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Impact of subventricular zone interaction on clinical outcomes in patients with intracerebral hematoma

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ABSTRACT

Aim: To investigate the impact of subventricular zone (SVZ) interaction on the clinical outcomes of patients undergoing surgery for intracerebral hematoma (ICH). Specifically, we aimed to analyze radiological parameters and assess whether access of the hematoma to the SVZ affects clinical outcomes and long-term clinical course.

Methods: We conducted a retrospective analysis of patients who underwent surgery for ICH, dividing them into two groups based on SVZ involvement. Preoperative clinical evaluations, including Glasgow Coma Scale (GCS) assessments, and preoperative cranial tomographies were performed. The study assessed hematoma localizations, volumes, and extension to the SVZ. Postoperative outcomes, including reoperation rates, Glasgow Outcome Scores (GOS) at 6 months, and hydrocephalus development, were monitored.

Results: Out of 121 patients, 40 had SVZ involvement while 81 did not. There were no significant differences in demographic characteristics between the groups. However, significant differences were observed in hematoma locations, volumes, midline shifts, and development of hydrocephalus between patients with and without SVZ involvement. At 6 months, patients with SVZ involvement had significantly different GOS scores compared to those without SVZ involvement.

Conclusions: Our study suggests that SVZ involvement plays a crucial role in the prognosis of patients with ICH. Patients with hematoma reaching the SVZ had different clinical outcomes, highlighting the potential significance of this brain region in brain injury repair mechanisms. These findings emphasize the need for further research into the role of the SVZ in recovery processes after brain injury and the development of innovative treatment strategies for ICH.

Key words: Intracerebral hematoma, subventricular zone, clinical outcome, neurological complications, surgical intervention.

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1. Introduction

Intracerebral hematomas (ICH) are a type of acute neurological emergency that can have serious consequences. They can compress the tissues around the hemorrhages that form inside the brain, causing edema, brain compression, and severe neurological damage [1]. Hematomas can

cause brain damage and complications that can affect long-term clinical outcomes in patients [2]. The subventricular zone (SVZ) is a structure located along the lateral walls of the brain ventricles and contains various cellular components, including neural stem cells. The SVZ is capable of self-renewal into adulthood and has been associated with neurogenesis, making it an important region in the brain's natural regeneration process [3].

The SVZ has been identified as a potential therapeutic target for brain injuries and diseases due to its proximity to the brain's ventricles and the presence of neural stem cells [4]. These cells can aid in the repair of damaged brain tissue and promote nerve cell regeneration [5].

The interaction between cerebral hemorrhages, such as ICH, and SVZ and its effects on the clinical course in patients are not yet fully understood. Therefore, it is important to investigate the role and potential of SVZ in developing innovative approaches to the treatment of brain injuries. Future research and treatment strategies should take into account the potential of SVZ in the treatment of brain injuries and diseases. Understanding the effects of SVZ access on the clinical course of patients with ICH may aid in the development of novel therapeutic approaches to reduce neurological complications and promote brain injury repair.

This study examined radiological parameters to investigate the effects of hematoma access to the SVZ on the clinical course of patients undergoing surgery for ICH. The study aimed to determine the potential impact of SVZ interaction on the treatment and clinical outcomes of patients with ICH. This study is important due to the limited number of similar studies in the literature and the uncertainty surrounding the effect of SVZ interaction on patient outcomes. The data obtained will contribute to understanding changes in the long-term clinical course of patients and improving treatment strategies.

The study results may aid in developing more effective and personalized approaches to treating and following up with patients who have ICH. In addition, a more comprehensive understanding of the impact of SVZ interaction on clinical outcomes may facilitate the identification of new treatment strategies. This study aims to investigate the relationship between SVZ interaction and clinical course in patients with ICH. We investigated whether access of the hematoma to the SVZ affects clinical outcomes and long-term clinical course.

2. Materials and metods

2.1. Study design: This study aimed to analyze radiologic parameters of patients who underwent surgery for ICH. Patients were divided into two groups based on whether the hematoma reached the SVZ. Preoperative clinical evaluations were performed using the Glasgow Coma Scale (GCS). Preoperative cranial tomographs were examined to calculate midline shift, hematoma localizations, and volumes. The study also assessed whether the hematoma extended to the SVZ using preoperative tomography images. Postoperative status was monitored to record any reoperations due to hematoma. Glasgow Outcome Scores (GOS) were evaluated after 6 months, and the development of hydrocephalus post-hemorrhage was analyzed. Long-term clinical outcomes were compared with SVZ involvement.

2.2. Patient selection

Inclusion criteria:

- Patients diagnosed with ICH who underwent surgery and
- Patients who had a preoperative cranial tomography to assess hematoma involvement with the SVZ.

- Patients clinically evaluated using the GCS.
- Availability of images for calculating hematoma localizations and volumes.
- Adequate data documenting the postoperative follow-up process.
- Patients whose GOS and hydrocephalus development were assessed at the 6-month follow-up.

Exclusion criteria:

- Patients unsuitable for hematoma localization due to the spread of hematoma to other regions.
- Patients in whom the hematoma could not be clearly identified on preoperative images.
- Cases with insufficient data retrieval due to missing patient files.
- Cases with unclear results due to additional neurological or systemic complications were excluded.

2.3. GOS consists of five different categories:

1. Death: The worst outcome category. The patient could not be successfully rescued.

2. Vegetative state: The patient is in a semi-awake state and responds minimally to environmental stimuli. Loss of consciousness persists.

3. Severe disability: The patient may be dependent on life support devices and unable to carry out daily activities. May need specialized care.

4. Moderate disability: The patient can carry out activities of daily living but has some significant limitations.

5. Good recovery: The patient is almost completely back to normal and can carry out activities of daily living independently.

2.4. Ethical approval

The study was approved ethically by non-interventional ethics committee of Istanbul Medipol University (date: 2024/02/29 – No: 295).

2.5. Statistical analysis

The study's statistical analysis primarily consists of descriptive statistics of the patients' demographic characteristics, such as age, gender, and other variables. This includes mean, standard deviation, median, and frequency distributions. Then, comparisons were made between patients who reached the SVZ and those who did not, considering GCS, presence of midline shift, hematoma localization, hematoma volumes (6), and other variables. Appropriate nonparametric tests were used to determine significance in the group comparisons. Additionally, Pearson or Spearman correlation analyses were performed to evaluate the relationships between variables, such as hematoma volume, localization, and SVZ interaction.

During the postoperative follow-up period, the groups were compared in terms of re-operation due to hematoma, GOS at the end of the 6th month, and development of hydrocephalus. Appropriate tests and analyses were used to perform these comparisons. The statistical significance level was generally accepted as $p < 0.05$, and p values were reported. Finally, multiple regression analyses were conducted to evaluate the association between SVZ interaction and long-term clinical outcomes.

3. Results

Out of the 121 patients who underwent surgery for ICH, 51.2% (62) were women and 48.8% (59) were men. Among the ICH, 40 included SVZ while 81 did not. There was no statistically significant difference in gender between those with and without SVZ (p=0.17). The age range of the patients was between 55 and 87 years with a mean age of 74.9 years. There

Table 1. Distribution of data according to subventricular zone.

Parameters		Total (n=121)	SVZ involvement (n=40)	No SVZ involvement (n=81)	
		n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	*p*
Gender	Female	62 (51.2%)	17 (14.0%)	45 (37.2%)	*0.17*
	Male	59 (48.8%)	23 (19.0%)	36 (29.8%)	
Age		74.9 ± 8.26 [55 - 87]	75.5 ±1.29 [62 - 87]	74.6 ±0.93 [55 - 87]	*0.59*
GCS		8.5 ± 2.46 [3 - 12]	8.28 ± 0.44 [3 - 12]	8.62 ± 0.26 [3 - 12]	*0.47*
Location	Temporal	35 (28.9%)	14 (11.6%)	21 (17.4%)	*<0.05**
	Parietal	28 (23.1%)	8 (6.6%)	20 (16.5%)	
	Frontal	23 (19.0%)	14 (11.6%)	9 (7.4%)	
	Occipital	35 (28.9%)	4 (3.3%)	31 (25.6%)	
Reoperation for hematoma	Yes	6 (5.0%)	3 (2.5%)	3 (2.5%)	*0.37*
	No	115 (95.0%)	37 (30.6%)	78 (64.5%)	
6.month GOS	1	9 (7.4%)	4 (3.3%)	5 (4.1%)	*<0.05**
	2	14 (11.6%)	11 (9.1%)	3 (2.5%)	
	3	57 (47.1%)	22 (18.2%)	35 (28.9%)	
	4	34 (28.1%)	2 (1.7%)	32 (26.4%)	
	5	7 (5.8%)	1 (0.8%)	6 (5.0%)	
Volume of hematoma (cm^3)		37.20 ± 5.81 [30 - 50]	35.20 ± 6.10 [30 - 50]	38.20 ± 5.44 [31 - 50]	*<0.05**
Midline shift		11.6 ± 4.52 [5 - 20]	10.10 ± 4.20 [5 - 19]	12.40 ± 4.50 [5 - 20]	*<0.05**
Hydrocephalus	Yes	22 (18.2%)	15 (12.4%)	7 (5.8%)	*<0.05**
	No	99 (81.8%)	25 (20.7%)	74 (61.2%)	

GCS: Glasgow coma scal; GOS: Glasgow outcome scale; SVZ: Subventricular Zone; SD: Standart Deviation; Min: minimum; Max: maximum; p<0.05: Statistically significant.*

was no statistically significant difference in age between patients with and without SVZ (p=0.59). The GCS scores of the patients ranged from 3 to 12, with a mean of 8.5. There was no significant difference in GCS between patients with and without sub-ventricular zone (SVZ) involvement (p=0.47). Six patients (5.0%) required reoperation due to ICH, with three patients having SVZ involvement and three patients without SVZ involvement. There was no significant difference in reoperation rates between patients with and without SVZ involvement (p=0.37). Of the ICH, 35 (28.9%) were located in the temporal region, 28 (23.1%)

in the parietal region, 23 (19.0%) in the frontal region, and 35 (28.9%) in the occipital region.

There was a significant difference in the locations of hematomas with and without SVZ (p<0.05). The total volume of the ICH ranged from 30 to 50 cm^3 with a mean volume of 37.2 cm^3. The mean volume of hematomas with SVZ was 35.20 cm^3, while the mean volume of hematomas without SVZ was 38.20 cm^3. Midline shifting ranged from 5 to 20 mm in all patients, with a mean of 11.6 mm. Patients with SVZ had a mean midline shift of 10.10 mm, while those without had a mean of 12.40 mm.

There was a statistically significant difference in ICH volume and midline shift between patients with and without SVZ (p<0.05). Hydrocephalus developed in 22 (18.2%) patients, with 15 of those including SVZ and 7 not including SVZ.

There was a statistically significant difference in the development of hydrocephalus between patients with and without SVZ (p<0.05). Upon analyzing the 6th month GOS scores of the patients, it was found that 9 (7.4%) patients had a GOS score of 1, 14 (11.6%) had a score of 2, 57 (47.1%) had a score of 3, 34 (28.1%) had a score of 4, and 7 (5.8%) had a score of 5. A significant difference in GOS was observed between patients with and without SVZ (p<0.05) (Table 1).

Statistically significant differences were observed at the end of the 6th month between GOS 1-4, 2-4, and 2-5, depending on whether the ICH contained SVZ or not. Additionally, a significant difference was observed between low GOS and SVZ (p<0.05). The presence or absence of hydrocephalus also had a significant effect on the difference between GOS 2 and 4.

Table 2. Comparison of factors that may affect GOS at 6 months.

Parameters	6. Month GOS					
	1. Death (n=9)	2. Vegetative State (n=14)	3. Severe Disability (n=57)	4. Moderate Disability (n=34)	5. Good Recovery (n=7)	
	n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	n (%) / Mean ± SD [min - max]	*p*
SVZ involvement	4 (3.3%)	11 (9.1%)	22 (18.2%)	2 (1.7%)	1 (0.8%)	*<0.05**
Hydrocephalus	2 (1.7%)	6 (5.0%)	13 (10.7%)	1 (0.8%)	0 (0.0%)	*<0.05***
Reoperation for hematoma	3 (2.5%)	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	*<0.05****
Volume of Hematoma (cm3)	41.10 ± 6.97 [31-50]	37.70 ± 6.98 [30 - 50]	36.10 ± 5.57 [30 - 50]	38.50 ± 5.29 [31 - 47]	33.70 ± 1.60 [31-35]	*>0.05*
GCS	5.22 ± 3.38 [3 - 12]	7.86 ± 2.74 [4 -12]	8.67 ± 2.30 [3 - 12]	8.71 ± 1.34 [7 - 12]	11.7 ± 0.49 [11 - 12]	*<0.05#*
Midline Shift (mm)	15.7 ± 5.34 [6-20]	11.0 ± 4.57 [5-20]	10.8 ± 4.15 [5 - 19]	13.4 ± 3.56 [5 -17]	5.57 ± 1.13 [5 - 8]	*<0.05##*
Age	74.4 ± 7.50 [62 -84]	73.6 ± 8.34 [62 - 83]	76.5 ± 7.50 [62 - 87]	73.9 ± 9.21 [55 - 87]	69.9 ± 9.25 [62 - 86]	*>0.05*

: Statistical difference is due to GOS 1-4, 2-4, 2-5; **: Statistical difference is due to GOS 2-4; *: Statistical difference is due to GOS 1-3; #: Statistical difference is due to GOS 1-4, 1-5, 2-5, 3-5, 4-5; ##: Statistical difference is due to GOS 1-3, 1-5, 2-5, 3-4, 3-5, 4-5; GCS: Glasgow coma scale; GOS: Glasgow outcome scale; SVZ: Subventricular Zone; SD: Standard Deviation; Min: minimum; Max: maximum; p<0.05: Statistically significant.*

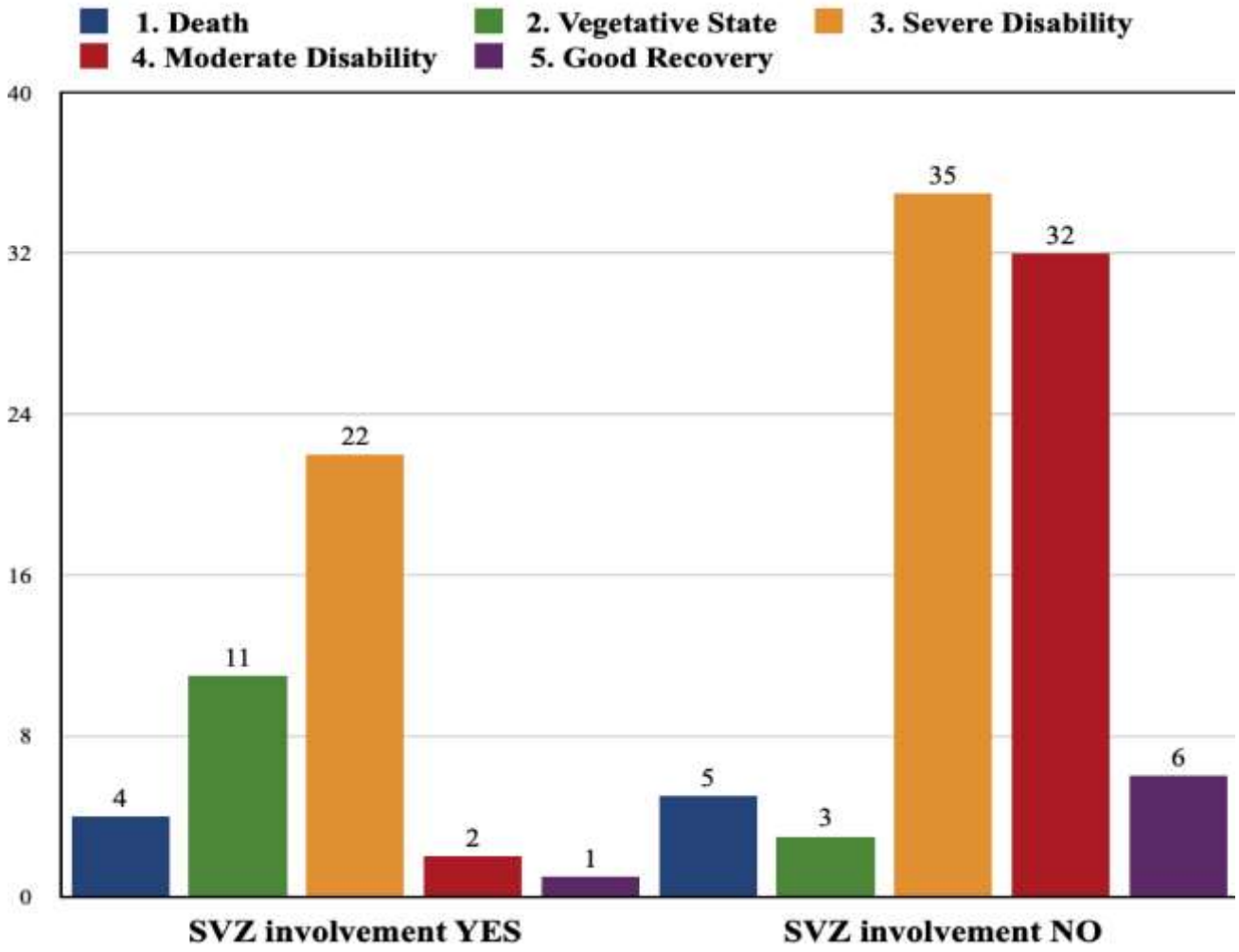

Figure 1. Distribution of 6th month GOS scores according to whether the intracerebral hematoma contains. (SVZ or not. SVZ; GOS: Glasgow outcome scale; SVZ: Subventricular Zone).

Furthermore, the presence of reoperation for hematoma significantly affected the difference between GOS 1 and GOS 3. Reoperation for hematoma has a statistically significant effect on the difference between death and severe disability ($p<0.05$). There was no statistically significant difference between ICH volume and GOS ($p>0.05$). GCS had a significant effect on the difference between GOS 1-4, 1-5, 2-5, 3-5, 4-5. There is a significant difference between those with low GCS and those with high GOS ($p<0.05$). The study found that midline shift had a significant effect on the difference between GOS scores of 1-3, 1-5, 2-5, 3-4, 3-5, and 4-5 ($p<0.05$). However, there was no significant difference between age and GOS scores ($p>0.05$) (Table 2) (Figure 1).

4. Discussion

ICHs are a medical condition that can result from various causes, such as trauma, high blood pressure, or vascular disease, and require prompt intervention. The prognosis of ICH is influenced by several factors, including the size, location, and cause of the hematoma [7]. For example, a large hematoma can impair normal brain function and lead to severe complications. The

prognosis of ICH can be influenced by various factors, including the rate of hemorrhage development, the patient's age, and general health condition.

Treatment options for ICH may vary depending on the patient's condition and the size of the hematoma [8]. In cases of small and stable hematomas, monitoring the patient and controlling bleeding with medication may be sufficient. However, in cases of large and life-threatening hematomas, surgical intervention may be necessary [9,10]. At 6 months postoperatively, our study suggests that there is no significant correlation between hematoma volume and prognosis. It is important to note that our study only included hematomas that required surgery, which are already large enough to potentially damage the brain. Furthermore, our study did not examine the impact of small-sized hematomas. It is worth noting that once a hematoma reaches the surgical nerves, its size is no longer a significant factor in prognosis.

The prognosis of ICH is influenced by various factors, including the patient's age, general health, as well as the size and location of the hematoma [11]. Early detection of small hematomas usually results in a better prognosis, while larger and life-threatening hematomas can have a worse prognosis. Furthermore, the patient's risk of complications, brain damage, and neurological sequelae can also affect the prognosis [12].

In our study, we did not find any significant impact of age and hematoma localization on the 6-month prognostic outcome. However, it is worth noting that younger patients were excluded from the study, which may have affected our ability to fully evaluate the impact of these factors. Including younger patients in future studies could provide a more comprehensive understanding of the relationship between age, hematoma localization, and prognostic outcomes. Perhaps the limited age diversity among older patients may have hindered our ability to fully clarify the issue. Therefore, it may be beneficial for future studies to include a more diverse patient population with varying age groups to comprehensively examine the effects of age on prognostic outcomes. This data could potentially provide a better understanding of the impact of age and hematoma localization on prognostic outcomes.

The SVZ is situated adjacent to the lateral ventricles of the brain and is home to cells that play vital roles in brain development and regeneration [13]. Neural stem cells located in this region are responsible for the generation of new neurons and glial cells during brain development. Furthermore, the activation of neural stem cells in this region is also crucial for the repair and regeneration of brain damage [14]. During brain development, it has been observed that neural stem cells in the SVZ tend to proliferate and differentiate into neurons and glial cells in different parts of the brain under the influence of various signals. This process is considered to be critical for brain development and maturation. Additionally, it has been noted that neural stem cells in the SVZ can be activated after brain damage to form new neurons and repair the damaged area [15].

Damage to the brain, such as trauma, stroke, or neurological diseases, has been found to activate and regenerate neural stem cells in the SVZ. These cells have the potential to repair brain damage and replace lost neurons with new ones, which is crucial for restoring neurological functions [16]. Neural stem cells in the SVZ have been shown to play a significant role in brain development and regeneration. The SVZ and its neural stem cells play a crucial role in the formation of new neurons and glial cells, as well as in repairing brain damage [17]. The SVZ and its neural stem cells play a crucial role in the

formation of new neurons and glial cells, as well as in repairing brain damage. Therefore, studying this area is of great importance for researching brain injuries and regeneration [18]. Additionally, information regarding the status of cells in the SVZ in adult humans is readily available. It has been observed that neural stem cells are present in the SVZ of adult individuals and have the potential to contribute to brain regeneration. However, it is worth noting that these cells tend to lose their activity and reproductive capacity as individuals age, but can be reactivated under certain conditions [19]. In adults, it is common for neural stem cells in the SVZ to remain in a quiescent state, while still retaining the potential to respond to environmental stimuli. However, certain conditions such as brain injury, trauma, or neurological diseases can activate these cells, allowing them to repopulate, differentiate, and repair the damaged brain region [20].

The relationship between the SVZ and stroke is often associated with the regeneration process that follows stroke and the repair of brain damage. According to several studies, neural stem cells located in the SVZ may play a crucial role in the repair and regeneration of brain damage after stroke, actively contributing to this process [21,22].

Our research has found that there is a notable difference in prognostic conditions assessed at the end of the sixth month, particularly in cases where hematomas have reached and affected the SVZ (SVZ). Specifically, we have observed that SVZ involvement has a significant impact on the outcome of patients, differentiating those who have ended up in a vegetative state or passed away from those who have had a good recovery and are less disabled. The clinical evidence suggests that the SVZ may have an important role in brain repair mechanisms. It appears that the SVZ's impact on this critical brain region could significantly affect patients' prognosis if hematomas reach this area. These findings emphasize the need for further research into the SVZ's role in recovery processes after brain injury. Further studies could potentially aid in comprehending the role of SVZ in the mechanisms of recovery after brain injury and in developing novel therapeutic approaches. Therefore, it is important to continue focusing research on the importance of SVZ in the effects of hematomas and prognosis after brain injury.

4.1. Conclusion

In conclusion, our study suggests that subventricular zone (SVZ) involvement may play a crucial role in the prognosis of patients with ICH. The observation that SVZ involvement differentiates between patients in a vegetative state or deceased and those with less disability and good recovery highlights the potential significance of this brain region in brain repair mechanisms. Further research into the role of the SVZ in recovery processes after brain injury is important for developing innovative treatment strategies. By understanding the impact of SVZ access on the clinical course of patients with ICH, we can potentially improve neurological outcomes and promote brain injury repair. In conclusion, our study suggests that there is a need for additional research to fully understand the role of the SVZ in addressing the effects of hematomas and predicting outcomes after brain injury.

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