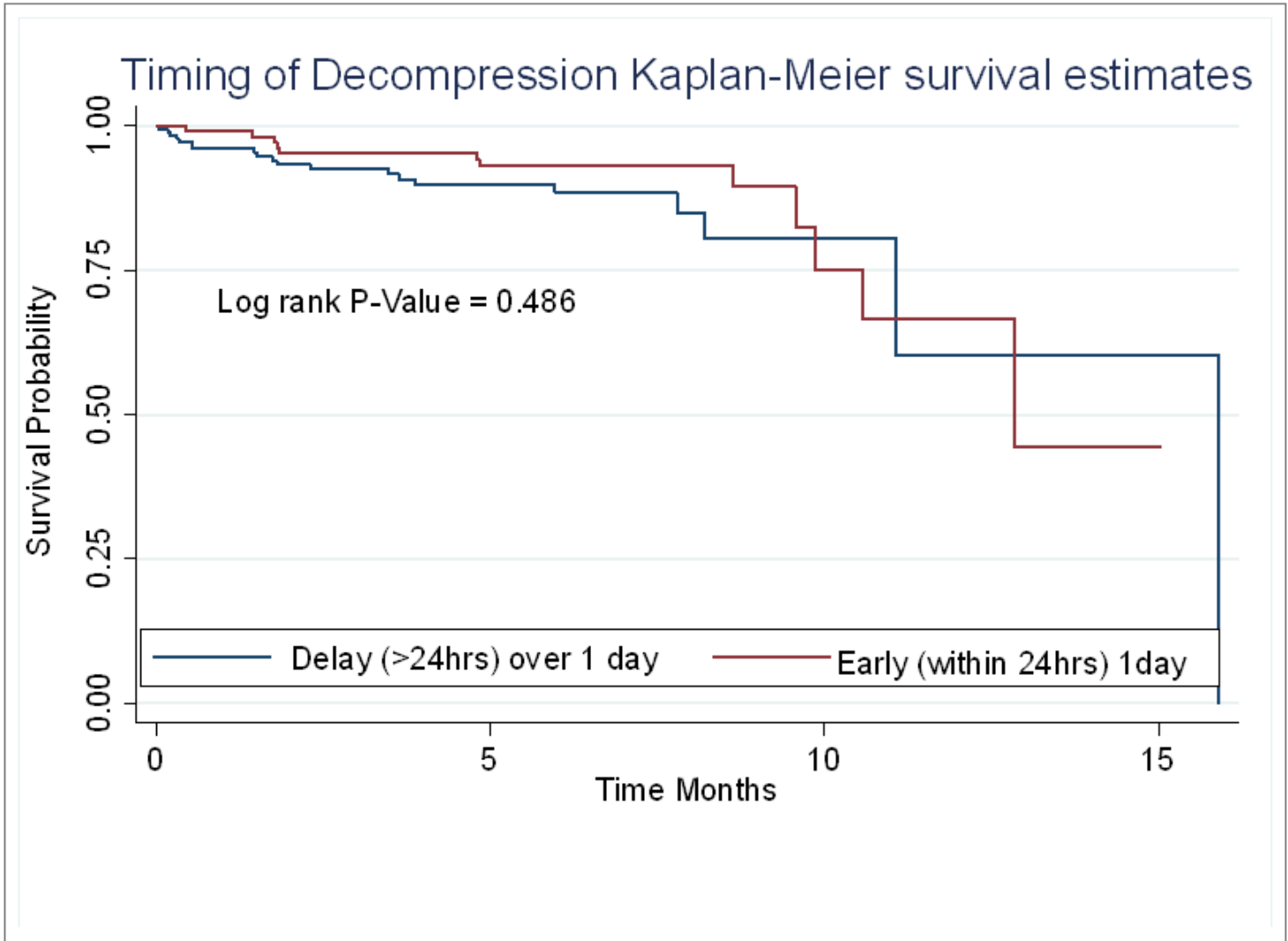


Figure 5

Effect of surgical timing on survival

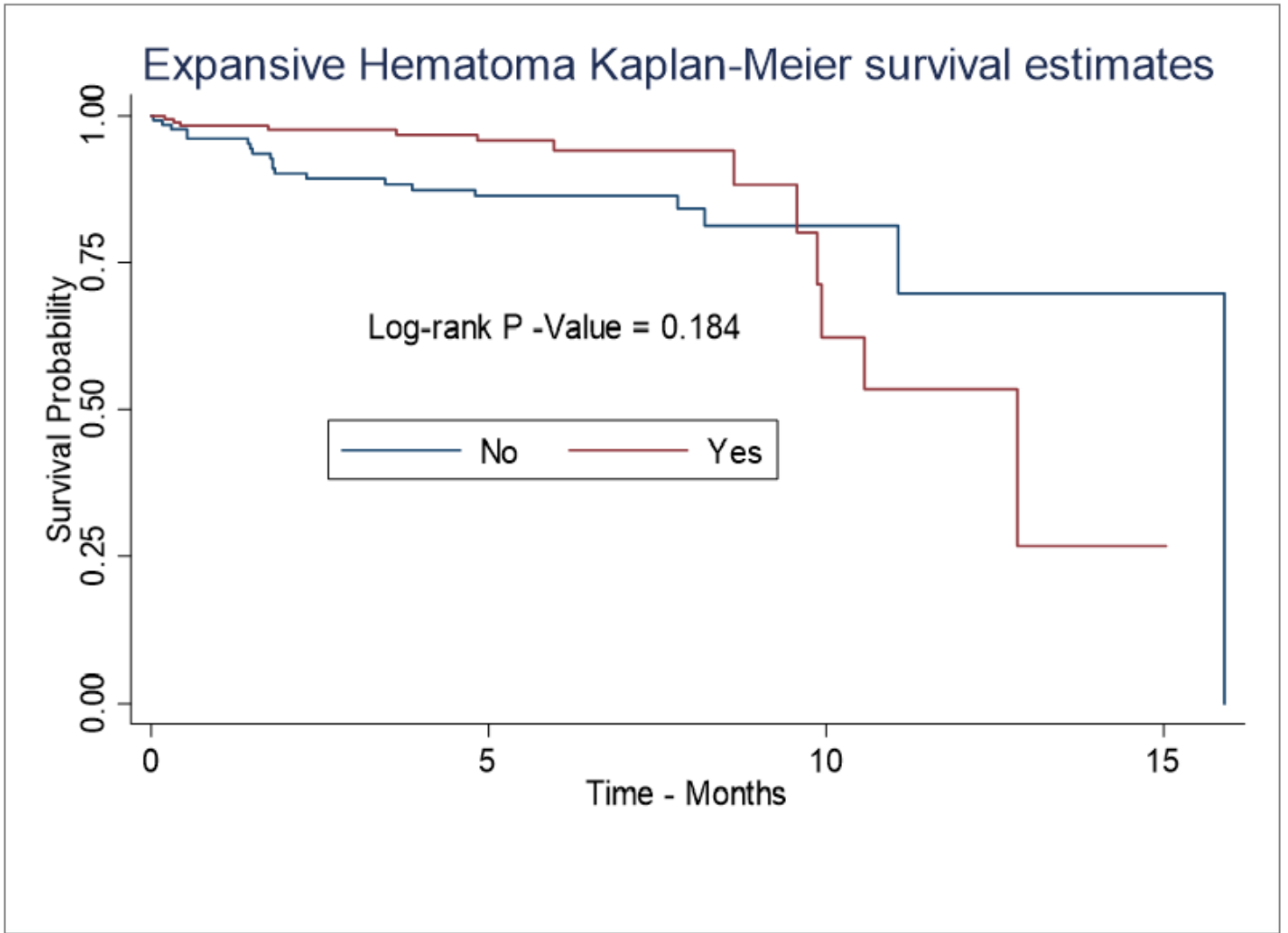
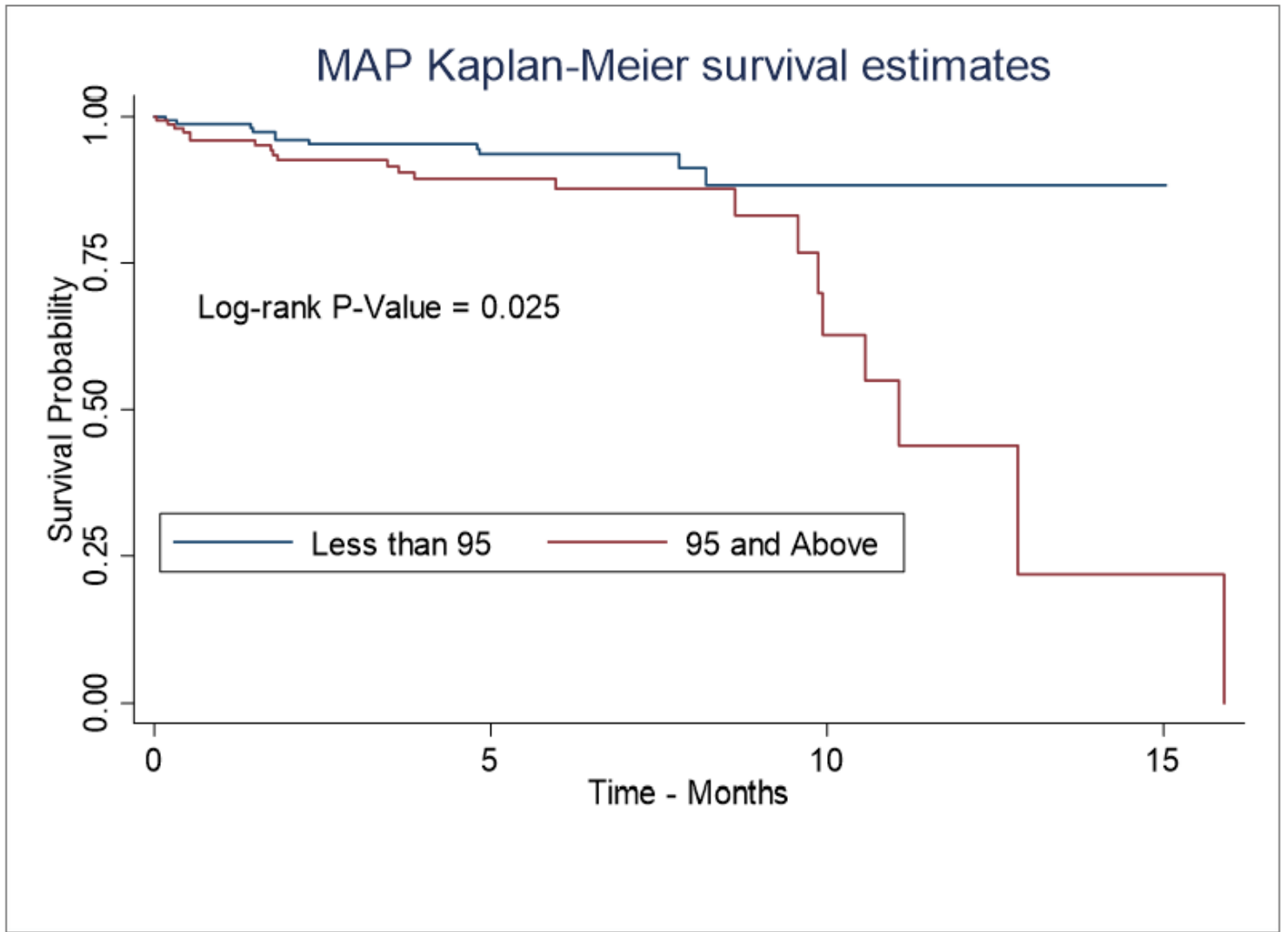


Figure 6

The overall survival (OS) of patients with EIH after surgery





**Figure 7**

Effect of mean arterial pressure on survival of patients with EIH

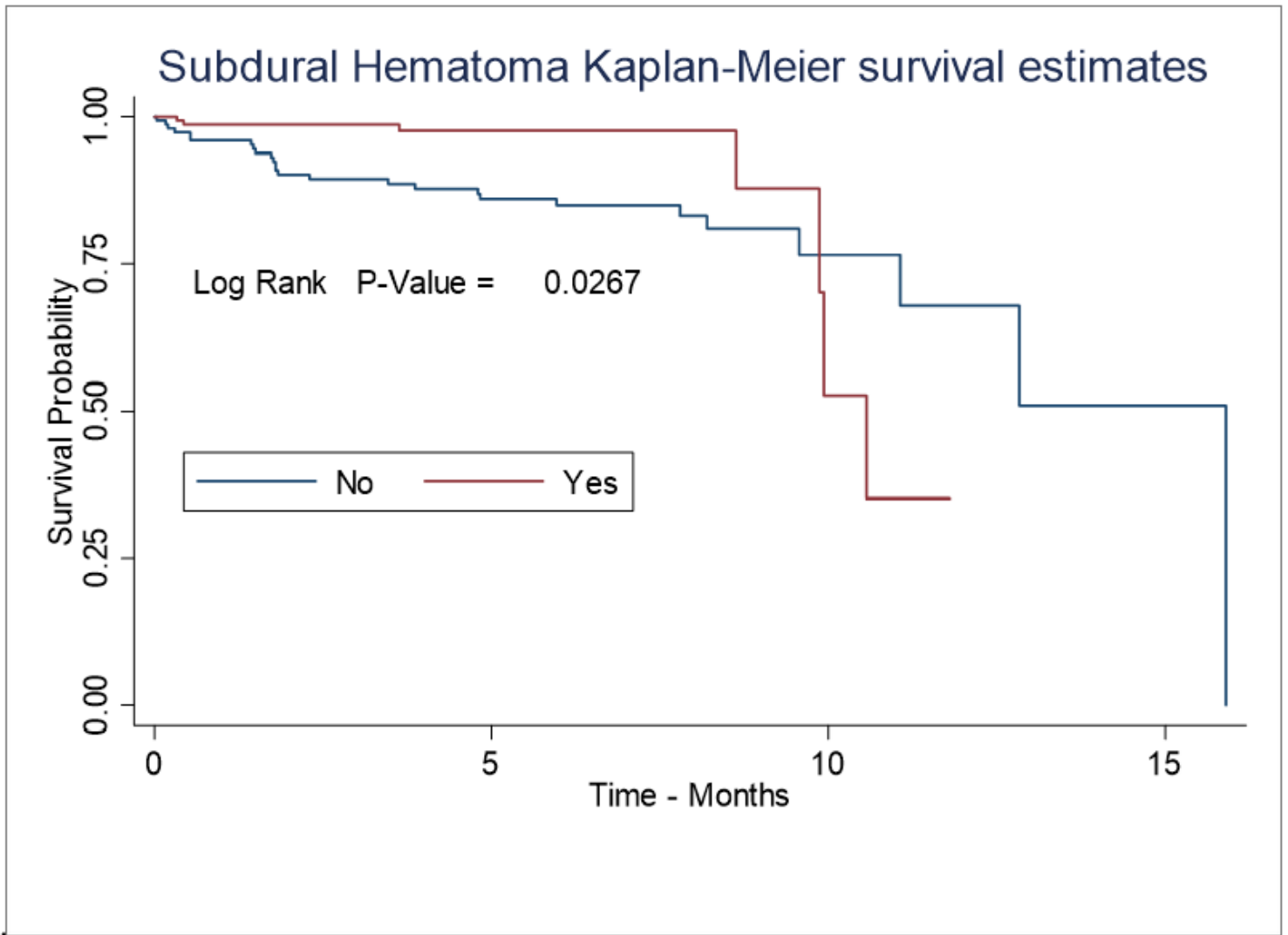


Figure 8

Survival of expansive hematoma patients with acute subdural hematoma

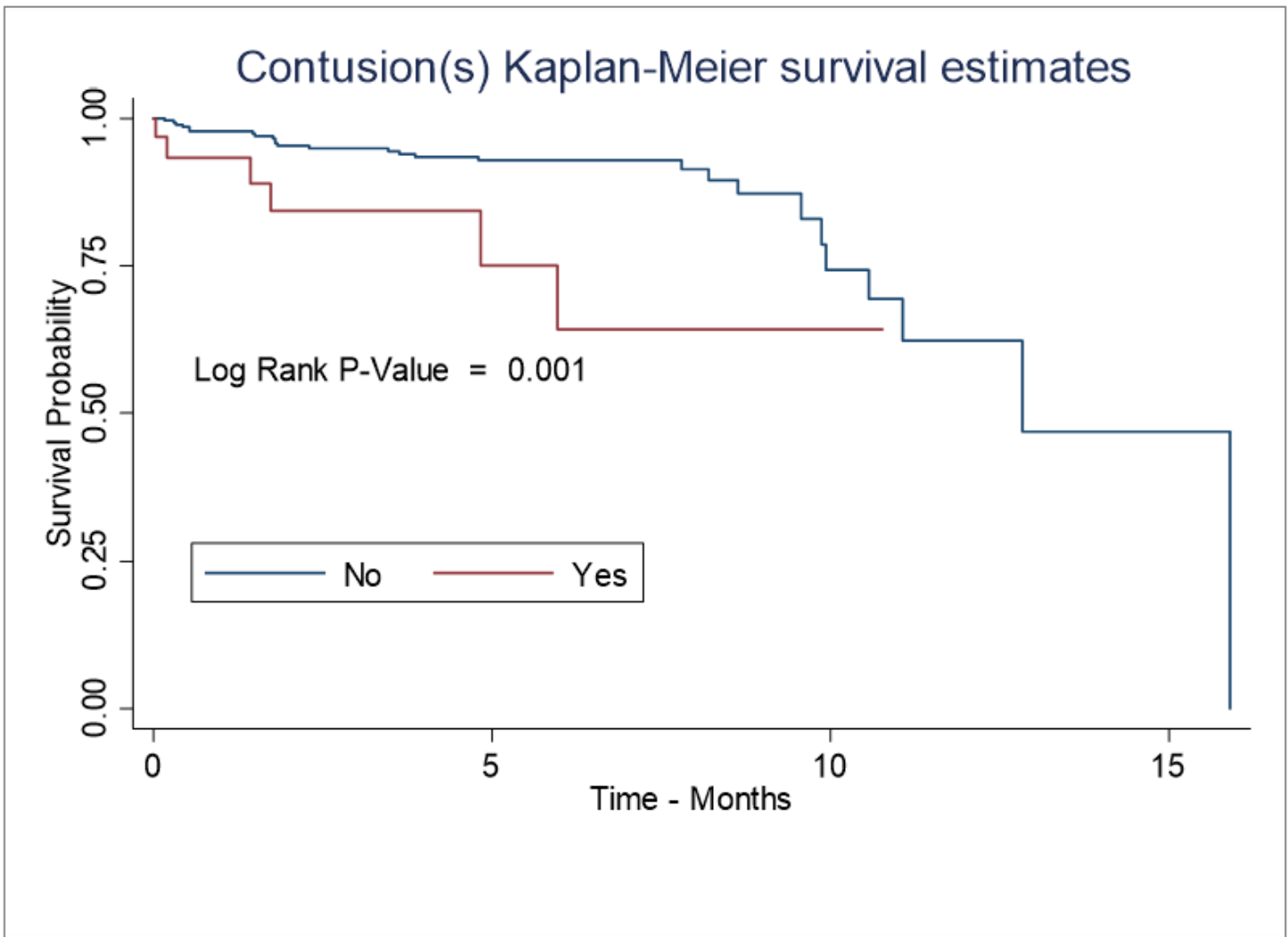


Figure 9

Survival of expansive hematoma patients with contusion

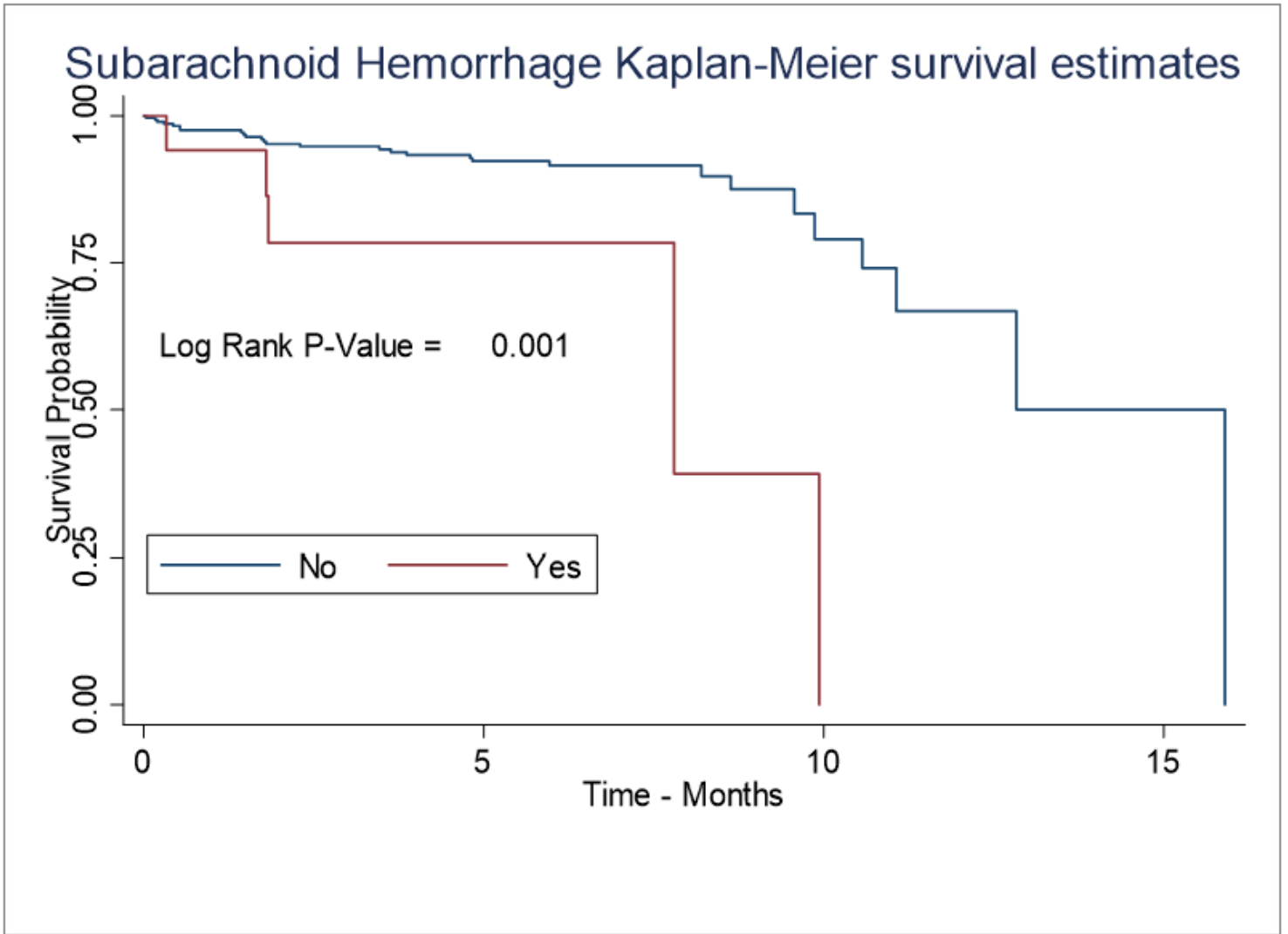


Figure 10

Survival of expansive hematoma patients with subarachnoid hemorrhage

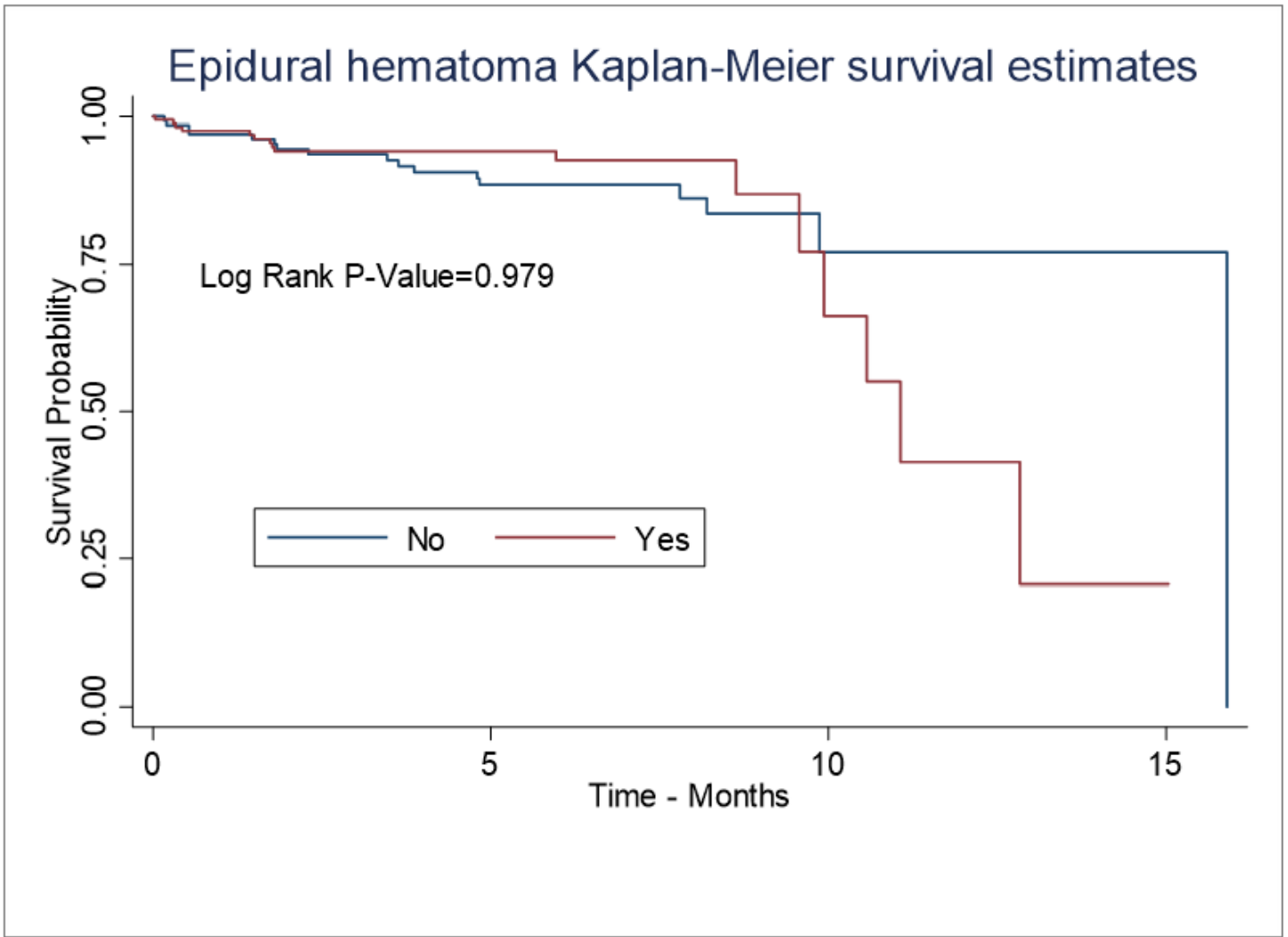


Figure 11

Survival of expansive hematoma patients with epidural hematoma.

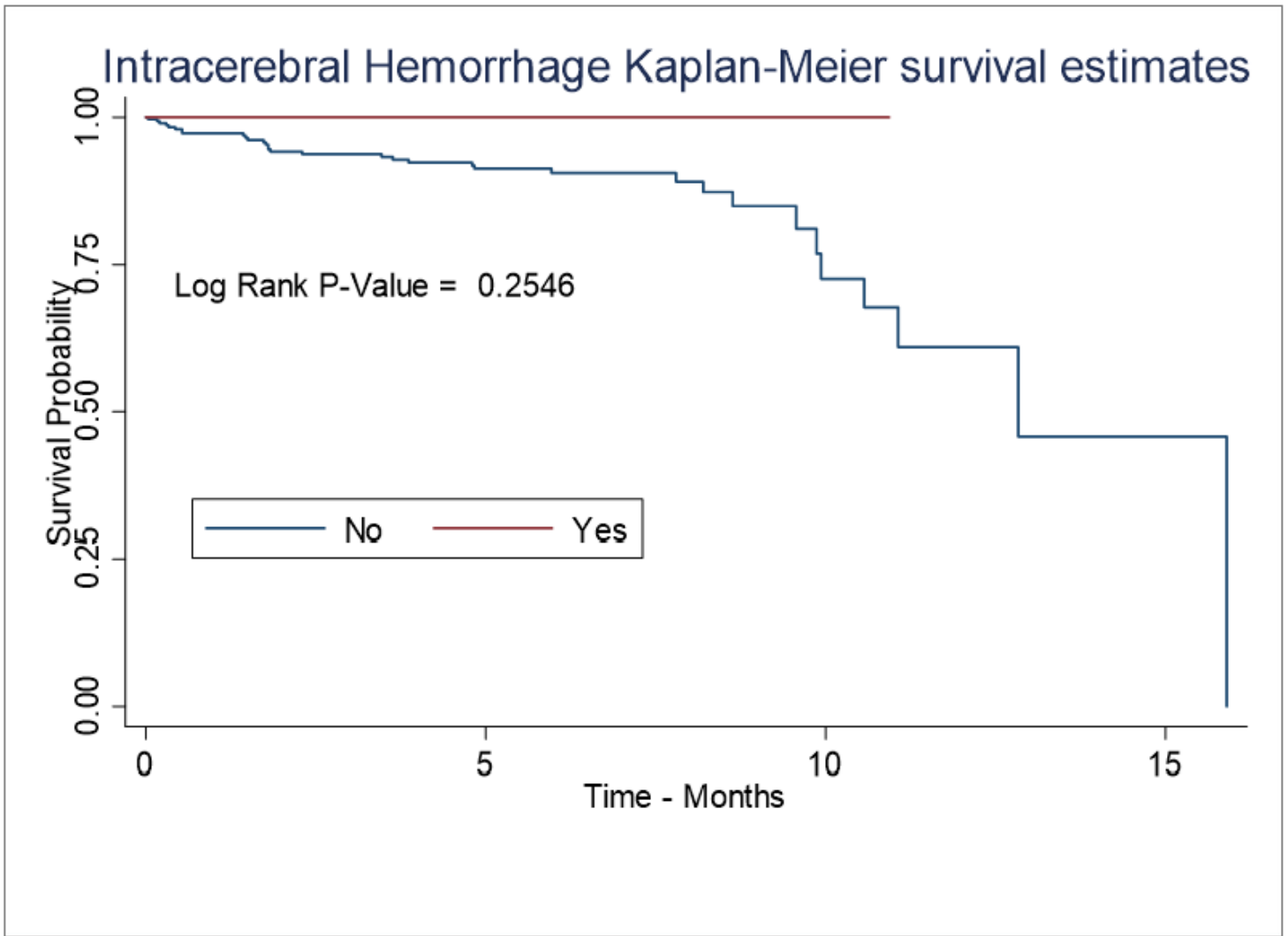


Figure 12

Survival of expansive hematoma patients with intracerebral hematoma

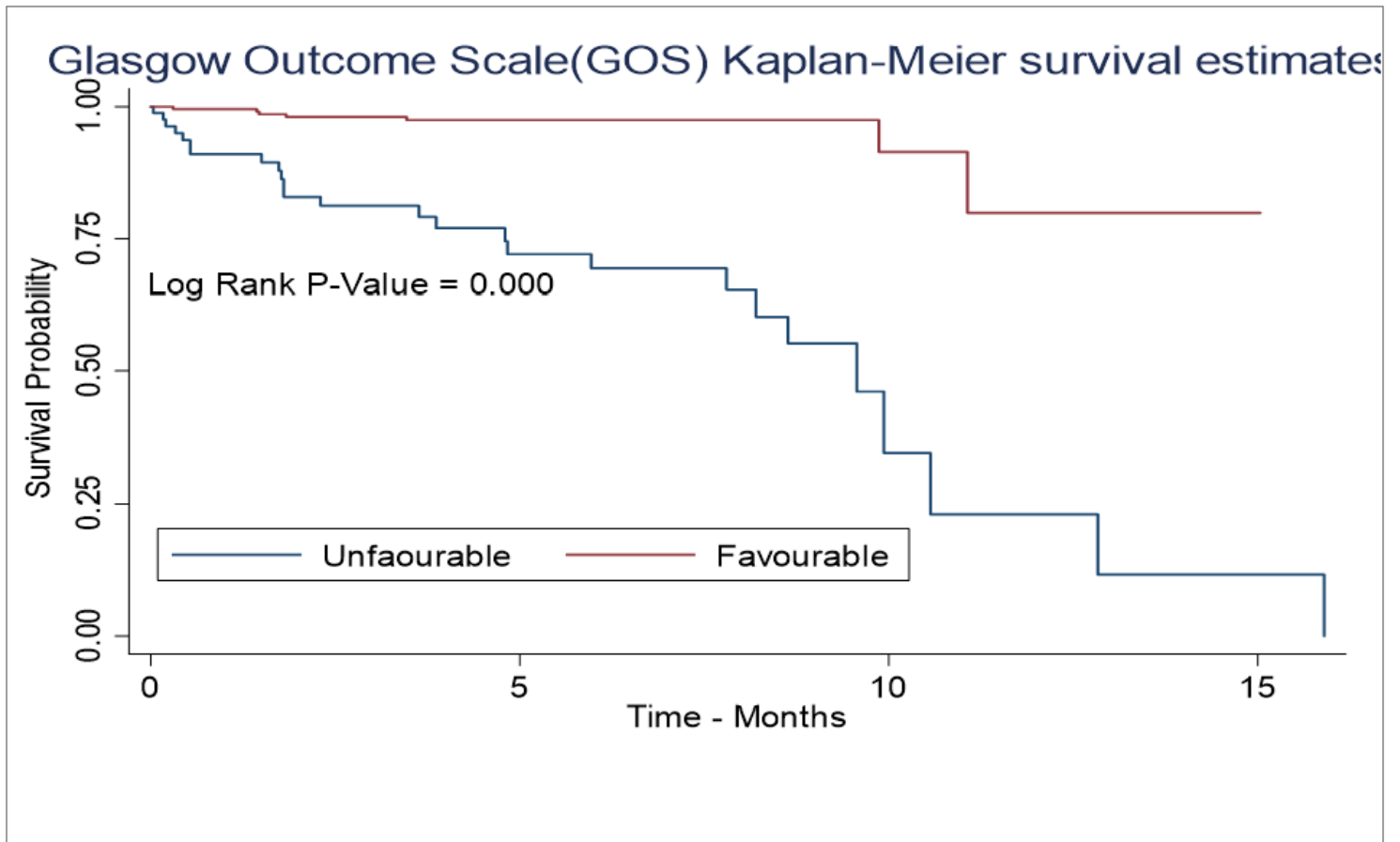
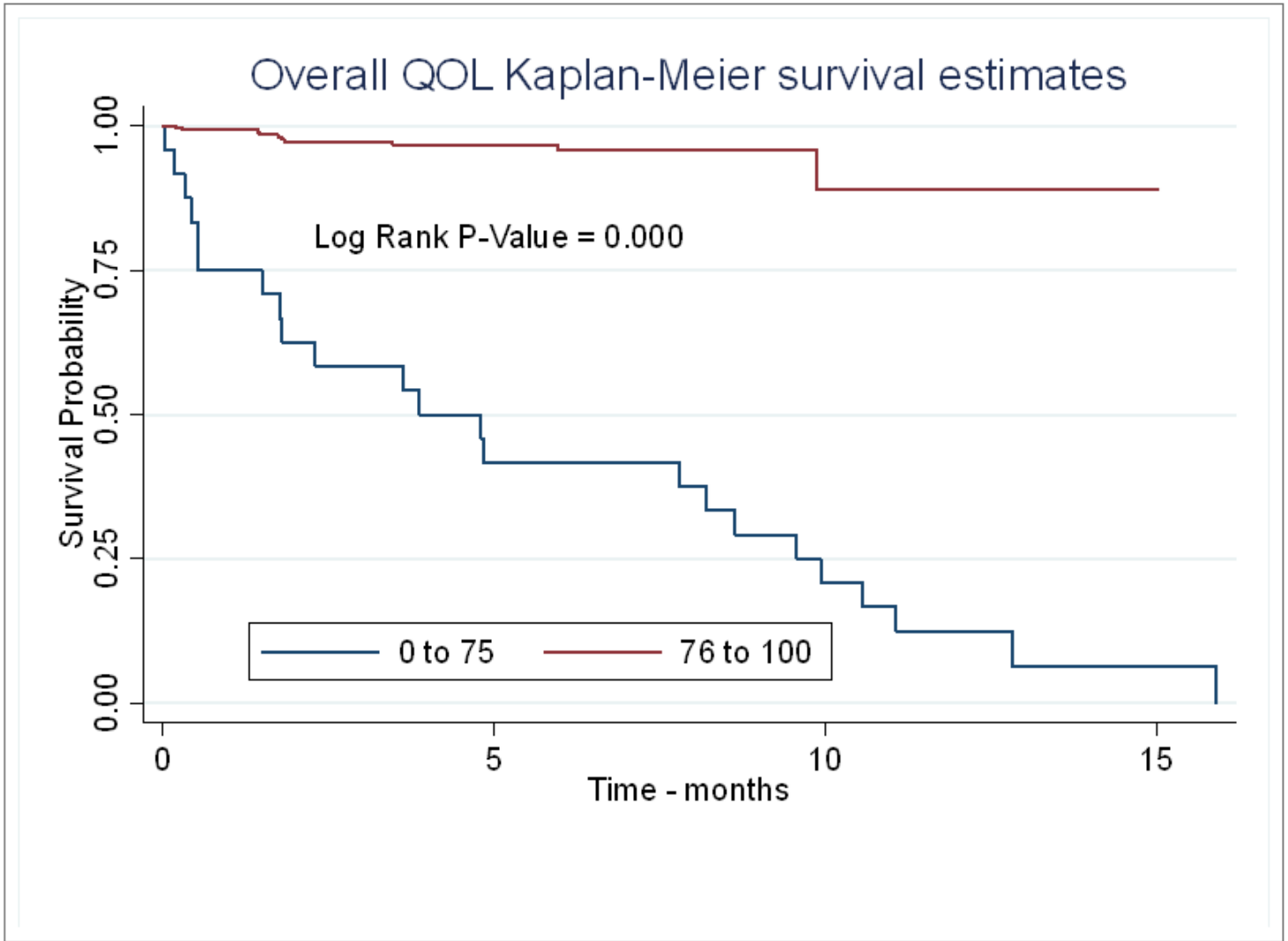


Figure 13

Effect of functional outcome on survival of expansive hematoma



**Figure 14**

Effect of health related quality of life on survival of expansive hematoma