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J.D. Banjarnahor^{1,2}, R.H. Dahlan^{1,2,3}, S.E. Ompusunggu^{1,2,3}

¹ Hasan Sadikin General Hospital, Bandung, Indonesia

² Universitas Padjadjaran, Bandung, Indonesia

³ RFS Spine Care, Bandung, Indonesia

THE EFFECT OF TIME INTERVAL TO SURGERY ON THE CLINICAL OUTCOME OF PATIENTS WITH INTRAMEDULLARY TUMOR AT HASAN SADIKIN GENERAL HOSPITAL

Objective: the authors analysed the outcome of intramedullary spinal cord tumor surgery, focusing on the preoperative & postoperative neurological status and influence of time interval on clinical outcome of surgery.

Methods: retrospective analysis of medical records of 25 intramedullary tumour patients, operated at our institute between Jan 2012 – Jan 2018 was done. Pre – and postoperative neurological status was determined. Ambulatory status were evaluated using the modified McCormick Scale (MMS).

Results: 44% of the patients were in 41-60 years of age group (age range, 18-80 years; mean age 37 years). Region most commonly affected was thoracic (48%). The preoperative McCormick grade was I in 0 (0%), II in 2 (8%), III in 6 (24%), IV in 10 (40%), and V in 7 (28%) patients. Histologically 60% of the lesions were ependymomas. Overall postoperative neurological status improved in 8 (32%) of the patients, remained unchanged in 27 (68%) of cases, and deteriorated in 0 (0%) patients.

Conclusion: better outcome correlated with good preoperative Modified McCormick Scale. Time interval for surgery does not significantly affected clinical outcome. We favor early preoperative Modified McCormick Scale as a stronger indicator to predict outcome and time to do optimal resection in IMSCT patients.

Keywords : intramedullary spinal cord tumor, Time interval, Modified McCormick Scale.

Introduction

Intramedullary Spinal Cord Tumor/IMSCT is a rare malignancy of the central nervous system (CNS), with prevalence rate at 2-4% of the overall neoplasm of CNS, and 15-20% of all spine malignancies [1-6]. In majority of the cases, ependymoma identified as the etiology, followed by astrocytoma and other neoplasm types, such as hemangioblastoma, ganglioglioma, germinoma, primary CNS lymphoma and melanoma [4, 7, 8]. Thus we can conclude that the majority of IMSCT are benign and originated from glial cells, neurons or cells of connective tissue. According to their cells of origin, these glial cell tumors can be diagnosed with astrocytoma, ependymoma, and oligodendroglioma [5, 8]. Of these three types, astrocytoma is a neoplasm that is originated from astrocytes of the spinal cord, hence tumor resection can become a technical challenge [2, 6]. Additionally, despite its less prevalence, IMSCT can also be the product of distant metastasis of other types of tumor elsewhere [1, 4].

Due to its anatomical nature, IMSCT is a malignancy that can potentially cause severe neurological

impairment, disabilities, leading to low quality of life and painful death. At the onset of the disease, the most common symptom identified in patients with IMSCT is backpain, including diffuse and/or radicular pain. Moreover, IMSCT can also cause motoric and sensoric functions, such as paresthesia, spasticity, or even muscle weakness. In some cases, contractility of visceral organs are also severely impaired, leading to inability to urinate and defecate. Thus, mortality seemed inevitable unless treatment is correctly planned and executed [1, 2, 3, 6, 7].

To date, confirmation of the diagnosis of this tumor type can only be obtained with histopathology examination. Concordantly, microsurgery is the preferred therapy to optimise tumor resection [6, 9, 10]. Despite progress in certain aspects, treatment of intramedullary tumor remained clinically challenging for spine practitioners as the available choices of treatment are very limited. Thus, a consensus on the standardized treatment for intramedullary tumor are yet to be achieved [1, 2, 7].

Nevertheless, some authors have proposed strategies to be adapted as a standard treatment for intra-

medullary tumors. Despite existing disagreements, all agreed that in order to obtain optimum post-operative functional results, an early diagnosis and treatment, including tumor resection, is key [2, 5, 7]. Ideally, tumor resection of this tumor type should always be concluded in a total removal of the tumor tissue, hence possibility for future recurrences can be minimized and long term survival rates can be expected. Unfortunately, this has not always been doable [1-7].

One way to increase the possibility to be able to remove the tumor tissue totally is to confirm the diagnosis as early as possible [1, 8]. Moreover, some authors have also suggested that interval of surgery, pre-operative and post-operative neurological state, tumor location, histopathological analysis and patients' quality of life contribute significantly to tumor recurrences and overall outcomes [9, 11].

Despite it has been hypothesized that the time interval to surgery is an important factor that affects the overall outcome of treatment, only a few of the data have been published [9, 12]. Kane et al. concluded that Gait abnormality was only found worsen in 6 of 54 cases (12%) [13]. Some authors believe that intramedullary tumor resection has to be performed as soon as Gait abnormality is identified, without waiting for any further worsening of the symptom itself.

In this study, the authors aim to investigate the effect of the time interval to surgery on the outcome. Hence, Modified McCormick Scale was used as a parameter to assess spinal cord functionalities. Results from functional assessment during preoperative period were then compared with the results of the postoperative period in every patient. Final results were classified into 3 different subgroups: "Improved", "Unchanged" and "Worsen".

RESULTS

Patients' Characteristics

Initially, this study included 28 intramedullary tumor patients from 2012-2017 in department of Neurosurgery at Hasan Sadikin Hospital. Among these 28 patients, 3 patients were excluded from the study, including 1 patient who died at the hospital, and 2 patients who requested a forced discharge before further examinations. The patients approved written informed consent before the inclusion in this study.

Of 25 patients who were included in this study, 13 patients (52%) are male, and 12 patients (48%) are women, suggesting gender differences is not existing in this study. (Table 1). Patients' age were vary between 18-84 year-old, while the mean age is 37.32-year-old. The majority of patients (11 patients) were aged between 41-60 years (44%), while the minority (2 patients) aged >60-year-old (8%).

Table 1

PATIENTS' GENDER DISTRIBUTION IN THIS STUDY, INCLUDING 13 PATIENTS ARE MALE, WHILE 12 PATIENTS ARE FEMALE.

Sex	Male	13	52 %
	Female	12	48 %
Age	18 – 20	4	16 %
	21 – 40	8	32 %
	41 – 60	11	44 %
	> 60	2	8 %
Tumor Location	Cervical	11	44 %
	Thoracal	12	48 %
	Lumbal & Conus	2	8 %

Location of Tumors

Results from MRI examination acknowledged that the majority of intramedullary tumor was located in thoracic vertebra (12 patients ~ 48%) and cervical (11 patients ~ 44%), suggesting that there is no significant difference on the predilection of tumor in these 2 regions. Of all, only 2 patients had tumor at lumbal and conus (8%).

Time Interval to Surgery, Intraoperative Findings and Examination Results

Of 25 intramedullary tumor patients who were included in this study, more than 50% were operated in more than 12 months after having onset of symptoms, and only 2 patients had their surgery in the duration of 1-3 months after onset of symptoms. The mean time interval to surgery is 16.68 months after the onset of symptoms was identified (Figure 1).

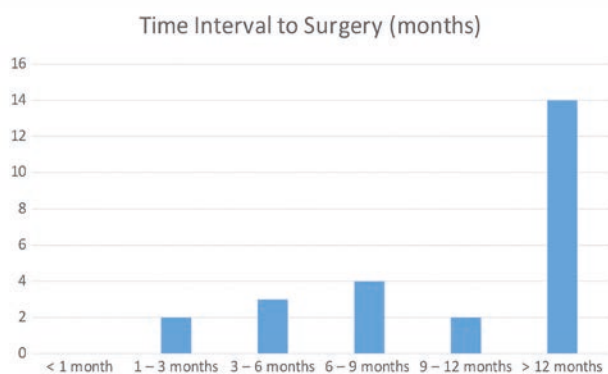


Figure 1 – Most patients who were diagnosed with IMSCT had surgery >12 months after the onset of symptom(s)

Pre-Operative and Post-Operative Modified McCormick Scale in IMSCT Patients

Results of this study showed that most of our IMSCT patients (n=10) had preoperative Modified McCormick Scale of IV, indicating that most patients were presented with a severe deficit of motoric and/or sensoric functions, thus needing other people's assistances. As many of 7 patients (28%) were presented with preoperative Modified McCormick Scale of V, suggesting that they were presented with tetraplegic or paraplegic. Conversely, there were only 2 of our patients (8%) who came with mild neurological deficit (Figure 2).

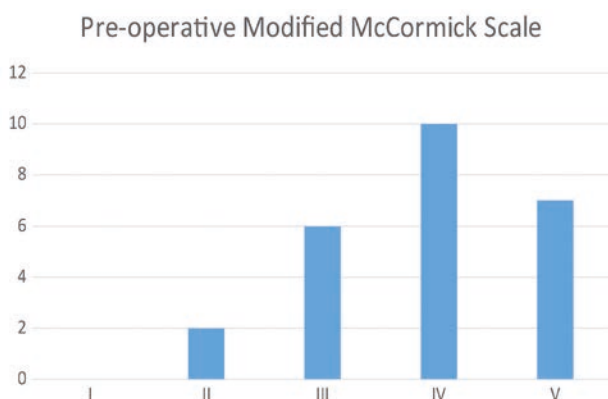


Figure 2 – Majority of IMSCT patients had preoperative Modified McCormick Scale of IV

Post-operative examinations revealed that the majority of patients (n=9) had post-operative modified McCormick scale of IV, indicating that severe sensoric and motoric deficit persisted, thus patients remained dependent of caregivers. Furthermore, 7 patients (~28%) remained tetraplegic or paraplegic. Only 5 patients (20%) had post-operative modified McCormick scale of II, and the other 4 patients (16%) were identified for having modified McCormick scale III (Figure 3).

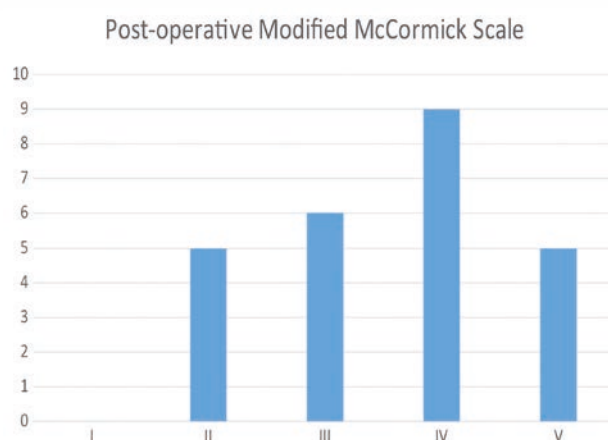


Figure 3 – Post-operative Modified McCormick scale in IMSCT patients showed that the majority of patients had the scale of IV, while the rest of the patients had varies scale of III, II and IV, respectively. No patients that were operated at Hasan Sadikin had scale of I

Histopathology Analyses of the Tumor

Based on histopathology analyses of the tumor tissue that were collected during the tumor removal surgery at Hasan Sadikin General Hospital, the majority of IMSCT specimens were identified as ependymoma (n=15, ~60%), followed by astrocytoma (n=7, ~28%) and varies of other IMSCT tumor types, such as cavernous angioma (n=1, ~4%) and arachnoid cyst (n=1, ~4%) (Figure 4).

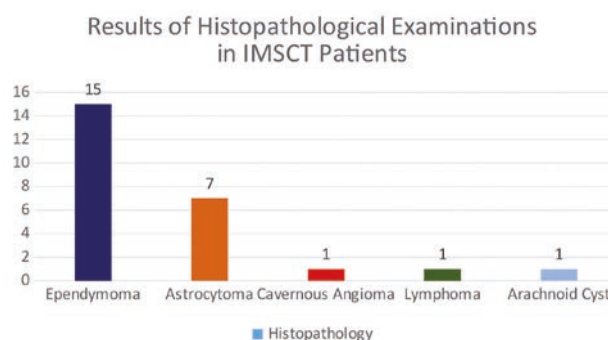


Figure 4 – Histopathology examinations of IMSCT patients' tumor tissue revealed ependymoma as the tumor type in majority of patients, followed by astrocytoma, cavernous angioma, lymphoma and arachnoid cyst

Improvement of Modified McCormick Scale in IMSCT Patients at Post-operative Period

To assess the impact of tumor removal on IMSCT patients' Modified McCormick Scale, we compare pre-operative Modified McCormick Scale with post-operative Modified McCormick Scale in every patient. As expected, as many as 8 patients experienced an increase of modified McCormick scale at post-operative period. Of these 8 patients, 7 patients (~87,5%) had timeinterval to surgery of less than 12

months. The majority of patients (6 patients ~75%) who showed an improvement of Postoperative modified McCormick scale had a pre-operative modified

McCormick scale of III and IV. The results of this study also showed that the number of improvement in these patients are limited to 1 scale.

Table 2
Table of Bivariate Analysis shows proportion and correlation between pre-operative and post-operative modified McCormick scale in IMSCT patients

BIVARIATE ANALYSIS OF PRE-OPERATIVE MODIFIED MCCORMICK SCALE AND POST-OPERATIVE MODIFIED MCCORMICK SCALE

Pre-operative Modified McCormick Scale	Post-operative Modified McCormick Scale					Correlation (r)	P Value
	I	II	III	IV	V		
I						0,766	0,000 *
II		2					
III		3	3				
IV			3	7			
V				2	5		
Total		5	6	9	5		

As shown on table 2, patients with pre-operative modified McCormick scale of II had no change of post-operative modified McCormick scale, while only 2 out of 7 patients who were admitted with pre-operative modified McCormick scale of V had an increase of 1 scale when examined at post-operative period.

None of the patients had an increase of more than 1 scale. As such, statistical analysis using Pearson's Chi-Square test showed that the correlation between pre-operative and post-operative modified McCormick scale is statistically significant (p value<0,05).

Table 3
Bivariate analysis on time interval to surgery and post-operative modified McCormick scale in IMSCT patients

CORRELATION BETWEEN TIME INTERVAL TO SURGERY AND POST-OPERATIVE MODIFIED MCCORMICK SCALE

Time interval to surgery (months)	Post-operative Modified McCormick Scale (n patients)					Correlation (r)	P Value
	I	II	III	IV	V		
<1 month						0,600	0,298
1 – 3 months		1	1	1			
3 – 6 months			1	1			
6 – 9 months		2	2	1	1		
9 – 12 months		2					
>12 months		5	2	6	4		

Table 3 shows that despite the data suggests there may be some correlations between time interval to surgery and post-operative modified McCormick scale, the p value suggests that any possible correlations are statistically insignificant (p value>0,05).

Nonetheless, the data shows that patients with time interval to surgery of >12 months are more likely to acquire unfavorable post-operative outcomes showed by modified McCormick scale of IV and V (10 patients ~ 40%).

Table 4

Bivariate analysis on tumor histopathology and post-operative modified McCormick scale in IMSCT patients

**CORRELATION BETWEEN TUMOR HISTOPATHOLOGY
WITH POSTOPERATIVE MODIFIED MCCORMICK SCALE**

Tumor Histopathology	Postoperative Modified McCormick Scale					Number of Patients	Correlation (r)	P Value
	I	II	III	IV	V			
Ependymoma		3	3	7	2	15	0,615	0,230
Astrocytoma			1	3	3	7		
Cavernous Angioma			1			1		
Lymphoma		1				1		
Arachnoid Cyst		1				1		
Total		5	6	9	5	25		

Even though the data shows that the effect of tumor histopathology on post-operative modified McCormick scale is insignificant, the r value suggests that tumor histopathology and post-operative modified McCormick scale is strongly correlated ($r=0,615$). This data acknowledges that patients who were diagnosed with astrocytoma acquire more unfavorable post-operative modified McCormick scale of IV and V ($n=9 \sim 60\%$).

Discussion

Intramedullary Spinal Cord Tumor (IMSCT) is a rare yet fatal neoplasm of the spinal cord that is mainly diagnosed in productive patients. Due to its location, this tumor type leads to disabilities in its patients, thus severely impaired their quality of lives.

Although progress in neurosurgical operative techniques have better equipped neurosurgeon when treating patients with IMSCT, overall outcomes remain far from ideal, therefore further understanding in disease pathogenesis and treatment, including patient's characteristics may offer valuable insights to further optimize the treatment of IMSCT patients.

In this study, we evaluated the effect of time interval to surgery on the IMSCT patients' treatment outcome. To do so, we used pre-operative and post-operative modified McCormick scale (MMS) as the standardized description of patient's condition. MMS is a parameter that can be used to evaluate the functionalities of spinal cord, therefore can be applied as an overview of the quality of life in patients who are diagnosed with IMSCT.

Table 5

Evaluation of spinal cord function with Modified McCormick Scale 9

Grade	Explanation
I	Neurologically intact, ambulates normally, may have minimal dysesthesia
II	Mild motor or sensory deficit; patient maintains functional independence
III	Moderate deficit, limitation of function, independent with external aid
IV	Severe motor or sensory deficit, limit of function with a dependent patient
V	Paraplegic or quadriplegic, even if there is flickering movement

As expected, the longer the time interval to surgery is, the more unfavorable the outcome in patients after surgery will be. As shown on table 3, 10 patients who underwent surgery in >12 months after the onset of symptoms acquired post-operative modified McCormick scale of IV and V. Nonetheless, to our surprise, the effect of time interval to surgery on the outcome of patient's treatment is not statisti-

cally significant. Likewise, despite the possible effect of tumor histopathology on patient's outcome, such correlation is also statistically insignificant.

Interestingly, bivariate analysis of pre-operative and post-operative modified McCormick scale showed that these 2 parameters are significantly correlated, suggesting that the pre-operative neurological conditions in IMSCT patients affect post-operative outcomes. As



shown on table 2, although patients with pre-operative MMS of II did not acquire any improvement of neurological functions after surgery, patients with pre-operative MMS of \geq III have higher possibilities to acquire improvement of neurological functions when they underwent operation with better pre-operative MMS.

To our knowledge, evaluation of neurological functions with MMS is influenced by several factors, such

as duration of disease, tumor location, tumor malignancy and tumor type. Based on this, we can conclude that the insignificance effect of tumor location, time interval to surgery and tumor histopathology is mainly due to sample size. Hence, we recommend future studies would include larger sample size.

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Banjarnahor^{1,2}, R.H. Dahlan^{1,2,3}, S.E. Ompusunggu^{1,2,3}

¹ X. Садикин атындағы жалпы аурухана, Бандунг қ., Индонезия

² Паджаджаран университеті, Бандунг қ., Индонезия

³ RFS Spine Care, Бандунг қ., Индонезия

ХАСАН САДИКИН АТЫНДАҒЫ ЖАЛПЫ АУРУХАНАДА ИНТРАМЕДУЛЯРЛЫ ІСІКТЕРІ БАР НАУҚАСТАРҒА ЖАСАЛҒАН ОПЕРАЦИЯЛАРДЫҢ КЛИНИКАЛЫҚ НӘТИЖЕСІНЕ УАҚЫТ АРАЛЫҒЫНЫҢ ҮЙІПАЛЫ

Мақсаты: Операцияға дейінгі және операциядан кейінгі неврологиялық жағдайға және операцияның клиникалық нәтижесіне уақыт аралығының әсер етуіне назар аударып, интрамедулярлы жұлын ісігі операциялары (IMSCT) үшін хирургияның нәтижелері талданды.

Міндеттері: 2012 жылдың қаңтар айынан бастап 2018 жылдың қаңтарына дейін жатқызылған интрамедулярлы ісігі бар 25 науқастың медициналық есептеріне ретроспективті талдау жасалды. Операцияға дейінгі және операциядан кейінгі неврологиялық жағдайға бағалау жүргізілді. Амбулаториялық жағдай McCormick модификацияланған шкаласы (MMS) арқылы бағаланды.

Нәтижелері: науқастардың 44% -ы 41-60 аралығындағы (жалпы жас аралығы 18-80, орташа – 37 жас) жас тобында болған. Көбіне кеуде аймағы зардап шеккен (48%). Операцияға дейінгі кезеңде пациенттер McCormick шкаласы бойынша төмендегідей үлестірілді: I деңгейде 0 (0%), II-де 2 (8%),

II-де 6 (24%), IV-де 10 (40%) және V-де 7 (28%). Гистологиялық тұрғыдан алғанда, зақымданулардың 60% эпендимом болды. Жалпы 8 (32%) науқаста жалпы операциядан кейінгі неврологиялық жағдай жақсарды, 27 (68%) жағдайда өзгеріссіз қалды және 0 (0%) науқаста нашарлады.

Қорытынды: Операциядан кейінгі жақсырақ нәтижелер науқастардың операцияға дейін McCormick модификацияланған шкаласы бойынша жақсы көрсеткіштерге ие болуымен тікелей байланысты. Уақыт аралығы хирургияның клиникалық нәтижесіне айтарлықтай әсер етпеді. McCormick модификацияланған шкаласы IMSCT бар науқастардың нәтижелерін және оңтайлы резекцияның уақытын болжаудың маңызды көрсеткіші болып табылады деп есептейміз.

Негізгі сөздер: интрамедулярлы жұлын ісігі, уақыт аралығы, McCormick модификацияланған шкаласы.

J.D. Banjarnahor^{1,2}, R.H. Dahlan^{1,2,3}, S.E. Ompusunggu^{1,2,3}

¹ Общая больница им. X. Садикин, г. Бандунг, Индонезия

² Университет Паджаджаран, г. Бандунг, Индонезия

³ RFS Spine Care, г. Бандунг, Индонезия

ВЛИЯНИЕ ВРЕМЕННОГО ИНТЕРВАЛА НА КЛИНИЧЕСКИЙ ИСХОД ОПЕРАЦИЙ БОЛЬНЫХ С ИНТРАМЕДУЛЯРНЫМИ ОПУХОЛЯМИ В ОБЩЕЙ БОЛЬНИЦЕ ИМЕНИ ХАСАН САДИКИН

Цель: Авторы проанализировали результаты хирургии интрамедулярных опухолей спинного мозга (IMSCT), сосредоточив внимание на дооперационном и послеоперационном неврологическом статусе и влиянии временного интервала на клинический исход операции.

Методы: Проведен ретроспективный анализ медицинских карт 25 пациентов с интрамедулярной опухолью, оперированных в период с января 2012 года по январь 2018 года. Оценивался пред-

и послеоперационный неврологический статус. Амбулаторный статус оценивался с использованием модифицированной шкалы Маккормика (MMS).

Результаты: 44% пациентов были в возрастной группе 41-60 лет (возрастной диапазон 18-80 лет; средний возраст 37 лет). Чаще всего поражен грудной отдел (48%). В предоперационном периоде по шкале Маккормика пациенты были распределены следующим образом; I у 0 (0%), II у 2 (8%), III у 6 (24%), IV у 10 (40%) и V у 7 (28%)



пациентов. Гистологически 60% поражений были эпендимомы. Общий послеоперационный неврологический статус улучшился у 8 (32%) пациентов, оставался неизменным в 27 (68%) случаях и ухудшился у 0 (0%) пациентов.

Заключение: Лучший результат прямо коррелировал с хорошей предоперационной модифицированной шкалой Маккормика. Временной интервал для операции существенно не влиял

на клинический исход. Мы полагаем, что Модифицированная Шкала Маккормика является значимым показателем при прогнозировании исхода и времени для оптимальной резекции у пациентов с IMSCT.

Ключевые слова: интрамедуллярная опухоль спинного мозга, временной интервал, модифицированная шкала Маккормика.