Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.

Evaluation of levels of bradykinin, intercellular adhesion molecule-ICAM and electrolytes in patients with ischemic stroke

I. A. A. K. Al-Samarai, A. J. Al Samer

University of Samarra, Saleh Aden, Iraq

Article info

Received 26.08.2025
Received in revised form 01.10.2025
Accepted 19.10.2025

Department of Applied Chemistry, College of Applied Science, University of Samarra, Saleh Aden, Iraq.
Tel.: +0-772-737-24-37.
E-mail: israa.a@uosamarra.edu.iq

Al-Samarai, I. A. A. K., & Al Samer, A. J. (2025). Evaluation of levels of bradykinin, intercellular adhesion molecule-ICAM and electrolytes in patients with ischemic stroke. Regulatory Mechanisms in Biosystems, 16(4), e25172. doi:10.15421/0225172

Stroke is one of the leading causes of death worldwide, especially among the elderly. Fifty blood samples were collected from patients (25 females and 25 males) suffering from ischemic stroke (IS) who visited the central health laboratories at the Medical City. The patients belonged to different age groups ranging from 45–65 years. Twenty samples (10 females and 10 males) were collected from healthy individuals who did not suffer from any diseases as a control group. Several biochemical parameters were tested, such as intercellular adhesion molecule (ICAM), bradykinin, sodium and potassium in the patient's blood serum. The results of the present study indicated a significant elevation in ICAM, bradykinin, Na, K in the blood serum of the patient group compared to the control group. The results also showed a highly significant positive correlation between bradykinin concentration and ICAM in the blood serum of the patient group, as the value of the correlation coefficient was 0.724. The results also showed that the area under the curve value for the studied variables, ICAM, bradykinin, was excellent, so they can be considered important diagnostic variables for patients with ischemic stroke.

Keywords: Ischemic stroke; bradykinin; intercellular adhesion molecule; sodium; potassium.

Introduction

Stroke is one of the most common causes of death worldwide, and its incidence is increasing in developing countries. Blocked arteries cause ischemic stroke and are responsible for the majority of strokes (Campbell, 2019). It poses a major global health challenge, with 12.2 million new strokes occurring annually worldwide, a death rate of 6.5 million cases, and a total disability of 143 million disability-adjusted life years (Feigin, 2022). In the United States, a stroke occurs every 40 seconds, making it the fifth leading cause of death and the first leading cause of disability in the country Thus, the high prevalence of stroke, coupled with high survival rates, places increased pressure on already limited healthcare resources; as the cost of treatment increases (Ottenbacher, 2004), and this is limited to the clinical setting (Lang, 2007), resulting in 50% of survivors who reach the chronic stage suffering from severe motor disability in the upper extremities (Gresham, 1979). Thus, before the advent of modern stroke treatment, the mortality rate in the acute phase was 10% for patients with moderate to severe disability. A key side of acute stroke treatment is that "time is brain." Reperfusion, or the rapid restoration of cerebral blood flow to salvageable ischemic brain tissue at risk of cerebral infarction, is the most important treatment (Hasan, 2021). Therefore, the Acute Stroke Trials Classification System was developed in the early 1990s, which classifies ischemic strokes into five subtypes, based on the pathological mechanism, including large-arterial atherosclerosis, myocardial infarction, and stroke of other specific causes (Adams, 1993; Ay, 2007). Cell adhesion molecules are glycoproteins expressed on the cell surface and have a major role in inflammation and tumors. Cell adhesion molecules and ligands that may play a role in pathological conditions have been discussed as potential therapeutic approaches that require regulating the expression of these molecules. These molecules are essential for the functioning of the immune system in both pathological and healthy conditions (Koh & Park, 2018). The intact part of the intercellular adhesion is one of the glycoproteins that are present on the cell surface and is an adhesion receptor that plays a role in regulating and transporting white blood cells from the blood circulation to the site of inflammation. It also acts as a stimulator of the inflammatory response on the surface of immune epithelial cells. Also, it acts as a biosensor to transmit external signals by linking its cytoplasmic domain with the actin cytoskeleton (Bui, 2020). Endothelial dysfunction is a precursor to atherosclerosis, which is characterized by overexpression of adhesion molecules, including intercellular adhesion molecule-1 (Habas, 2018). Bradykinin is a peptide belonging to the kallikrein-kinin system, which acts as a vasodilator and inflammatory mediator (Rex, 2022). It stimulates the peripheral circulation by reducing arterial smooth muscle tone and increasing blood flow (Mombouli, 1995). In addition, it causes the exit of plasma from the blood vessels by merging with the lining of the capillaries, and narrows the blood vessels by stimulating the venous smooth muscle fibers. Bradykinin signaling is also of interest in chronic pain, vasculopathy, neuropathy, and diabetes (Dagnino, 2020; Lau, 2020; Rex, 2022).

Sodium is the main ion in the extracellular fluids of the body, as it is the most important element in the extracellular fluids, and its normal limit in blood serum is (Chen, 2012; Portolés, 1996) 135–145 mmol/L, as it has an important role in the work and activation of tissues that transmit nerve impulses (Guyton, 2015). Sodium is essential for muscle, nerve, and stomach functions and for maintaining proper blood pH and electrolyte balance. Potassium is the primary intracellular alkaline cation, with approximately 95–98% of potassium being found inside cells (Guyton, 2015). Potassium ions inside the cell participate in transmitting nerve impulses, help in contracting cardiac, skeletal, and smooth muscles, and maintain blood pressure (Bishop et al., 2000). The current study aimed to evaluate the relationship between bradykinin and ICAM-1 levels and electrolyte levels to predict the severity of ischemic stroke and the extent to which these variables affect its severity and subsequent outcomes.

Materials and methods

The study was conducted in the laboratories of the College of Applied Sciences/Department of Applied Chemistry and some external laboratories in Baghdad. Ethical approval was obtained from the Scientific Committee of the Department of Applied Chemistry, Samarra University. All patients were informed of the study, and their informed consent was obtained. Confidentiality of patient data was ensured. The current study involved collecting 50 blood samples from ischemic stroke subjects (25 males and 25 females) who visited the central health laboratories at the Medical City, and 20 blood samples from healthy subjects (10 males and 10 females). 5 mL of venous blood from patients and healthy subjects was taken, placed in gel tubes, and centrifuged at 3000 rpm to obtain serum. It was stored at –20 °C until biochemical tests were performed.

The study involved the assessment of serum (ICAM, bradykinin) levels by using an ELISA assay kit provided by Fine Test-China. The Na concentration was assessed according to the kit prepared by the German company Spectrum. The K concentration was also estimated according to the kit prepared by the German company Spectrum (Hillman, 1967).

We calculated the mean ± standard deviation (SD) of the studied biochemical parameter between patients and healthy controls at a probability level of $P \leq 0.05$ using the F-test. The correlation between bradykinin and biochemical parameters was also studied according to SPSS V27. The area under the curve was calculated using MedCalc V20 for biochemical parameters, and the figures were drawn according to Graphpad Prism V9.

Results

The results of the current study showed significant differences in the concentration of biochemical variables between the stroke group and the healthy group. The result showed a significant ($P < 0.0001$) elevation in the mean bradykinin and ICAM levels in patients, 67.6 ± 17.6 pg/mL, 13.0 ± 2.8 ng/mL, respectively, compared to the control group, 24.1 ± 5.5 pg/mL, 5.5 ± 1.1 ng/mL, respectively, at $P \leq 0.05$ (Fig. 1 and 2). Also, the results showed a significantly ($P \leq 0.005$) elevated mean (Na, K) concentration in patients, 141.9 ± 2.0 mEq/L, 4.34 ± 0.44 mmol/L, respectively, compared to the control group, 140.3 ± 1.1 mEq/L, 3.63 ± 0.50 mmol/L, respectively (Fig. 1 and 2).

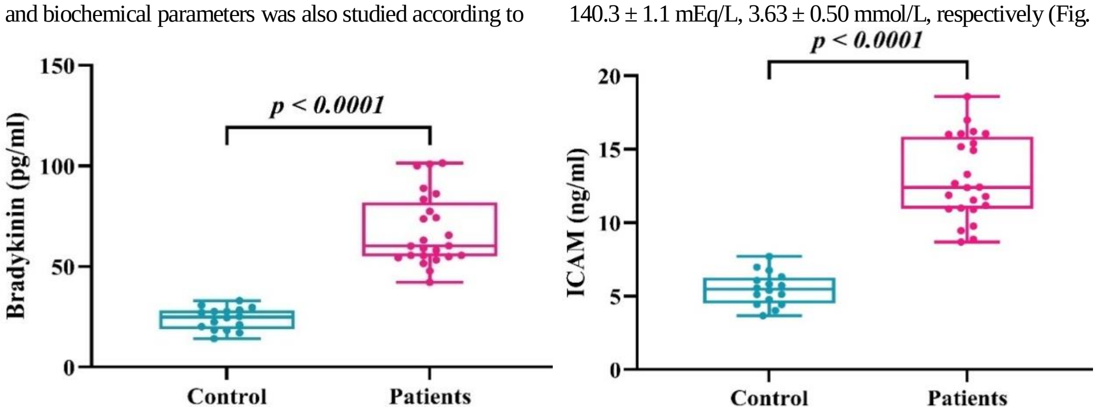

Fig. 1. Concentration of bradykinin and ICAM in patients and healthy people

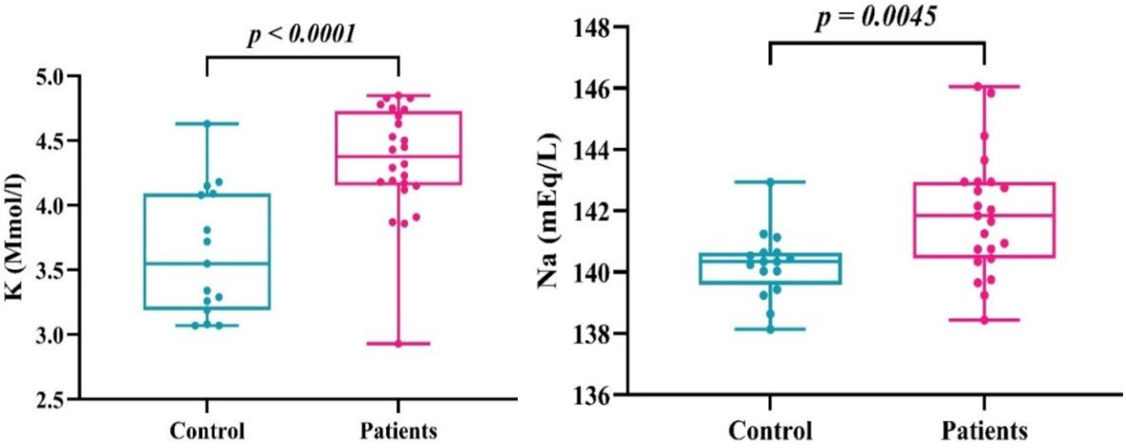

Fig. 2. Concentration of Na and K in patients and healthy people

The area under the curve results (Fig. 3) demonstrate the ability to discriminate biochemical variables in predicting ischemic stroke from serum bradykinin, ICAM, Na, and K. The AUC value for bradykinin was 1.000 (sensitivity of 100%) with specificity of 100% for IS (G1) vs control group (C), while the AUC for ICAM in the group of patients with IS was 1.000 (the sensitivity 100% and specificity of 100%) in the group of patients with IS (G1) and control group (C). Also, the AUS for Na was 0.776 (sensitivity of 73.9%) with specificity of 81.2% for the IS (G1) vs the healthy group (C), while the AUC for K in the group of patients with IS was 0.868 (the sensitivity 83.3% and specificity of 80.0%) in the group of patients with IS (G1) and healthy group (C). So the variables in this study may be considered to have high specificity and an important predictive indicator for diagnosing ischemic stroke.

Table 3 shows the correlation of the effectiveness of the bradykinin peptide with the parameter studied, as a highly significant positive correlation was found between bradykinin concentration and ICAM, with a value of the correlation coefficient of 0.724 in the patient group with IS.

Table 3
Relationship of bradykinin with biochemical parameters

Parameters	Control		IS	
	r	P-value	r	P-value
ICAM	0.486	0.056	0.724**	<0.001
Na	0.404	0.120	–0.289	0.182
K	0.029	0.917	–0.187	0.381

Note: ** – correlation is significant at the 0.01 level (2-tailed).

Discussion

Stroke is a leading cause of death worldwide, especially among the elderly. Evidence suggests that ischemic injury and inflammation are responsible for its development. Therefore, the expression of soluble adhesion molecules, including ICAM-1, plays an important role in inflammation and the development of ischemic injury after acute stroke (Supanc, 2011). The results of the current study revealed an increase in ICAM levels in the serum of stroke patients compared to healthy individuals. The study by Fassbender (1995) found no significant difference in the adhesion molecule ICAM-1 between patients and healthy subjects, which is inconsistent with the results of the current study. But the study by Clark (1992) also indicated an elevated ICAM-1 concentration in patients with ischemic stroke; the reason may be that blood samples were taken within 72 hours of the onset of symptoms.

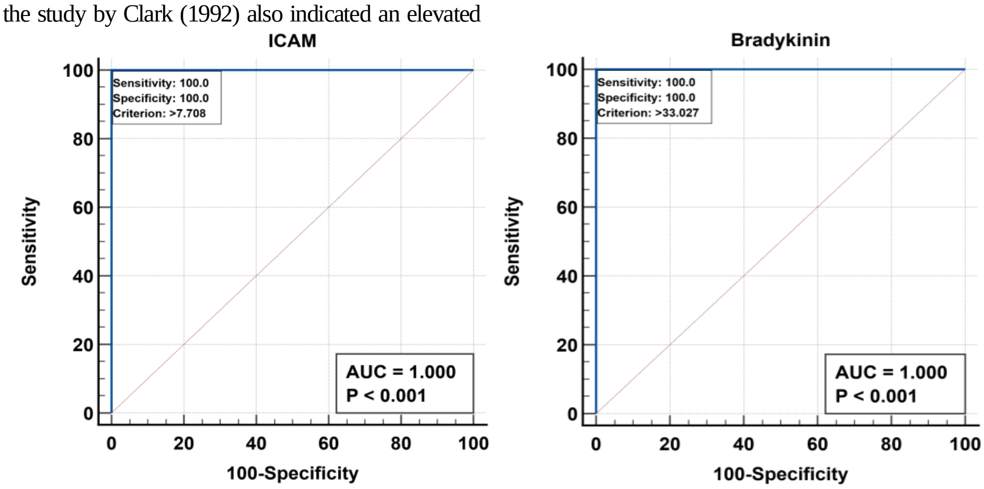

Fig. 3. ROC analysis of bradykinin and ICAM in patients and healthy people

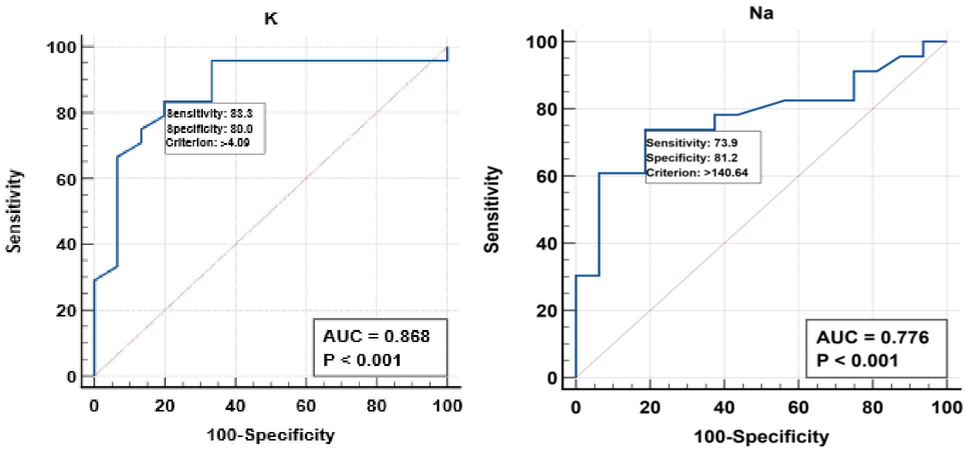

Fig. 4. ROC analysis of Na and K in patients and healthy people

Adhesion molecules play functional roles in the pathophysiology of ischemic stroke (Wang, 2006), and genetically elevated sICAM-1 concentration is linked with adverse outcomes after stroke (Wang et al., 2023). Inflammation exacerbates brain injury during the acute phase of stroke. During this process, ICAM plays a crucial role in facilitating the migration of immune cells to the damaged area (Rakhimbaeva, 2023). It has also been found that elevated levels of ICAM-1 may be caused by ischemia, and this is closely associated with the entrapment of vascular endothelial cells (EPCs) in the ischemic limb. Therefore, the expression of ICAM-1 may be important in regulating the process of neovascularization through its ability to recruit vascular endothelial cells (Yoon, 2006). A study by Nielsen (2020) showed an increase in ICAM-1 concentration in acute stroke patients and found that they increased significantly within 8 hours of stroke onset.

The results of the present study also indicate higher levels of bradykinin peptide in the blood serum of patients compared to healthy people, as brain damage resulting from ischemia or toxic factors in the exposed areas selectively leads to delayed neuronal death similar to programmed cell death. Therefore, the production of bradykinin peptide is an indicator of ischemic and toxic brain injury (Lalkovičová, 2015).

Bradykinin peptide works to release excitatory amino acid neurotransmitters, is a powerful stimulator of cytokines, and acts as a chemoattractant for white blood cells (Relton, 1997). Thus, stroke leads to disruption of the blood-brain barrier, sometimes leading to life-threatening cerebral edema. Even short-term use of bradykinin has been shown to cause significant and prolonged dilation of cerebral arteries and increased cerebral vascular permeability (Sarker, 2000). Bradykinin concentration in the blood or cerebrospinal fluid of stroke patients rises as a result of its activation within the kallikrein-kinin system during cerebral ischemia. When blood flow to brain tissue is interrupted, the cell membrane is ruptured and protein enzymes (plasma and tissue kallikrein) are activated, leading to the production of high amounts of bradykinin from kininogen. Bradykinin (BK), whose levels are elevated during ischemic stroke, enhances blood-brain barrier permeability and raises intracranial capillary pressure, leading to cerebral edema. Furthermore, bradykinin stimulates glutamate release from neurons and astrocytes via activation of bradykinin type 2 receptors, suggesting bradykinin involvement in glutamate neurotoxicity. It has recently been shown that individuals lacking functional natriuretic peptides suffer from acute strokes (Rubattu, 2004; Rubattu, 1999). BK administration and B2R activation are known to disrupt the blood-brain/retinal barrier (BBB/BRB) by stimulating eNOS and PLA2, leading to increased production of NO and prostaglandins, resulting in plasma protein leakage and angioedema formation (Vink, 2003; Moreau, 2005). A study indicated that activation of the kallikrein-kinin system after stroke contributes to vascular leakage, inflammation, and deterioration of nervous tissue. It was also shown that the generated recombinant tissue kallikrein-1 may produce bradykinin locally, which leads to vasodilation and improved cerebral perfusion via synchronous pathways, which has implications for stroke (Kasner, 2025). Also, the results showed higher sodium levels in stroke patients compared to healthy individuals. Sodium deficiency is a common complication after stroke, However, some patients exhibit elevated sodium levels as a result of therapeutic factors or a physiological response to stress, such as the use of hypertonic solutions or stimulation of cortisol secretion, which requires interpretation of the results according to the clinical context of each patient. Hyponatremia is a common electrolyte imbalance, easily observed in patients with ischemic and hemorrhagic stroke. Hyponatremia is often caused by low osmolality and may be due to the syndrome of insufficient antidiuretic hormone or cerebral salt-losing syndrome (Ehtesham, 2019).

Sodium imbalance is common in acute stroke patients and is associated with increased mortality. Sodium concentration can be affected in hospitalized stroke patients by dehydration due to decreased fluid intake, impaired neurocognition and consciousness, or by taking medications (such as mannitol). Sodium and water imbalances can also be exacerbated by the development of endocrine complications after acute stroke, including secondary adrenal insufficiency (Yuen, 2022). Therefore, when hypernatremia occurs in acute stroke, it is usually the result of patients not receiving enough water or the development of diabetes insipidus. Hypernatremia after stroke is very rare due to decreased thirst, which is secondary to damage to the thirst center (Ramthun, 2011).

On the other hand, higher potassium levels were found in stroke patients compared to healthy controls. High potassium levels in stroke patients may be attributed to cellular damage resulting from ischemia, metabolic acidosis, or impaired renal excretion. This does not necessarily conflict with the clinical picture, but may reflect the severity of the injury or the stage of recovery. Therefore, electrolyte disturbances are common in stroke patients (Hossain, 2023).

The results of the study indicated that the area under the curve of the adhesion molecule ICAM was excellent, so it can be considered a biochemical indicator to predict the severity of stroke patients. It was found that stroke patients suffer from a lack of oxygen, which results in the release of inflammatory cytokines that stimulate the expression of ICAM-1 on cerebral vascular cells. Therefore, high levels of AUC allow white blood cells to adhere to vessels and enter nervous tissue, increasing inflammation and nerve cell damage. Therefore, a high AUC value indicates a prolonged inflammatory response that reflects the severity of brain damage and the extent of neurovascular inflammation associated with a stroke. On the other hand, an elevated AUC value for bradykinin peptide indicates activation of the kallikrein-kinin pathway, which leads to increased bradykinin secretion. This, in turn, causes vasodilation, increased permeability, and cerebral edema. Therefore, both ICAM and bradykinin peptide can be considered biomarkers for predicting stroke severity. The study showed that ICAM-1 levels were significantly more elevated in the serum of patients with a poor prognosis than in patients with a good prognosis. The area under the curve (AUC) results also showed that the sensitivity and specificity of ICAM-1 in serum for predicting AIS diagnosis were 74% and 76%, respectively. This compares to the current study, which reported a sensitivity and specificity of 100% (Wang, 2021). A study by Rakhimbaeva (2023) indicated that the AUC for ICAM concentration was 0.829, so it could be one of the predictive indicators for diagnosing stroke.

On the other hand, sodium and potassium had good AUC values, indicating electrolyte imbalances that can occur in many diseases other than stroke. This suggests a limited ability to differentiate between patients and healthy individuals. This may be because changes in electrolyte levels, including sodium and potassium, are not predictive of stroke and are influenced by therapeutic and physiological factors, reducing their sensitivity and specificity. The study (Yakar, 2024) also indicated that the AUC value for both sodium and potassium was weak, reaching 0.55 and 0.63, respectively. The study results also indicated a highly significant correlation between bradykinin and ICAM. This correlation is explained by the fact that elevated bradykinin levels are typically accompanied by elevated ICAM levels in stroke patients, which in turn leads to increased inflammatory migration and worsening brain damage.

Suppose a study indicates the role of endothelial cells in stroke. In that case, bradykinin may contribute to the deterioration of endothelial cell function, which leads to increased expression of ICAM-1 and increased inflammation (Gong, 2025). It was also found that activation of bradykinin type 1 receptors enhances inflammation and increases the permeability of the blood-brain barrier, which contributes to the exacerbation of neurological damage after stroke (Huang, 2022). While the study results found no correlation between bradykinin peptide and electrolyte levels, this may be because increased bradykinin levels lead to vasodilation and increased permeability, but they do not alter kidney function significantly enough to alter electrolyte concentrations directly.

Conclusion

It is concluded that the vasculitis markers bradykinin and ICAM-1 are elevated in stroke patients and persist at high levels over time, as reflected by the high area under the curve for these markers compared to electrolytes, which showed only moderate or good AUC. This biochemical pattern explains that cerebral ischemia activates local kallikreins and kinins, leading to the production of bradykinin in high quantities. The high AUC value of bradykinin indicates evidence of persistent vasodilatory activity after a stroke. Elevated ICAM-1 also enhances leukocyte adhesion and transmigration into damaged tissue, complementing bradykinin's mechanism of amplifying inflammation and edema. The high AUC value of ICAM-1 indicates the continued interaction between the vascular endothelium and inflammatory cells as a central pathological mechanism in the post-stroke stages. As for electrolyte levels, their changes are not specific to stroke as they are direct indicators of inflammation. For this reason, the ability of sodium and potassium to distinguish patients from controls (AUC) was less than that of indicators of vascular inflammation.

References

Adams Jr., H. P., Bendixen, B. H., Kappelle, L. J., Biller, J., Love, B. B., Gordon, D. L., & Marsh 3rd, E. E. (1993). 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, 24(1), 35–41.

Ay, H., Benner, T., Arsava, E. M., Furie, K. L., Singhal, A. B., Jensen, M. B., Ayata, C., Towfighi, A., Smith, E. E., Chong, J. Y., Koroshetz, W. J., & Sorensen, A. G. (2007). A computerized algorithm for etiologic classification of ischemic stroke: The Causative Classification of Stroke System. Stroke, 38(11), 2979–2984.

Bishop, M. L., Duben-Engelkirk, J. L., & Fody, E. P. (2000). Clinical chemistry: Principles, procedures, correlations. Lippincott Williams and Wilkins, Baltimore.

Bui, T. M., Wiesolek, H. L., & Sumagin, R. (2020). ICAM-1: A master regulator of cellular responses in inflammation, injury resolution, and tumorigenesis. Journal of Leukocyte Biology, 108(3), 787–799.

Campbell, B. C. V., De Silva, D. A., Macleod, M. R., Coutts, S. B., Schwamm, L. H., Davis, S. M., & Donnan, G. A. (2019). Ischaemic stroke. Nature Reviews. Disease Primers, 5(1), 70.

Chen, W., Zhu, H. L., Shi, Y., Zhao, M. M., Wang, H., & Zeng, Y. Q. (2012). Comparative analysis on antioxidative ability of muscle between Laiwu pig and Large White. Asian-Australasian Journal of Animal Sciences, 25(8), 1190–1196.

Clark, W. M., Coull, B. M., Briley, D. P., Mainolfi, E., & Rothlein, R. (1993). Circulating intercellular adhesion molecule-1 levels and neutrophil adhesion in stroke. Journal of Neuroimmunology, 44(1), 123–125.

Dagnino, A. P. A., Campos, M. M., & Silva, R. B. M. (2020). Kinins and their receptors in infectious diseases. Pharmaceuticals, 13(9), 215.

Ehtesham, M., Mohmand, M., Raj, K., Hussain, T., Kavita, F., & Kumar, B. (2019). Clinical spectrum of hyponatremia in patients with stroke. Cureus, 11(8), e5310.

Fassbender, K., Mössner, R., Motsch, L., Kischka, U., Grau, A., & Hennerici, M. (1995). Circulating selectin- and immunoglobulin-type adhesion molecules in acute ischemic stroke. Stroke, 26(8), 1361–1364.

Feigin, V. L., Brainin, M., Norrving, B., Martins, S., Sacco, R. L., Hacke, W., Fisher, M., Pandian, J., & Lindsay, P. (2022). World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. International Journal of Stroke, 17(1), 18–29.

Gong, R., Tan, J. L., Liu, G., Liu, X. F., Ma, L., & Shi, S. (2025). Mechanism of disturbed endothelial cell function on angiogenesis following ischemic brain stroke (review). Experimental and Therapeutic Medicine, 29(4), 61.

Gresham, G. E., Phillips, T. F., Wolf, P. A., McNamara, P. M., Kannel, W. B., & Dawber, T. R. (1979). Epidemiologic profile of long-term stroke disability: The Framingham study. Archives of Physical Medicine and Rehabilitation, 60(11), 487–491.

Guyton, A. C., & Hall, J. E. (2015). Textbook of medical physiology. 12th edition. Elsevier Health Sciences.

Habas, K., & Shang, L. (2018). Alterations in intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1) in human endothelial cells. Tissue and Cell, 54, 139–143.

Hasan, T. F., Hasan, H., & Kelley, R. E. (2021). Overview of acute ischemic stroke evaluation and management. Biomedicines, 9(10), 1486.

Haupeltshofer, S., Mencl, S., Szepanowski, R. D., Hansmann, C., Casas, A. I., Abberger, H., Hansen, W., Blusch, A., Deuschl, C., Forsting, M., Hermann, D. M., Langhauser, F., & Kleinschnitz, C. (2024). Delayed plasma kallikrein inhibition fosters post-stroke recovery by reducing thrombo-inflammation. Journal of Neuroinflammation, 21(1), 155.

Hillmann, G., & Beyer, G. (1967). Schnellbestimung von Serum-Kalium Durch Trübungsmessung mit Kalignost nach Eiweissfällung [Rapid determination of serum potassium by turbidity measurement with kalignost after protein precipitation]. Zeitschrift fur Klinische Chemie und Klinische Biochemie, 5(2), 93–94.

Hossain, M. F., Kharel, M., Husna, A. U., Khan, M. A., Aziz, S. N., & Taznin, T. (2023). Prevalence of electrolyte imbalance in patients with acute stroke: A systematic review. Cureus, 15(8), e43149.

Huang, L., Liu, M., Jiang, W., Ding, H., Han, Y., Wen, M., Li, Y., Liu, X., & Zeng, H. (2022). Bradykinin/bradykinin 1 receptor promotes brain microvascular endothelial cell permeability and proinflammatory cytokine release by downregulating Wnt3a. Journal of Biochemical and Molecular Toxicology, 36(12), e23213.

Kasner, S. E., Bath, P. M., Hill, M. D., Volpi, J. J., Giuffre, M., Masuoka, L., Wambeke, D., & Madeddu, P. R. (2025). Recombinant human tissue kallikrein-1 for treating acute ischemic stroke and preventing recurrence. Stroke, 56(3), 745–753.

Koh, Y., & Park, J. (2018). Cell adhesion molecules and exercise. Journal of Inflammation Research, 11, 297–306.

Lalkovičová, M., Bonová, P., Burda, J., & Danielisová, V. (2015). Effect of bradykinin postconditioning on ischemic and toxic brain damage. Neurochemical Research, 40(8), 1728–1738.

Lang, C. E., MacDonald, J. R., & Gnip, C. (2007). Counting repetitions: An observational study of outpatient therapy for people with hemiparesis post-stroke. Journal of Neurologic Physical Therapy, 31(1), 3–10.

Lau, J., Rousseau, J., Kwon, D., Bénard, F., & Lin, K. S. (2020). A systematic review of molecular imaging agents targeting bradykinin B1 and B2 receptors. Pharmaceuticals, 13(8), 199.

Mombouli, J. V., & Vanhoutte, P. M. (1995). Kinins and endothelial control of vascular smooth muscle. Annual Review of Pharmacology and Toxicology, 35, 679–705.

Moreau, M. E., Garbacki, N., Molinaro, G., Brown, N. J., Marceau, F., & Adam, A. (2005). The kallikrein-kinin system: Current and future pharmacological targets. Journal of Pharmacological Sciences, 99(1), 6–38.

Nielsen, H. H., Soares, C. B., Høgedal, S. S., Madsen, J. S., Hansen, R. B., Christensen, A. A., Madsen, C., Clausen, B. H., Frich, L. H., Degn, M., Sibbersen, C., & Lambertsen, K. L. (2020). Acute neurofilament light chain plasma levels correlate with stroke severity and clinical outcome in ischemic stroke patients. Frontiers in Neurology, 11, 448.

Ottenbacher, K. J., Smith, P. M., Illig, S. B., Linn, R. T., Ostir, G. V., & Granger, C. V. (2004). Trends in length of stay, living setting, functional outcome, and mortality following medical rehabilitation. The Journal of the American Medical Association, 292(14), 1687–1695.

Portolés, M. T., Catalá, M., Antón, A., & Pagani, R. (1996). Hepatic response to the oxidative stress induced by *E. coli* endotoxin: Glutathione as an index of the acute phase during the endotoxic shock. Molecular and Cellular Biochemistry, 159(2), 115–121.

Rakhimbaeva, G. S., & Abdurakhmonova, K. B. K. (2023). ICAM-1 and CRP as biomarkers of 3-month outcome in acute ischaemic stroke. BMJ Neurology Open, 5(2), e000516.

Ramthun, M., Mocelin, A. J., & Alvares Delfino, V. D. (2011). Hypernatremia secondary to post-stroke hypodipsia: Just add water! Nephrology Dialysis Transplantation Plus, 4(4), 236–237.

Relton, J. K., Beckey, V. E., Hanson, W. L., & Whalley, E. T. (1997). CP-0597, a selective bradykinin B2 receptor antagonist, inhibits brain injury in a rat model of reversible middle cerebral artery occlusion. Stroke, 28(7), 1430–1436.

Rex, D. A. B., Deepak, K., Vaid, N., Dagamajalu, S., Kandasamy, R. K., Flo, T. H., & Keshava Prasad, T. S. (2022). A modular map of bradykinin-mediated inflammatory signaling network. Journal of Cell Communication and Signaling, 16(2), 301–310.

Rex, D. A. B., Vaid, N., Deepak, K., Dagamajalu, S., & Prasad, T. S. K. (2022). A comprehensive review on current understanding of bradykinin in COVID-19 and inflammatory diseases. Molecular Biology Reports, 49(10), 9915–9927.

Rubattu, S., Ridker, P., Stampfer, M. J., Volpe, M., Hennekens, C. H., & Lindpaintner, K. (1999). The gene encoding atrial natriuretic peptide and the risk of human stroke. Circulation, 100(16), 1722–1726.

Rubattu, S., Stanzione, R., Di Angelantonio, E., Zanda, B., Evangelista, A., Tarasi, D., Gigante, B., Pirisi, A., Brunetti, E., & Volpe, M. (2004). Atrial natriuretic peptide gene polymorphisms and risk of ischemic stroke in humans. Stroke, 35(4), 814–818.

Sarker, M. H., Hu, D. E., & Fraser, P. A. (2000). Acute effects of bradykinin on cerebral microvascular permeability in the anaesthetized rat. The Journal of Physiology, 528(1), 177–187.

Schrier, R. W. (1990). Body fluid volume regulation in health and disease: A unifying hypothesis. Annals of Internal Medicine, 113(2), 155–159.

Sharma, J. N. (2014). Basic and clinical aspects of bradykinin receptor antagonists. Progress in Drug Research, 69, 1–14.

Supanc, V., Biloglav, Z., Kes, V. B., & Demarin, V. (2011). Role of cell adhesion molecules in acute ischemic stroke. Annals of Saudi Medicine, 31(4), 365–370.

Vink, R., Young, A., Bennett, C. J., Hu, X., Connor, C. O., Cernak, I., & Nimmo, A. J. (2003). Neuropeptide release influences brain edema formation after diffuse traumatic brain injury. Acta Neurochirurgica, Supplement, 86, 257–260.

Wang, J. Y., Zhou, D. H., Li, J., Zhang, M., Deng, J., Gao, C., Li, J., Lian, Y., & Chen, M. (2006). Association of soluble intercellular adhesion molecule 1 with neurological deterioration of ischemic stroke: The Chongqing Stroke Study. Cerebrovascular Diseases, 21, 67–73.

Wang, L., Chen, Y., Feng, D., & Wang, X. (2021). Serum ICAM-1 as a predictor of prognosis in patients with acute ischemic stroke. BioMed Research International, 2021, 5539304.

Wang, M., Zhang, Z., Liu, D., Karhunen, V., Georgakis, M. K., Ren, Y., Ye, D., Gill, D., & Liu, M. (2023). Soluble adhesion molecules and functional outcome after ischemic stroke: A Mendelian randomization study. Journal of Stroke and Cerebrovascular Diseases, 32(6), 107136.

Yakar, Ş., & Baykan, N. (2024). Association of potassium and sodium parameters with the type of stroke. Journal of Surgery and Medicine, 8(5), 81–84.

Yoon, C. H., Hur, J., Oh, I. Y., Park, K. W., Kim, T. Y., Shin, J. H., Kim, J. H., Lee, C. S., Chung, J. K., Park, Y. B., & Kim, H. S. (2006). Intercellular adhesion molecule-1 is upregulated in ischemic muscle, which mediates trafficking of endothelial progenitor cells. Arteriosclerosis, Thrombosis, and Vascular Biology, 26(5), 1066–1072.

Yuen, K. C. J., Sharf, V., Smith, E., Kim, M., Yuen, A. S. M., & MacDonald, P. R. (2022). Sodium and water perturbations in patients who had an acute stroke: Clinical relevance and management strategies for the neurologist. Stroke and Vascular Neurology, 7(3), 258–266.