

# **Cellular and Molecular Biology**

E-ISSN: 1165-158X / P-ISSN: 0145-5680

www.cellmolbiol.org

# Management of Acute Cerebral Infarction by Intravenous Thrombolysis with Recombinant T Cell Receptor and Plasminogen Activator and Association of Emergency Nursing Route in the Prognosis

Yuqi Liu<sup>1</sup>, Chengyong Wang<sup>2</sup>, Yuanpeng Han<sup>3</sup>

<sup>1</sup> Emergency Department, Xuanwu Hospital Capital Medical University, Beijing, China. <sup>2</sup> Zaitaku care, Towa hospital, Osaka, Japan

<sup>3</sup> The First Operating Room, SecondAffiliated Hospital of Dalian Medical University, Dalian, China

admitted and begin receiving specialised care.

The purpose of this study is to determine the impact and prognosis of the emergency nursing approach in

conjunction with the use of recombinant T cell receptors and plasminogen activators in patients who have just

had an acute stroke. In this study, 100 patients were randomly selected that were equally divided into experimental and control groups. The period of hospital admission, the results of the Montreal Cognitive Assessment

(MoCA) and the Mini-mental State Examination (MMSE), the results of the Glasgow Outcome Scale (GOS),

and the results of the Activities of Daily Living were all analysed before and after the intervention.. Both the amount of time it took to get a diagnosis after being admitted and the amount of time it took to receive special-

ised therapy after receiving a diagnosis were significantly reduced in the observation group (both P values less than 0.05). At one month after discharge, the scores of ADL, MoCA, MMSE, and GOS rose in both groups,

with more significant changes occurring in the observation group (all P<0.05). This was due to the fact that

ADL scores declined while scores for MoCA, MMSE, and GOS increased. The percentage of people who were

disabled in the observation group was significantly lower than the percentage in the control group (P < 0.05).

Including emergency, nursing might drastically reduce the time it takes for patients with acute stroke to be

# ARTICLE INFO ABSTRACT

#### Original paper

Article history: Received: May 11, 2023 Accepted: August 22, 2023 Published: August 31, 2023

Keywords:

Acute cerebral infarction, emergency nursing, recombinant T-Cell receptor, plasminogen activator

Doi: http://dx.doi.org/10.14715/cmb/2023.69.8.3

Copyright: © 2023 by the C.M.B. Association. All rights reserved.

CMB Association

#### Introduction

The risk of permanent disability or death from a cerebrovascular emergency, such as an acute cerebral infarction or stroke, is significantly increased if the patient is not effectively treated within the golden rescue time. The risk of death and disability is significantly increased if the patient is not effectively treated during the golden rescue time As of 2011, the World Health Organization ranked it as the world's second leading cause of death. (1, 2) Patients experiencing a stroke need to be evaluated and treated as soon as possible for the best possible clinical outcome. There needs to be a rapid and precise diagnosis of a stroke. This is achieved by reducing blood flow to the brain or by rupturing arteries suddenly, both of which are devastating to brain tissue. Directly resulting from this problem is an alteration in the cerebral blood flow. As a result of the sudden start, patients who are resuscitated at the wrong time often die very quickly. In acute stroke, the first three to six hours are the most crucial; therefore, early thrombolysis and surgery are important therapeutic options that may reduce the death and disability rate. (3) A green channel tailored to people with acute cerebral infarction is thus required to save their lives.

In the early 1990s, researchers developed a classification scheme called the Trial of Acute Stroke Therapy (TOAST). This method is extensively used, and there is strong interobserver agreement among those who use it. According to the paper, there are five distinct forms of ischemic stroke, each characterised by a distinct pathophysiological process. Stroke may be caused by a number of different factors, including (A) atherosclerosis in the major arteries, (B) cardio-embolism, (C) obstruction of a smaller blood vessel, (D) additional causes of a stroke that have been identified, and (E) an unknown cause of the stroke. There are five further classifications inside each of these categories. For patients with moderate to severe neurological impairments who come within 4.5 hours of the beginning of symptoms, intravenous recombinant tissue plasminogen activator (r-tPA) remains the therapy of choice, although the incidence of t-PA usage remains at less than 4%. The best results are still seen in those who satisfy these conditions. (5) Patients with moderate to severe neurological deficits due to proximal artery occlusion after an acute ischemic stroke have been demonstrated to benefit from endovascular reperfusion therapy.

After a cerebral infarction, there is a two-step process wherein the peripheral immune response is modified. Early activation of peripheral leukocytes is followed by significant immunosuppression and splenic atrophy in this phase. The progression of the infarct is exacerbated by the influx of inflammatory cells, as well as the timing and

<sup>\*</sup> Corresponding author. Email: hanyuanpeng2021@163.com Cellular and Molecular Biology, 2023, 69(8): 18-24

magnitude of accumulation of various inflammatory cell types in the brain. When the blood-brain barrier is compromised by an ischemia event, myelin-reactive antigens are released into the circulation. Afterward, the antigens are presented to the peripheral immune system, which recognises them as pathogens. Thus, an autoaggressive immune response develops, facilitating the infiltration of immune cells into the brain. Recombinant T-cell receptor (TCR) has been found to reduce infarct volume and brain inflammation when given to mice following middle cerebral artery occlusion. (6,7)

This was found after administering the receptor to the mice (MCAO). By sending partial agonist signals to the T-cell receptor, it is able to selectively alter harmful autoaggressive CD4+ T-cells, which in an animal model of multiple sclerosis reversed clinical paralysis. (9) Hence, RTLs that target brain-reactive T-cells may prevent T-cell-mediated CNS inflammation without causing systemic immunosuppression.

Serine proteases like tissue plasminogen activator (tPA) are important in the healing process (enzymes that cleave peptide bonds in proteins). That's why it's so important for preventing blood clots and for breaking them up when they do form. Catalyzing the conversion of plasminogen into plasmin, the enzyme primarily responsible for thrombus dissolution. In order to produce the serine protease plasmin, it specifically cleaves the zymogen plasminogen at the Arg561-Val562 peptide link. Indications for the use of tPA include thrombolysis, pulmonary embolisms in massive pulmonary embolisms that cause severe instability due to high pressure on the heart, ischemic stroke, and myocardial infarction if there would be a delay of more than 1 to 2 hours before percutaneous transluminal coronary angioplasty. Thrombolysis is another use for tissue plasminogen activator (tPA). (10)

In the past, the primary focus of emergency stroke treatment was on improving and maintaining vital signs. This implies that preventing deaths took precedence over assessing other factors, such as quality of life or mental health, that may have been affected by the sickness. (11) A novel approach with life-saving potential is the emergency nursing route. Before to arrival, during check-in, thereafter, a thorough evaluation and prognosis, and finally, emergency care are the four phases that make up this process. (12) Acute myocardial infarction, acute stroke, and other acute critical conditions are now often treated using the emergency nursing technique. Positive effects on resuscitation have been shown in studies using this method. (13)

The main objective of the present study is to evaluate the benefits of the emergency nursing route along with intravenous thrombolysis by recombinant T Cell receptor & plasminogen activator in acute cerebral infarction conditions.

#### **Materials and Methods**

For the purpose of this prospective research, a total of one hundred people who had an acute stroke and were hospitalised were considered participants. Patients were assigned to one of two groups using a random number generator: an observation group consisting of fifty patients and a control group consisting of another fifty patients. The individuals for the study were chosen according to the inclusion and exclusion criteria, and each subject gave their informed permission before the study began. The hospital's Ethics Committee gave its assent to the research before it was carried out.

## **Inclusion criteria:**

- Age of the patient: between 40-70 years
- Glasgow Coma Score >8
- Patients who got early admission to hospital that is less than 5 hours.

## **Exclusion criteria:**

- Patients with other brain diseases
- Patients with other organ dysfunction such as kidney, liver

The experimental group was implemented with an emergency nursing route along with the treatment of recombinant T Cell receptors & plasminogen activator. The emergency nursing route included three aspects:-(14)

To inform a professional emergency care team that included trained nursing and medical staff from different departments such as neurosurgery, medicine, and anesthesiology. All the members together help to improve the resuscitation techniques and level.

Another crucial step is to prepare for receiving the patient at the reception. This comprises a comprehensive description of the patient's medical history, as well as the beginning symptoms and the time of onset, so that the status of the patient may be evaluated. In addition, additional preparations, such as the medicines, equipment, and instruments necessary for resuscitation, are produced in advance to cut any delays that could occur.

As a last step, initiate emergency treatment on-site. As soon as the patient arrived at the hospital, the emergency channel was activated so that the patient's life might be saved. Intravenous access is established, and a resuscitation plan is developed based on the patient's pupils, limb reflexes, blood pressure, and pulse, among other factors. The resuscitation plan primarily consists of opening the airway, administering oxygen and medication intravenously, and suctioning the sputum from the airway. This includes the use of recombinant T Cell receptor & plasminogen activator therapy. Besides this, staff also participated in resuscitation together, and perform a thorough examination by the radiology department to confirm the disease and condition. Other necessary investigations such as biochemical tests, complete blood count and coagulation are performed before preparing the patient for surgery or intravenous thrombolysis.

On the other hand, the control group was provided with normal emergency treatment throughout the whole experiment. As soon as the patient arrived at the emergency room, the personnel quickly performed an assessment of their condition, ensured that their airways were clear, and administered any necessary lifesaving treatments (Table 1).

The following indicators were used to verify the outcomes in two groups:

- The length of time it took to get a specialist's help once a diagnosis was made, both before and after admission.
- Before treatment and at two weeks post-intervention, patients' neurological function will be evaluated

Yuanpeng Han et al. / Recombinant T Cell Receptor for Acute Cerebral Infarction, 2023, 69(8): 18-24

Table 1.	Components	of Experimental	and Control	Groups.
----------	------------	-----------------	-------------	---------

Experimental Group=50	Control group=50			
Implemented with the emergency nursing route along				
with the treatment of recombinant T Cell receptor &	Implemented with emergency routine care.			
plasminogen activator.				

using the National Institutes of Health Stroke Scale (NIHSS). In any situation, this is what will happen. There were a total of 42 points available on the scale. However much the score improves, the neurological damage remains the same. Thus, a score of 0-1 indicated normal neurological function, whereas a score of 21-42 indicated a severe stroke (15).

- The patients' cognitive function was measured using the Montreal Cognitive Assessment (MoCA) and the Mini-mental State Examination (MMSE) before to the intervention and again one month after they were released. There was a possible score of 30 points, with a higher score indicating better cognitive health. If a patient scored 26 or higher on the MoCA, or 27 or higher on the MMSE, they were classified as having normal cognitive function; however, if their score was lower than 26, or their MMSE score was lower than 27, they were regarded to have cognitive impairment (16).
- The patient's quality of life was assessed both before and after the intervention using the Generic Quality of Life Inventory-74 (GQOLI-74). 16 Each of the three categories—social function, bodily function, and psychological function—received a score of 20 out of a possible 100. The average was 78 out of a possible 380 points, with higher numbers indicating a better quality of life. The following was found to be the relationship between score and QoL.
- Patients' outcomes were evaluated both before and after treatment using the Glasgow Outcome Scale (GOS). It took a month following patients' releases for this to be completed. If the patient received a 5, it signified they had fully recovered and could return to their regular lives, whereas a 1 meant they had passed away (17). Patients' pre-intervention and post-intervention abilities to perform activities of daily living were evaluated using the Activity of Daily Living (ADL) scale.

The scale's total score was 56, and it was broken down into two parts: the Physical Self-Maintenance Scale (PSMS; 24 points) and the Instrumental Activities of Daily Living Scale (IADL; 20 points) (IADL; 32 points). The lower the score, the more independently the person can do day-to-day tasks (18).

#### **Statistical Analysis**

The information was analysed statistically once it was gathered. The significance of the data differences was examined using the t-test. A paired t-test was used to compare pre-and post-intervention outcomes for the same group, while an independent t-test was utilised to assess differences between the two. The significance threshold was set at p 0.05.

#### Results

General information about the patients such as age, medical history, stroke history, and habit history such as smoking, and drinking was obtained and statistically analysed. The experimental group mean age was  $54.5\pm8.5$  and in the control group, it was  $56.8\pm7.5$  and the time from onset of symptoms was  $3.60\pm1.22$  and  $7.81\pm1.31$ . It was observed that no statistical difference in general information (P>0.05), was found and both the groups that is experimental as well as control were comparable as shown in Table 2.

The length of time between admission and diagnosis, as well as the length of time between diagnosis and specialised treatment, were compared between the experimental group and the control group. Time from admission to diagnosis in the experimental group was  $12.34\pm4.44$  whereas in the control group, it was  $17.98\pm3.40$ . The time from diagnosis to receiving specialist treatment in the experimental group was  $18.72\pm4.30$  and in the control group, it was  $28.54\pm4.44$ . It was observed that the experimental

	Experimental group n=50	Control group n=50	P value
Age	54.5±8.5	56.8±7.5	0.544
Time from onset of symptoms	3.60±1.22	7.81±1.31	0.583
Hypertension	12	12	
Diabetes	8	4	0.658
Coronary artery disease	6	6	
History of stroke			
Yes	20	8	0.709
No	30	42	
Smoking			
Yes	34	24	0.231
No	20	26	
Drinking			
Yes	18	12	0.416
No	36	38	

Table 2. Detailed information about participants.



**Figure 1.** Comparison of rescue time from admission to diagnosis between the Experimental Group and Control Group.

group time was shorter than those of the control group (P<0.05), as shown in Table 3 and Fig 1.

In the experiment group, before intervention value of ADL, GQOLI and GOS are 33.05±4.41, 185.27±20.19 one month after discharge was 17.29±2.77, 256.57±21.64 and 3.27±0.82whereas in the control group before intervention values are 31.54±6.90, 176.85±16.34 and  $2.45\pm0.63$  and after one month discharge it was  $24.06\pm3.25$ , 222.20±15.34 and 2.85±1.74. Because of this, when the data were analysed, it was determined that there was not a significant difference in the scores of ADL, GQOLI, or GOS between the two groups of patients before the intervention (P>0.05). Nevertheless, the scores of both groups of patients were higher than they were before the intervention one month after they were discharged, and the scores of the experimental group rose significantly (P < 0.05), as can be shown in Table 4 and Fig 2.

In the experiment group, before intervention values of MoCA and MMSE are  $16.75\pm2.22$ ,  $22.54\pm1.75$  and one months after intervention it is  $24.37\pm3.98$  and  $25.43\pm4,34$ . whereas in the control group before intervention values are  $18.45\pm3.78$  and  $23.66\pm2.34$  and one month after discharge it was  $34.22\pm1.65$  and  $25.16\pm4.25$ . Hence, when doing the

 Table 3. Rescue times between two patient groups.

study, it was determined that there was not a significant difference in the scores of MoCA and MMSE between the two groups of patients before the intervention (P>0.05). Yet, the MoCA and MMSE scores of the two groups of patients were higher than those before the intervention one month after discharge, as shown in Table 5 and Fig 3, and the experimental group rose significantly (P 0.05).

In the experimental group value was  $45.5\% \pm 3.5\%$  and in the control group, it was  $20.19\% \pm 4.2\%$  whereas the mean value was  $23.3\% \pm 2.4\%$ . Patients were administered



Figure 2. Comparison of ADL, GQOLI-74 and GOS.



	Experimental group	Control group
Time from admission to diagnosis	12.34±4.44	17.98±3.40
Time from diagnosis to receiving specialist treatment	18.72±4.30	28.54±4.44

Table 4. Comparison of ADL, GQOLI-74 and GOS.

Group	Time	ADL	GQOLI	GOS
Experimental group	Before intervention	33.05±4.41	185.27±20.19	2.15±1.24
	One month after discharge	17.29±2.77	256.57±21.64	3.27±0.82
Control group	Before intervention	31.54±6.90	$176.85{\pm}16.34$	2.45±0.63
	One month after discharge	24.06±3.25	222.20±15.34	2.85±1.74

Table 5. Comparison of MoCA and MMSE.

Group	Time	MoCA	MMSE
Experimental group	Before intervention	16.75±2.22	22.54±1.75
	One month after discharge	24.37±3.98	25.43±4,34
Control group	Before intervention	$18.45 \pm 3.78$	23.66±2.34
	One month after discharge	34.22±1.65	25.16±4.25



with combined therapy of RTL and t-PA. A significant difference was observed. RTL and t-PA (10 mg/kg) was infused through the jugular vein within 4 hours of the onset of symptoms. The fact size reduces drastically when both were used (Table 6 and Fig. 4). During the tenure of the experiment, two patients died in the experimental group whereas three patients died in the control group.

#### Discussion

Insufficient blood flow to the brain causes cerebral ischemia, which causes irreversible changes to the structure of the brain's blood vessels. Hypoperfusion of a bodily portion often results from the occlusion of a supplying artery. The severity of neurological damage measured by the National Institutes of Health Stroke Scale (NIHSS) is related to the site of arterial blockage. Patients with a primary intracranial artery occlusion almost never have a National Institutes of Health Functional Status Scale (NIHSS) score under 10. There is only a little amount of accuracy in making a clinical diagnosis of vascular territory (carotid versus vertebrobasilar) (20).

Eye muscle and vision problems are among the first and most obvious indicators of a stroke affecting the posterior circulation. Some stroke sufferers still pass away or are left with severe neurological and cognitive disabilities despite advances in treatment and organisational improvements. Stroke mortality rates decreased by 37% between 1990 and 2010 in high-income countries and by 22% in low-income countries globally. These cuts have occurred on a global scale. In 2010, worldwide, the incidence-tomortality ratio was 0.35. An extensive investigation was done on a statistically-representative population sample (21) to determine the impact that important risk factors have on stroke occurrence. Because of differences in risk between sexes and with age, the likelihood of having arterial hypertension might vary between 1.6% to 4.2%. (22)

Atherosclerosis in large arteries, arteriosclerosis in cerebral small vessels, and lipohyalinosis in these vessels are all the result of persistently high blood pressure's influence on the remodelling of vessel walls. The ensuing arterial wall hardening interferes with the brain's ability to regulate its blood flow. Endothelial dysfunction, a potential outcome of diabetes, influences cerebrovascular autoregulation. Atherosclerotic irregularities may develop in the body due to hyperlipidemia and smoking. Atrial fibrillation, or AF, is a risk factor for ischemic stroke and is now generally considered to be the leading risk factor. (23) Studies have demonstrated that emergency resuscitation using the emergency nursing technique helps bring patients back from the verge of death in cases of acute myocardial infarction, acute stroke, and other acute critical conditions. This form of care requires strict supervision throughout its whole, from the time a patient is admitted to the moment they are discharged from the hospital. This model's objective is to speed up emergency response by shortening the time spent on diagnosis. (12)

According to the findings of O'Keeffe and coworkers, the emergency nursing strategy significantly shortened the time it took for patients admitted with acute stroke to get specialised care. The number of disabled people dropped as a consequence. (24) Researchers found that by using an emergency nursing strategy, both patient wait times and the success of treatment may be greatly improved. It was expected that the emergency nursing approach would make the most efficient use of available resources while waiting for the patient to arrive. Nevertheless, no significant difference in mortality rates was seen between the two groups.

Focal cerebral ischemia has been linked to spleen and thymus degeneration. Cellular emigration from the spleen to the brain, which has deleterious effects, contributes to this phenomenon. Multiple sclerosis (MS) is an inflammatory demyelinating disease caused by CD4+T lymphocytes that become dysregulated and recognise myelin protein antigens as foreign. RTLs were first created as a treatment for MS. Myelin sheath disease, often known as multiple sclerosis, disrupts the protective covering of nerve fibres. (25,26) Treatment with RTL dramatically reduced the secondary infiltration of immune cells like macrophages and the generation of chemokines and chemokine receptors required for entry into the central nervous system, as indicated by research by Sinha and colleagues (CNS). Since it specifically targets infarct-associated brain regions after a stroke rather than a systemic inflammatory response, RTL seems to be a viable treatment method. Based on the results of the present study, it seems that RTL and t-PA may be used together to lessen the size of the infarct after 24 hours. To improve the prognosis of individuals who have just had an acute ischemic stroke, recanalization therapy with t-PA is the most effective method. Furthermore, the FDA has approved it as the sole treatment for stroke. (27, 28)

RTL therapy alone improves outcomes and provides additional protection in t-PA-treated mice with experimental ischemic stroke. These features make RTL an attractive, safe, and effective option in the treatment of so-called "cocktail" strokes, as well as in the treatment of stroke patients who were hospitalised after the therapeutic time window of t-PA had passed. Further, RTL serves as a platelet ligand. When applied to collagen-coated surfaces and subjected to physiologically relevant pressure gradients, it prevents the formation of occlusive thrombus. Platelet aggregation induced by collagen is suppressed in vitro. Therefore, in addition to the anti-inflammatory protection mechanism, RTL may also inhibit platelet re-aggregation after t-PA-induced thrombolysis. (29-34)

Acute stroke patients who received emergency nursing care had significantly less neurological impairments after surgery or medication compared to those who received routine care. That held true whether the patients underwent operations or took medication. Because of the rapid onset and development of acute stroke, the sooner the problem is detected and treatment started, the less brain damage the patient will sustain. The emergency nursing strategy cut down on patients' wait times in the ER, allowing them to see doctors sooner and get better care. This meant reduced damage to patients' nerve cells and nerve functions. The fact that only a very limited number of people were chosen to participate in the research is the primary drawback of this study. Hence, the benefit of pursuing a career in emergency nursing requires more research before it can be confirmed.

## Conclusion

The incorporation of an emergency nursing path could significantly shorten the time from admission to specialist treatment for patients who are experiencing an acute stroke. This would promote the recovery of neurological and cognitive functions, which would be advantageous to the patient's prognosis.

# References

- 1. Leigh R, Knutsson L, Zhou J and van Zijl PC. Imaging the physiological evolution of the ischemic penumbra in acute ischemic stroke. J Cereb Blood Flow Metab 2018; 38: 1500-1516.
- 2. Ahmed B, Ali A, Usage of traditional chinese medicine, western medicine and integrated Chinese-western medicine for the treatment of allergic rhinitis, SPR, 2021, 1(1), 01-10.
- Nwuke C, Ibeh B, Antidiarrheal potential of methanol extract of Combretum dolichopetalum and its fractions in wistar albino rats, SPR, 2021,1(1), 11-23
- 4. Fact sheet N°310. [Accessed July 2013] The top 10 causes of death. Media center of World Health Organization website.
- Giacalone G, Zanoletti M, Re R, Germinario B, Contini D, Spinelli L, Torricelli A and Roveri L. Time-domain near-infrared spectroscopy in acute ischemic stroke patients. Neurophotonics 2019; 6: 015003.
- Adams, H.P., Jr.; Bendixen, B.H.; Kappelle, L.J.; Biller, J.; Love, B.B.; Gordon, D.L.; Marsh, E.E., 3rd. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993, 24, 35–41.
- Wang Y, Zhang Z, Chow N, et al. An activated protein C analog with reduced anticoagulant activity extends the therapeutic window of tissue plasminogen activator for ischemic stroke in rodents. Stroke. 2012; 43:2444–2449. Gelderblom et al. 2009;Stevens et al. 2002;Wang et al. 1993).
- Stevens SL, Bao J, Hollis J, Lessov NS, Clark WM, Stenzel-Poore MP. The use of flow cytometry to evaluate temporal changes in inflammatory cells following focal cerebral ischemia in mice. Brain Res. 2002; 932:110–119.
- 9. Wang PY, Kao CH, Mui MY, Wang SJ. Leukocyte infiltration in acute hemispheric ischemic stroke. Stroke. 1993; 24:236–240.
- Burrows GG, Chou YK, Wang C, Chang JW, Finn TP, Culbertson NE, Kim J, Bourdette DN, Lewinsohn DA, Lewinsohn DM, Ikeda M, Yoshioka T, Allen CN, Offner H, Vandenbark AA. Rudimentary TCR signaling triggers default IL-10 secretion by human Th1 cells. J Immunol. 2001;167:4386–4395.
- Burrows GG, Adlard KL, Bebo BF Jr, Chang JW, Tenditnyy K, Vandenbark AA, Offner H. Regulation of encephalitogenic T cells with recombinant TCR ligands. J Immunol. 2000; 164:6366– 6371.
- 12. Heiferman DM, Li DD, Pecoraro NC, Smolenski AM, Tsimpas A, Ashley WW. Intra-Arterial Alteplase Thrombolysis during

Mechanical Thrombectomy for Acute Ischemic Stroke. J Stroke Cerebrovasc Dis. 2017 Dec;26(12):3004-3008.

- Baron JC. Protecting the ischaemic penumbra as an adjunct to thrombectomy for acute stroke. Nat Rev Neurol 2018; 14: 325-337.
- 14. Dawood M and Gamston J. An intervention to improve retention in emergency nursing. Emerg Nurse 2019: 27: 21-25.
- 15. Pouryahya P, Guiney N, Meyer A and Goldie N. Evaluating the implementation and outcomes of a sepsis pathway in the emergency department. N Z Med J 2020; 133: 35-49.
- 16. Li M and Liu HM. Implementation of a clinical nursing pathway for percutaneous coronary intervention: a prospective study. Geriatr Nurs 2018; 39: 593-596.
- 17. Kwah LK and Diong J. National institutes of health stroke scale (NIHSS). J Physiother 2014; 60: 61-67.
- Trivedi D. Cochrane review summary: mini-mental state examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. Prim Health Care Res Dev 2017; 18: 527-528.
- Dikmen S, Machamer J, Manley GT, Yuh EL, Nelson LD and Temkin NR; TRACK-TBI Investigators. Functional status examination versus glasgow outcome scale extended as outcome measures in traumatic brain injuries: how do they compare? J Neurotrauma 2019; 36: 2423-2429.
- Harper KJ, Riley V, Jacques A, MacDonald K and Spendier N. Australian modified Lawton's instrumental activities of daily living scale contributes to diagnosing older adults with cognitive impairment. Australas J Ageing 2019; 38: 199-205.
- Kilic E, Hermann DM, Hossmann KA. Recombinant tissue plasminogen activator reduces infarct size after reversible thread occlusion of middle cerebral artery in mice. Neuroreport. 1999; 10:107–111. [PubMed: 10094143].
- 22. Flossmann ETP9, Redgrave JN, Briley D, Rothwell PM. Reliability of clinical diagnosis of the symptomatic vascular territory in patients with recent transient ischemic attack or minor stroke. Stroke. 2008 Sep;39(9):2457-60.
- 23. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA et al.; Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet. 2014 Jan 18;383(9913):245-54.
- 24. Park TH, Ko Y, Lee SJ, Lee KB, Lee J, Han MK et al. Identifying Target Risk Factors Using Population Attributable Risks of Ischemic Stroke by Age and Sex. J Stroke. 2015 Sep;17(3):302-11.
- Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J et al.; EMBRACE Investigators and Coordinators. Atrial fibrillation in patients with cryptogenic stroke. N Engl J Med. 2014;370:2467-77.
- 26. O' Keeffe A, O' Grady S, Cronin F, Dolan C, O' Hea A, O' Shea KL and Naughton C. Evaluation of an emergency department falls pathway for older people: a patient chart review. Int Emerg Nurs 2020; 51: 10086.
- Liesz A, Hagmann S, Zschoche C, Adamek J, Zhou W, Sun L, Hug A, Zorn M, Dalpke A, Nawroth P, Veltkamp R. The Spectrum of Systemic Immune Alterations After Murine Focal Ischemia. Immunodepression Versus Immunomodulation. Stroke. 2009.
- Offner H, Subramanian S, Parker SM, Wang C, Afentoulis ME, Lewis A, Vandenbark AA, Hurn PD. Splenic atrophy in experimental stroke is accompanied by increased regulatory T cells and circulating macrophages. J Immunol. 2006b; 176:6523–6531.
- 29. Sinha S, Subramanian S, Proctor TM, Kaler LJ, Grafe M, Dahan R, Huan J, Vandenbark AA, Burrows GG, Offner H. A promising therapeutic approach for multiple sclerosis: recombinant

T-cell receptor ligands modulate experimental autoimmune encephalomyelitis by reducing interleukin-17 production and inhibiting migration of encephalitogenic cells into the CNS. J Neurosci. 2007; 27:12531–12539.

- Beerny-Lang MA, Hurst S, Tucker EI, et al. Thrombin mutant W215A/E217A treatment improves neurological outcome and reduces cerebral infarct size in a mouse model of ischemic stroke. Stroke. 2011; 42:1736–1741. [PubMed: 21512172].
- Itakura A, Aslan JE, Sinha S, et al. Characterization of human platelet binding of recombinant T cell receptor ligand. J Neuroinflammation. 2010; 7:75.10.1186/1742-2094-7-75 [PubMed: 21059245].
- Umarova RM, Sperber C, Kaller CP, Schmidt CSM, Urbach H, Kloppel S, Weiller C and Karnath HO. Cognitive reserve impacts on disability and cognitive deficits in acute stroke. J Neurol 2019; 266: 2495-2504.

- Ahmed DI, Idris AAA, Role of Ag NORs in Improve diagnosis of breast cancer with different grades and subtypes' among Sudanese women, SPR, 2021, Volume 2, issue 1, Page No.: 528 - 533.
- Kumar G, Kumar R, Gautam GK, Rana H, The phytochemical and pharmacological properties of Catharanthus roseus (Vinca), SPR, 2021, Volume 2, issue 1, Page No.: 472 - 477
- 35. Adisel1,Sukarno,Onsardi,Ahmad Gawdy Prananosa. Hybrid Learning Implementation in Higher Education During The Covid-19 Pandemic in Indonesia: An Overview. Educational Administration: Theory and Practice 2022,Volume 28, Issue 4,pp:131-141
- Hasanuddin, Salamiah Sari Dewi, Erlina Sari Siregar. Predictor Of Multiple Intelligence In Educational Practice, Educational Administration: Theory and Practice 2022, Volume 27, Issue 2, pp:049-056