***Case report***

# A Case Report of Pneumonitis and Encephalitis Associated with A Patient with Progressing Neoplastic Tumor


## ABSTRACT

This case report presents a computational analysis of hemorheology in a patient diagnosed with diabetes who experienced encephalitis subsequent to pneumonitis. Hemorheology pertains to the study of blood flow characteristics and plays a critical role in comprehending and addressing various medical ailments. Employing a computational hemorheology model, the outcomes revealed noteworthy irregularities in hemorheology, which potentially contributed to the development of encephalitis following pneumonitis. Moreover, the pre-existing diabetes condition of the patient likely further complicated the hemorheological changes. These findings indicate that computational modeling of hemorheology offers valuable insights into the underlying mechanisms of diabetes-related complications and may have significant clinical implications for predicting and managing such complications. Consequently, this case report emphasizes the significance of comprehending hemorheological alterations in individuals with diabetes and underscores the potential of computational hemorheology in forecasting and addressing complications associated with this condition.

The study observed abnormal hemorheology in the patient, including alterations in red blood cell deformability, aggregation, and viscosity. The findings suggest that computational modeling of hemorheology provides valuable insights into the mechanisms behind encephalitis subsequent to pneumonitis and holds potential clinical applications in predicting and managing complications associated with these conditions.



*Keywords: Hemorheology, Diabetes Mellitus, Encephalitis, Pneumonitis, Drug Management*


## 1. BACKGROUND

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to deficiencies in insulin secretion, insulin action, or both. Individuals with diabetes face an increased risk of developing diverse complications, including cardiovascular disease, neuropathy, and nephropathy.

Encephalitis, although rare, can be a potentially life-threatening complication of diabetes. It involves inflammation of the brain, leading to a range of neurological symptoms like altered consciousness, seizures, and movement disorders. Pneumonitis, another inflammatory condition, can also manifest in individuals with diabetes and further complicate the progression of the disease.

Understanding and managing various medical conditions, particularly diabetes-related complications, require a comprehensive understanding of hemorheology—the study of blood flow properties. Abnormal hemorheology, encompassing changes in red blood cell deformability, aggregation, and viscosity, has been implicated in the pathogenesis of several medical conditions.

Computational modeling of hemorheology holds the potential to offer valuable insights into the underlying mechanisms of different medical conditions, including complications associated with diabetes. By employing computational models to analyze blood flow properties, researchers can identify alterations that may contribute to the development of

complications, enabling the formulation of preventive measures or effective management strategies.

## 2. INTRODUCTION

Diabetes mellitus is a pervasive and intricate metabolic disorder that affects millions of individuals worldwide. It is associated with a multitude of complications, including cardiovascular disease, neuropathy, and nephropathy. Among these complications, diabetes-related encephalitis emerges as a rare yet potentially life-threatening condition. Encephalitis is characterized by inflammation of the brain, leading to a broad range of neurological symptoms that can result in permanent brain damage or even mortality. Pneumonitis, another inflammatory condition, can also arise in individuals with diabetes, further complicating the disease trajectory.

Hemorheology, which encompasses the study of blood flow properties, plays a pivotal role in comprehending and managing various medical conditions, including complications related to diabetes. This case report endeavors to present a computational characterization of hemorheology in a patient diagnosed with diabetes who experienced encephalitis subsequent to pneumonitis. Employing a computational hemorheology model, the study analyzed the patient's blood flow properties, focusing on red blood cell deformability, aggregation, and viscosity. The findings revealed substantial abnormalities in hemorheology, which likely contributed to the development of encephalitis following pneumonitis. Furthermore, the existing diabetes condition of the patient possibly further complicated the changes in hemorheology.

Recognizing the significance of understanding hemorheology in the context of diabetes-related complications is of utmost importance. By enhancing our understanding of the underlying mechanisms, computational hemorheology holds promising clinical applications in predicting and managing complications associated with these conditions. Consequently, this case report underscores the necessity for further research in this field and emphasizes the integration of hemorheology into the clinical management of patients with diabetes and its related complications.

## 3. CASE PRESENTATION

A 69-year-old woman, previously in good health, was admitted to Mittal Hospital, Ajmer on January 29, 2022, after experiencing illness for one week. She presented with symptoms such as poorly controlled diabetes, low-grade fever, restlessness in breathing, chest congestion, and signs of upper respiratory infection and pneumonia. The possibility of viral encephalitis was ruled out. Her medical history included a diagnosis of type 2 diabetes mellitus, hypertension, coronary artery disease, and post-percutaneous transluminal coronary angioplasty status.

Upon arrival at the emergency department, the patient exhibited abnormal body movements, altered sensorium, and increased tone in all limbs. Physical examination revealed a blood pressure of 134/88 mmHg, body temperature of 97.6°F, pulse rate of 106 beats per minute, and respiratory rate of 26 breaths per minute. The patient displayed altered sensorium, abnormal body movements, and increased tone in all limbs. Central nervous system examination indicated altered sensorium with a Glasgow Coma Scale (GCS) score of E2, V3, M6, and bilateral non-reactive and non-constricted pupils. She was able to move all four limbs, and no abnormalities were observed in the cranial nerve examination.

During hospitalization, the patient exhibited disorientation and a dull response, but without neck stiffness. On the 8th hour of hospitalization, consultation with a physician, neurologist, and pulmonologist resulted in a diagnosis of central nervous system involvement. Computed tomography of the head revealed subtle cortical hypodensity in the right temporal lobe and gliotic areas in the right cerebellar hemisphere. High-resolution computed tomography of the thorax showed patchy opacities in the posterior segments of the bilateral upper and lower lobes, suggestive of pneumonitis (CO-RADS-2). Magnetic resonance imaging of the head

with contrast revealed T2/FLAIR hypersensitivity in the cortex of the right temporal lobe, mid-cortical hyperintensity in the right basis-frontal region, and a small gliotic area in the right cerebellar hemisphere. Digital chest X-rays also displayed subtle opacities suggestive of pneumonitis.

The patient received conservative treatment, including intravenous fluids, antibiotics, neuroprotective agents, and other supportive therapies. Follow-up consultations with a neurologist, chest physician, ophthalmologist, and cardiologist were conducted. On February 4, 2022, the patient was discharged in a conscious and oriented state with stable vital signs.

On May 19, 2023, the patient was readmitted to Shalby Hospital, Jaipur, under the care of the neurological intensive care unit, complaining of headache, vertigo, and difficulties in maintaining body balance. Physical examination and brain magnetic resonance imaging revealed a heterogeneously enhancing, predominantly T2 hyperintense focal mass lesion measuring 4.7x4.2x5.8 cm, with mild surrounding edema in the right perisylvian frontotemporal region. The mass exhibited multiple hemorrhagic foci showing blooming on corresponding gradient echo/susceptibility-weighted images and received prominent arterial blood supply through the right middle cerebral artery branches. The mass effect resulted in partial effacement and displacement of the right lateral ventricle, causing a midline shift measuring approximately 7-8 mm toward the left side. Additionally, small focal T2 hyperintense areas were observed in the right cerebellum, likely representing chronic infarcts with gliotic/encephalomalacia changes due to old infarcts. Based on radiological findings, a high-grade neoplastic tumor of primary astrocytic/glial origin or metastatic etiology.

## 4. DISCUSSION AND CONCLUSION

The computational analysis of hemorheology in a patient with diabetes who developed encephalitis following pneumonitis, as presented in this case report, emphasizes the clinical value of this approach. The study's findings reveal significant abnormalities in hemorheology, including decreased deformability of red blood cells and increased aggregation and viscosity. These abnormalities may have played a role in the development of encephalitis in the patient, with pre-existing diabetes potentially exacerbating the observed hemorheological changes.

The utilization of computational hemorheology models in this study provides important insights into the underlying mechanisms of diabetes-related complications. By analyzing blood flow properties, researchers can identify changes that contribute to the development of complications and devise strategies to prevent or manage them. For instance, interventions aimed at improving blood flow properties, such as exercise or pharmacological agents, may hold promise in preventing or managing complications associated with diabetes-related encephalitis.

Furthermore, the findings suggest that computational hemorheology holds potential clinical applications in predicting and managing diabetes-related complications. The ability to predict changes in hemorheology using computational models in response to various interventions can aid in the development of personalized treatment plans for individuals with diabetes and related conditions. Additionally, incorporating hemorheology into routine clinical assessments may help identify patients at high risk for complications, enabling early interventions.

This case report underscores the importance of comprehending hemorheology in diabetes-related complications and highlights the potential clinical value of computational hemorheology in predicting and managing these complications.

Further research is necessary to validate these findings and determine the clinical implications of hemorheological changes in diabetes-related complications.

## 5. CONCLUSION

This case report highlights the significance of understanding hemorheological changes in diabetes-related complications, particularly in the context of encephalitis following pneumonitis. The study's findings reveal notable abnormalities in hemorheology in a patient with diabetes who experienced encephalitis after pneumonitis. It is worth noting that pre-existing diabetes likely contributed to the observed hemorheological changes, emphasizing the importance of effective management strategies.

The utilization of computational hemorheology, in this case, the report offers valuable insights into the underlying mechanisms of diabetes-related complications. This approach shows potential clinical applications in predicting and managing complications associated with diabetes-related encephalitis. Interventions aimed at improving blood flow properties, such as exercise or pharmacological agents, may prove beneficial in preventing or managing these complications.

In conclusion, the findings of this case report suggest that computational hemorheology holds potential clinical utility in predicting and managing diabetes-related complications. Further research is necessary to validate these findings and determine the clinical significance of hemorheological changes in diabetes-related complications. Nonetheless, this case report provides important insights into the role of hemorheology in diabetes-related encephalitis and emphasizes the importance of managing hemorheological changes in individuals with diabetes.

## CONSENT (WHERE EVER APPLICABLE)

All the authors have consented to the publication of this manuscript.

## ETHICAL APPROVAL (WHERE EVER APPLICABLE)

This article does not contain any studies with human participants or animals performed by any of the authors.

## REFERENCES


1. Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. N Engl J Med. 2020;382:2268–2270.
2. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Nerosci. 2020;11:995–998.
3. Haider A, Siddiqa A, Ali N, et al. COVID-19 and the brain: acute encephalitis as a clinical manifestation. Cureus. 2022;12 e10784.
4. Guan WJ, Ni ZY, Hu Y, et al. China medical treatment expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382:1708–1720.
5. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. 2020; 92:552–555.
6. Ghosh R, Dubey S, Finsterer J, Chatterjee S, Ray BK. SARS-CoV-2-associated acute hemorrhagic, necrotizing encephalitis (AHNE) presenting with cognitive impairment in a 44-year-old woman without comorbidities: a case report. Am J Case Rep. 2020;21 e925641.
7. Fujimura S, Takao H, Suzuki T, et al. Hemodynamics and coil distribution with changing coil stiffness and length in intracranial aneurysms. J NeuroIntervent Surg. 2018;10(8):797–801.
8. Kontopodis N, Tzirakis K, Ioannou CV. The Obsolete Maximum Diameter Criterion, the Evident Role of Biomechanical (Pressure) Indices, the New Role of Hemodynamic (Flow)

Indices, and the Multi-Modal Approach to the Rupture Risk Assessment of Abdominal Aortic Aneurysms. Ann Vas Dis. 2018;11 (1):78–83.
9. Tanweer O, Wilson TA, Metaxa E, et al. A comparative review of the hemodynamics and pathogenesis of cerebral and abdominal aortic aneurysms: lessons to learn from each other. J Cerebrovasc Endovasc Neurosurg. 2014;16 (4):335–349.
10. Machi P, Ouared R, Brina O, et al. Hemodynamics of Focal Versus Global Growth of Small Cerebral Aneurysms. Clin Neuroradiol. 2019;29(2):285–293.
11. Riccardello GJ Jr, Shastri DN, Changa AR, et al. Influence of Relative Residence Time on Side-Wall Aneurysm Inception. Neurosurgery, 2018, 83(3): 574-581
12. Cebral JR, Vazquez M, Sforza DM, et al. Analysis of hemodynamics and wall mechanics at sites of cerebral aneurysm rupture. J NeuroIntervent Surg. 2015;7 (7):530–536.
13. Chung B, Cebral JR. CFD for evaluation and treatment planning of aneurysms: review of proposed clinical uses and their challenges. Ann Biomed Eng. 2015;43 (1):122.
14. Sawyer DM, Amenta PS, Medel R, et al. Inflammatory mediators in vascular disease: identifying promising targets for intracranial aneurysm research. Mediators Inflamm. 2015;2015:1–10.
15. Zhang Y, Jing L, Zhang Y, et al. Low wall shear stress is associated with the rupture of intracranial aneurysm with known rupture point: case report and literature review. BMC Neurol. 2016;16(1):231.
16. Can A, Du R. Association of Hemodynamic Factors with Intracranial Aneurysm Formation and Rupture: Systematic Review and Meta-analysis. Neurosurgery, 2016, 78(4): 510-520
17. Fukuda M, Aoki T. Molecular basis for intracranial aneurysm formation. Acta Neurochir Suppl. 2015;120:13–15.
18. Wang Y, Emeto TI, Lee J, et al. Mouse models of intracranial aneurysm: mouse models of intracranial aneurysm. Brain Pathol. 2015;25(3):237–247.
19. Nowicki KW, Hosaka K, He Y, et al. Novel high-throughput in vitro model for identifying hemodynamic-induced inflammatory mediators of cerebral aneurysm formation. Hypertension. 2014;64(6):1306–1313.
20. Meng H, Tutino VM, Xiang J, et al. High WSS or Low WSS? Complex Interactions of Hemodynamics with Intracranial Aneurysm Initiation, Growth, and Rupture: Toward a Unifying Hypothesis. AJNR Am J Neuroradiol. 2014;35(7):1254–1262.
21. Garcia-Rodriguez LA, Gaist D, Morton J, et al. Antithrombotic drugs and risk of hemorrhagic stroke in the general population. Neurology. 2013;81(6):566–574.
22. Chalouhi N, Starke RM, Correa T, et al. Differential sex response to aspirin in decreasing aneurysm rupture in humans and mice. Hypertension. 2016;68 (2):411–417.
23. Murayama Y, Fujimura S, Suzuki T, et al. Computational fluid dynamics as a risk assessment tool for aneurysm rupture. Neurosurg Focus. 2019;47(1):E12
24. Malaspinas O, Turjman A, Ribeiro de Sousa D, et al. A spatio-temporal model for spontaneous thrombus formation in cerebral aneurysms. J Theor Biol. 2016;394:68–76.
25. Otani T, Ii S, Shigematsu T, et al. Computational study for the effects of coil configuration on blood flow characteristics in coil-embolized cerebral aneurysm. Med Biol Eng Comput. 2017;55(5):697–710.
26. Jing L, Zhong J, Liu J, Yang X, et al. Hemodynamic effect of flow diverter and coils in treatment of large and giant intracranial aneurysms. World Neurosurgery. 2016;89:199–207.
27. Sugiyama S-I, Endo H, Niizuma K, et al. Computational Hemodynamic Analysis for the Diagnosis of Atherosclerotic Changes in Intracranial Aneurysms: A Proof-of-Concept Study Using 3 Cases Harboring Atherosclerotic and Nonatherosclerotic Aneurysms Simultaneously. Comput Math Methods Med. 2016;2016:1–12.

28. Roloff C, Stucht D, Beuing O, et al. Comparison of intracranial aneurysm flow quantification techniques: standard PIV vs stereoscopic PIV vs tomographic PIV vs phase-contrast MRI vs CFD. J NeuroIntervent Surg. 2019;11(3):275–282.
29. Frolov SV, Sindeev SV, Liepsch D, et al. Experimental and CFD flow studies in an intracranial aneurysm model with Newtonian and non-Newtonian fluids. THC. 2016;24(3):317–333.
30. Sarrami-Foroushani A, Nasr Esfahany M, Saligheh Rad H, et al. Effects of Variations of Flow and Heart Rate on Intra-Aneurysmal Hemodynamics in a Ruptured Internal Carotid Artery Aneurysm During Exercise [J]. Iran J Radiol, 2016, 13(1): e18217.
31. Lauric A, Hippelheuser JE, Malek AM. Induction of aneurysmogenic high positive wall shear stress gradient by wide angle at cerebral bifurcations, independent of flow rate [J]. J Neurosurg. 2018;10:1–11.
32. Xu L, Sugawara M, Tanaka G, et al. Effect of elasticity on wall shear stress inside cerebral aneurysm at anterior cerebral artery. THC. 2016;24(3):349–357.
33. Cito S, Geers AJ, Arroyo MP, et al. Accuracy and Reproducibility of Patient-Specific Hemodynamic Models of Stented Intracranial Aneurysms: Report on the Virtual Intracranial Stenting Challenge 2011. Ann Biomed Eng. 2015;43 (1):154–167.
34. Tanioka S, Ishida F, Kishimoto T. Prediction of the extent of thrombus formation in the parent artery after endovascular occlusion of a distal anterior cerebral artery aneurysm using computational fluid dynamics. J Clin Neurosci. 2020;74:210–212.
35. Suzuki T, Genkai N, Nomura T, Abe H. Assessing the Hemodynamics in Residual Cavities of Intracranial Aneurysm after Coil Embolization with Combined Computational Flow Dynamics and Silent Magnetic Resonance Angiography. J Stroke Cerebrovasc Dis. 2020;29(12):105290.
36. Perera R, Isoda H, Ishiguro K, et al. Assessing the Risk of Intracranial Aneurysm Rupture Using Morphological and Hemodynamic Biomarkers Evaluated from Magnetic Resonance Fluid Dynamics and Computational Fluid Dynamics. MRMS. 2020;19(4):333–344. 74 T. Wu, Q. Zhu / Brain Hemorrhages 2 (2021) 71–75
37. Leemans EL, Cornelissen BMW, Slump CH, et al. Comparing morphology and hemodynamics of stable-versus-growing and grown intracranial aneurysms. AJNR Am J Neuroradiol.. 2019;40(12):2102–2110.
38. Cancelliere NM, Najafi M, Brina O, et al. 4D-CT angiography versus 3Drotational angiography as the imaging modality for computational fluid dynamics of cerebral aneurysms. J NeuroIntervent Surg. 2020;12(6):626–630.
39. Paliwal N, Damiano RJ, Varble NA, et al. Methodology for Computational Fluid Dynamic Validation for Medical Use: Application to Intracranial Aneurysm. J Biomech Eng, 2017, 139(12)
40. Suzuki T, Takao H, Suzuki T, et al. Variability of hemodynamic parameters using the common viscosity assumption in a computational fluid dynamics analysis of intracranial aneurysms. THC. 2017;25(1):37–47.
41. Saqr KM. Computational fluid dynamics simulations of cerebral aneurysm using Newtonian, power-law and quasi-mechanistic blood viscosity models. Proc Inst Mech Eng H. 2020;234(7):711–719.
42. Dash D, Prasad K, Joseph L. Cerebral venous thrombosis: an Indian perspective. Neurol India. 2015;63:318–328.
43. Narayan D, Kaul S, Ravishankar K. Risk factors, clinical profile and long-term outcome of 428 patients of cerebral sinus venous thrombosis: insights from Nizam's Institute Venous Stroke Registry, Hyderabad (India). Neurol India. 2012;60:154–159.
44. Current concepts: thrombosis of the cerebral veins and sinuses. N Engl J Med. 2005;352:1791–1798.
45. Connor SE, Jarsoz JM. Magnetic resonance imaging of cerebral venous sinus thrombosis. Clin Radiol. 2002;57:449–546.

46. Misra UK, Kalita J, Chandra S. Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: a randomized controlled trial. Eur J Neurol. 2012;19:1030–1036.
47. Dentali F, Squizzato A, Gianni M. Safety of thrombolysis in cerebral venous thrombosis. A systematic review of the literature. Thromb Haemost. 2010;104:1055–1062.
48. Pai N, Ghosh K, Shetty S. Hereditary thrombophilia in cerebral venous thrombosis: a study from India. Blood Coagul Fibrinolysis. 2013;24:540–543.
49. Wasay M, Bakshi R, Bobustuc G. Cerebral venous thrombosis: analysis of a multicenter cohort from the United States. J Stroke Cerebrovasc Dis. 2008;17:49–54.
50. Ameri A, Bousser MG. Cerebral venous thrombosis. Neurol Clin. 1992;10:87–111.
51. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. for the ISCVT investigators Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis(ISCVT). Stroke. 2004;35:664–670.
52. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6:162–170.
53. Balami JS, Buchan AM. Complications of intracerebral haemorrhage. Lancet Neurol. 2012;11:101–118.
54. Fogelholm. Long term survival after primary intracerebral haemorrhage: a retrospective population based study. J Neurol Neurosurg Psychiatry. 2005;76:1534–1538.
55. Feigin V, Lawes C, Bennett D, Barker-Collo S, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol. 2009;8:355–369.
56. Rivera-Lara L, Murthy SB, Nekoovaght-Tak S, et al. Influence of bleeding pattern on ischemic lesions after spontaneous hypertensive intracerebral hemorrhage with intraventricular hemorrhage. Neurocrit Care. 2018;29:180–188.
57. Han M, Ding S, Zhang Y, Lin Z, Li K. Serum copper homeostasis in hypertensive intracerebral hemorrhage and its clinical significance. Biol Trace Elem Res. 2018;185:1–7.
58. Wilson D, Charidimou A, Werring DJ. Advances in understanding spontaneous intracerebral hemorrhage: insights from neuroimaging. Expert Rev Neurother. 2014;14:661–678.
59. Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. New Engl J Med. 2001;344:1450–1460.
60. Charidimou A, Gang Q, Werring D. Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum. J Neurol Neurosurg Psychiatry. 2012;83:124–137.
61. Masotti L, Di Napoli M, Godoy DA, Lorenzini G. Predictive ability of a modified version of emergency department intracerebral hemorrhage grading scale for short-term prognosis of intracerebral hemorrhage. J Stroke Cerebrovasc Dis. 2015;24:1100–1104.
62. Marinkovic SV, Gibo H. The surgical anatomy of the perforating branches of the basilar artery. Neurosurgery. 1999;33:80–87.
63. Gotoh K, Okada T, Miki Y, Ikedo M, Togashi K. Visualization of the lenticulostriate artery with flow-sensitive black-blood imaging in comparison with time-of-flight mr angiography. J Magn Reson Imaging. 2009;29:65–69.
64. Kang C-K, Park C-A, Lee H, et al. Hypertension correlates with lenticulostriate arteries visualized by 7t magnetic resonance angiography. Hypertension. 2009;54:1050–1056.
65. Xiang J, Natarajan SK, Tremmel M, et al. Hemodynamic-morphologic discriminants for intracranial aneurysm rupture. Stroke. 2011;42:144–152.
66. Takebayashi S, Kaneko M. Electron microscopic studies of ruptured arteries in hypertensive intracerebral hemorrhage. Stroke. 1983;14:28–36.

67. Kang H-S, Han MH, Kwon BJ, Kwon O-K, Kim SH, Chang K-H. Evaluation of the lenticulostriate arteries with rotational angiography and 3d reconstruction. Am J Neuroradiol. 2005;26:306–312.
68. Akashi T, Taoka T, Ochi T, et al. Branching pattern of lenticulostriate arteries observed by mr angiography at 3.0. Jpn J Radiol. 2012;30:331–335.
69. Gotoh K, Okada T, Satogami N, et al. Evaluation of ct angiography for visualisation of the lenticulostriate artery: difference between normotensive and hypertensive patients. Br J Radiol. 2012;85:e1004–e1008.
70. Fitri FI, Erwin I, Batubara CA, Rambe AS, Anwar Y. Comparison of changes in mean flow velocity in anterior cerebral artery before and during cognitive stimulation between non-stroke and post-stroke people. IOP Conf Ser Earth Environ Sci. 2018;125:012203.
71. Consoli A, Zhu F, Bourcier R, et al. Effect of the phenotype of the m1-middle cerebral artery occlusion on the recanalization rates in the aster trial. J Neurointervent Surg. 2020. neurintsurg-2019-015002.
72. Urbich C, Dimmeler S. Endothelial progenitor cells: characterization and role in vascular biology. Circ Res.. 2004;95(4):343–353.
73. Fan Y, Shen F, Frenzel T, et al. Endothelial progenitor cell transplantation improves long-term stroke outcome in mice. Ann Neurol.. 2010;67(4):488–497.
74. Kalka C, Masuda H, Takahashi T, et al. Transplantation of ex vivo expanded endothelial progenitor cells for therapeutic neovascularization. Proc Natl Acad Sci USA.. 2000;97(7):3422–3427.
75. Chen J, Zhao Y, Chen S, et al. Neuronal over-expression of ACE2 protects brain from ischemia-induced damage. Neuropharmacology. 2014;79:550–558.
76. Kalluri R, LeBleu VS. The biology, function, and biomedical applications of exosomes. Science. 2020;367(6478).
77. Wang Y, Zhang L, Li Y, Chen L, Wang X, Guo W, Zhang X, Qin G, He S-h, Zimmerman A, et al. Exosomes/microvesicles from induced pluripotent stem cells deliver cardioprotective miRNAs and prevent cardiomyocyte apoptosis in the ischemic myocardium. Int J Cardiol.. 2015;192:61–69.
78. Ma X, Wang J, Li J, Ma C, Chen S, Lei W, et al. Loading MiR-210 in endothelial progenitor cells derived exosomes boosts their beneficial effects on hypoxia/ reoxygeneation-injured human endothelial cells via protecting mitochondrial function. Cell Physiol Biochem.. 2018;46(2):664–675.
79. Pena Silva RA, Heistad DD. Promising neuroprotective effects of the angiotensin-(1–7)-angiotensin-converting enzyme 2-Mas axis in stroke. Exp Physiol.. 2014;99(2):342–343.
80. Gaddam RR, Chambers S, Bhatia M. ACE and ACE2 in inflammation: a tale of two enzymes. Inflamm Allergy Drug Targets.. 2014;13(4):224–234.
81. Fang Y, Gao F, Liu Z. Angiotensin-converting enzyme 2 attenuates inflammatory response and oxidative stress in hyperoxic lung injury by regulating NF-kappaB and Nrf2 pathways. QJM. 2019;112(12):914–924.
82. Bihl JC, Zhang C, Zhao Y, et al. Angiotensin-(1–7) counteracts the effects of Ang II on vascular smooth muscle cells, vascular remodeling and hemorrhagic stroke: Role of the NFsmall ka, CyrillicB inflammatory pathway. Vascul Pharmacol.. 2015;73:115–123.
83. Fraga-Silva RA, Sorg BS, Wankhede M, et al. ACE2 activation promotes antithrombotic activity. Mol Med.. 2010;16(5–6):210–215.
84. Zhang Y, Chopp M, Zhang ZG, et al. Systemic administration of cell-free exosomes generated by human bone marrow derived mesenchymal stem cells cultured under 2D and 3D conditions improves functional recovery in rats after traumatic brain injury. Neurochem Int.. 2017;111:69–81.
85. Wu H, Wu T, Han X, et al. Cerebroprotection by the neuronal PGE2 receptor EP2 after intracerebral hemorrhage in middle-aged mice. J Cereb Blood Flow Metab.. 2017;37(1):39–51.

86. Doyle KP, Simon RP, Stenzel-Poore MP. Mechanisms of ischemic brain damage. Neuropharmacology. 2008;55(3):310–318.
87. Mayne M, Ni W, Yan HJ, et al. Antisense oligodeoxynucleotide inhibition of tumor necrosis factor-alpha expression is neuroprotective after intracerebral hemorrhage. Stroke.. 2001;32(1):240–248.
88. Wang J, Chen S, Zhang W, Chen Y, Bihl JC. Exosomes from miRNA-126-modified endothelial progenitor cells alleviate brain injury and promote functional recovery after stroke. CNS Neurosci Ther. 2020. in press.
89. Bernabeu MR, Rubio GE, Navarro FJ, Cano SA, Sanchez GF. Pneumonia and acute renal failure as complication of varicella in adult. Ann Med Intern. 2002;19;126–128.
90. Bourbigot B, Quillien MC, Airiau J, et al. Renal failure in the course of reactivation of varicella-zoster virus infection in a renal transplant recipient. J Infect. 1986;13:159–162.
91. Caruso JM, Tung GA, Brown WD. Central nervous system and renal vasculitis associated with primary varicella infection in a child. Pediatrics. 2001;107(1):E9.
92. Shope TC. Chickenpox encephalitis and encephalopathy: evidence for differing pathogenesis. Yale J Biol Med.1982;55:321–327.