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Arterial blood gas analysis predicts futile recanalization in mechanical thrombectomy-treated acute ischemic stroke patients: a multicenter study

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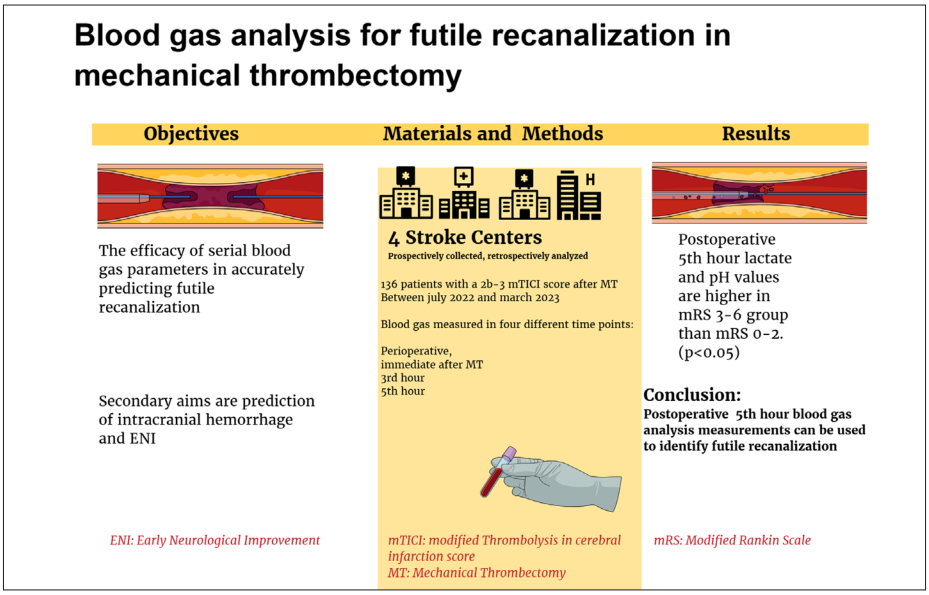
Abstract. – OBJECTIVE: It is known that providing recanalization alone in large vessel occlusions is not sufficient to provide a good 90-day clinical outcome. It is advocated that neuroprotection should be increased before endovascular treatment and that the penumbra should be protected from reperfusion damage after recanalization. However, the effects of blood gas parameters before and after mechanical thrombectomy on clinical outcomes are not clear. The objective of this study is to assess the effectiveness of serial blood gas measures in accurately predicting futile recanalization at an early stage.

PATIENTS AND METHODS: This study is a multicenter inquiry that collected data in a prospective manner and analyzed it retrospectively. Patients with a 2b-3 thrombolysis in cerebral infarction (TICI) score after mechanical thrombectomy for recanalization were consecutively analyzed from July 2022 to March 2023. Arterial blood gas parameters, including pH, oxygen saturation (SaO_2), partial carbon dioxide pressure ($PaCO_2$), partial oxygen pressure (PaO_2), lactate, and bicarbonate (HCO_3), were measured at four time points: before mechanical thrombectomy treatment (preoperative), immediately after recanalization (postoperative 1st), during the 3rd hour (postoperative 3rd), and at the 5th hour (postoperative 5th). The patients were categorized into groups based on their modified Rankin Scale (mRS) scores.



Blood gas analysis for futile recanalization in mechanical thrombectomy

Objectives

The efficacy of serial blood gas parameters in accurately predicting futile recanalization

Secondary aims are prediction of intracranial hemorrhage and ENI

ENI: Early Neurological Improvement

Materials and Methods

4 Stroke Centers
Prospectively collected, retrospectively analyzed

136 patients with a 2b-3 mTICI score after MT
Between july 2022 and march 2023

Blood gas measured in four different time points:

Perioperative,
immediate after MT
3rd hour
5th hour

mTICI: modified Thrombolysis in cerebral infarction score
MT: Mechanical Thrombectomy

Results

Postoperative 5th hour lactate and pH values are higher in mRS 3-6 group than mRS 0-2. (p<0.05)

Conclusion:
Postoperative 5th hour blood gas analysis measurements can be used to identify futile recanalization

mRS: Modified Rankin Scale

Graphical Abstract. Aims and structure of the study.

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RESULTS: The study included 136 patients with an average age of 69.71±11.22. The postoperative 1st-hour SaO_2 values were lower in the mRS 3-6 group (*p*=0.038). The postoperative pH and lactate mean were greater in the mRS 3-6 group than in the 0-2 group (*p*=0.038 and 0.018, respectively). In logistic regression, a unit rise in lactate increased poor functional outcomes 1,632 times (*p*=0.024). Early neurological recovery was associated with decreased postoperative 3rd-hour lactate (*p*=0.014). The mean postoperative PaO_2 (average of 1, 2, 3 PaO_2) was higher in those with symptomatic cerebral bleeding (*p*=0.044).

CONCLUSIONS: Monitoring lactate and pH levels in AIS patients who have had mechanical recanalization can be utilized to predict mortality and morbidity, especially in the first five hours after the procedure.

Key Words:

Blood gas analysis, Hyperoxia, Intracranial hemorrhage, Lactate, Oxygen saturation, Thrombectomy.

Introduction

Mechanical thrombectomy, or MT, is now widely acknowledged as a conventional therapy for acute stroke[1]. By employing state-of-the-art methods and advanced technology, recanalization rates of approximately 92% have been successfully attained. However, extensive research and meta-analyses[2], such as the HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke) meta-analysis, have demonstrated that the rates of favorable functional outcomes after three months vary between 46% and 51%. Consequently, the process called "futile recanalization" occurs when recanalization does not lead to a beneficial functional outcome. Neuroprotection is thought to be necessary to protect the penumbral tissue from reperfusion damage and prevent the expansion of the ischemic core after recanalization. This action would be taken to preempt the potential manifestation of the aforementioned scenario. Currently, there is a lack of a thorough study into the precise impact of blood gas parameters on mechanical thrombectomy in cases of acute ischemic stroke (AIS)[3].

To safeguard the penumbral tissue before recanalization, a neuroprotective mechanism entails enhancing blood oxygenation. Normobaric oxygen therapy (NBO), through its ability to enhance tissue oxygenation, has been demonstrated in various experimental studies to mitigate blood-brain barrier damage, decrease cerebral infarction volume, and enhance neurological impairment scores[4-7]. Conversely, it is believed to exacerbate the ischemic reperfusion injury that follows recanalization.

Blood gas analysis is a highly reliable tool that has demonstrated its effectiveness in both scoring systems and diagnostic algorithms. During a stroke where a large blood vessel is impeded, the flow of blood to the brain ceases, leading to a significant reduction in the delivery of oxygen and glucose to the affected area[8]. An intense and significant ion exchange is observed in the affected region[9]. Consequently, the anaerobic process is activated, resulting in alterations in the distribution of ion concentration within the bloodstream, which serves as an indication of ischemia[8]. The ischemic cascade arises due to numerous intricate mechanisms. Monitoring these rapid alterations in arterial blood gas levels can serve as a quick, effortless, and efficient approach to anticipate the occurrence of ischemia and assess neurological prognosis. Studies[10,11] have demonstrated that regional changes in pH, acid-base balance, and ion exchange take place gradually. Several studies[12-16] have been carried out on ischemic stroke, exploring its etiology, frequency, risks, predictive factors, and treatment modalities, as documented in the current scientific literature. However, no study has been conducted to observe and evaluate the neuroprognosis after successful recanalization in acute ischemic stroke through serial blood gas monitoring and changes.

This study primarily aimed to assess the influence of blood gas parameters on the clinical outcome 90 days after AIS and large vessel occlusion (LVO). The secondary aims were to precisely determine the impact of changes in serial blood gas parameters on early neurological improvement (ENI), as indicated by National Institutes of Health Stroke Scale (NIHSS) score improvement of more than 4 points at the 24th hour and symptomatic intracranial hemorrhage (sICH).

Patients and Methods

Study Design and Patient Selection

This prospectively collected, retrospectively analyzed study was held in 4 stroke centers between July 2022 and March 2023, and 150 consecutive patients presenting with LVO were screened with computed tomography angiography (CTA) performed at admission. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and approved by the Kartal Dr. Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Decision No.: 2023/514/254/29, Date: 19.07.2023).

The inclusion criteria were as follows:

1. Age ≥ 18 years,
2. Clinical diagnosis of AIS with anterior large vessel occlusion (proximal or distal internal carotid artery, M1 segment of Middle Cerebral Artery (MCA M1), M2 segment of Middle Cerebral Artery (MCA M2), anterior cerebral artery horizontal or pre-communicating segment (ACA A1), anterior cerebral artery vertical, post-communicating or infracallosal segment (ACA A2) or tandem occlusion;
3. Baseline NIHSS scores between 4-25 and Alberta Stroke Program Early CT (ASPECT) scores between 6-10;
4. Intra-arterial treatment with direct aspiration, stent retriever, or a combination of a stent retriever and aspiration;
5. Achievement of successful recanalization (TICI 2b-3).

The exclusion criteria were as follows:

1. Vascular recanalization after mechanical thrombectomy with TICI 0-2A;
2. Incomplete blood gas parameters;
3. Prestroke modified Rankin Scale (mRS) ≥3;
4. Having active and chronic obstructive pulmonary disease, such as chronic obstructive pulmonary disease, obstructive sleep apnea, and acute respiratory distress syndrome;
5. Decompensated congestive heart failure;
6. Severe hepatic or renal dysfunction.

A total of 136 patients with AIS met the study-selection criteria and were included in the analysis. Ten patients were excluded from the study due to unsuccessful recanalization (TICI 0-2A), and 4 patients were excluded due to missing blood gas parameters.

Clinical Data

Demographic characteristics of all patients, potential risk factors for stroke such as coronary artery disease (CAD), diabetes, hypertension, hyperlipidemia, atrial fibrillation, smoking and alcohol use, stroke severity, and intervention procedure were noted. Initial and discharge neurological status was assessed by the NIHSS score, and functional independence was assessed at discharge and at 90 days by the mRS score.

Patients who were suitable for intravenous thrombolysis were started on recombinant tissue plasminogen activator (rt-PA) at a dose of 0.9 mg/kg in the emergency department and underwent angiography. When vascular recanalization occurred, the remaining dose was not given. All endovascular procedures were performed using local anesthesia, with or without the administration of sedative agents. The interventional strategy was based on operator preference as direct aspiration, stent-retriever, or a combination of stent retriever and aspiration technique.

Imaging Assessment

Brain computed tomography (CT) and CT angiography were analyzed, and admission ASPECT scores and large vessel occlusions were noted. Post-procedural target vessel recanalization status was graded according to the modified Thrombolysis in Cerebral Infarction (mTICI) score on the final angiogram, and successful recanalization was defined as an mTICI score of 2b or 3. Ischemic or hemorrhagic areas, if any, were confirmed with control CT 24 hours after the procedure. It was noted whether the presence of bleeding was symptomatic. ASPECT and mTICI scores were evaluated by a blinded interventional neurologist.

Assessment of Blood Gas Parameters

All patients were monitored continuously in terms of 12-lead electrocardiogram, blood pressure, and saturation throughout the procedure. Mean arterial pressure and systolic and diastolic values were recorded every 15 minutes. The highest and lowest systolic and highest and lowest diastolic blood pressures and their averages were noted. Arterial blood gas analysis was performed immediately before the procedure (preoperative), immediately after recanalization (postoperative 1st hour), at the 3rd hour (postoperative 3rd hour), and at the 5th hour (postoperative 5th). The values of pH, partial oxygen pressure (PaO_2), oxygen saturation (SaO_2), partial carbon dioxide pressure ($PaCO_2$), bicarbonate (HCO_3), and lactate were documented.

Outcome Measures

The primary outcome measure was the modified Rankin Scale at 90 days. The 90-day outcome was assessed by either examination in the outpatient clinic or contact by phone. A score of 3-6 on the mRS in the third month following admission was considered a poor outcome.

Secondary outcome measures included ENI, as indicated by NIHSS score improvement of more than 4 points at the 24th hour, and sICH.

Statistical Analysis

Statistical analysis was performed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The conformity of the variables to the normal distribution was examined by histogram graphics and the Kolmogorov-Smirnov test. While presenting descriptive analysis, mean, standard deviation, median, IQR, and min-max values were used. Categorical variables were compared with the Pearson Chi-square test. The Mann-Whitney U test was utilized when evaluating no normally distributed (nonparametric) variables between two groups, and the Kruskal-Wallis test was used when evaluating differences between more than two groups. The results with a *p*-value below 0.05 were considered statistically significant.

Results

The study included a total of 136 patients who underwent successful mechanical thrombectomy. Among them, 71 (52.21%) were male and 65 (47.79%) were female. The mean age of the patients was 69.71±11.22. Modalities of treatment and patient characteristics are listed in Table I.

Considering the comorbidities, the most common were hypertension (n=95) and diabetes mel-

Table I. Modalities of treatment and patient characteristics of the study.

		n/mean±s.d.	**Median % (min-max)**
Gender	Male	71	(52.21)
	Female	65	(47.79)
Age		69.71 ± 11.22	71 (28-91)
mRS score		2.38 ± 1.95	2 (0-6)
mRS score groups	0-2	76	(55.88)
	3-5	45	(33.09)
	6	15	(11.03)
Medical treatment history	Not taking medication	58	(42.65)
	Antiaggregant	47	(34.56)
	Anticoagulant	28	(20.59)
	Both of them	3	(2.21)
Early neurological improvement	No	55	(40.44)
	Yes	81	(59.56)
TICI score after thrombectomy	0	0	(.00)
	1	0	(.00)
	2A	0	(.00)
	2B	16	(11.76)
	2C	38	(27.94)
	3	82	(60.29)
Intravenous tpa administration	No	117	(86.03)
	Yes	19	(13.97)
Occlusion side	Right	78	(57.35)
	Left	58	(42.65)
Occlusion site	MCA M1	86	(63.24)
	MCA M2	8	(5.88)
	Cervical or distal segment of ICA (I.L.T occlusion)	16	(11.76)
	Tandem	26	(19.12)
Thrombectomy technique	Aspiration	27	(19.85)
	Stent retriever	2	(1.47)
	Combination of aspiration and stent retriever	107	(78.68)
Need for intubation during the procedure	No	133	(97.79)
	Yes	3	(2.21)
Anesthesia procedure	Local anesthesia	110	(80.88)
	Neurosedation	26	(19.12)

Continued

Table I ***(Continued).*** Modalities of treatment and patient characteristics of the study.

		n/mean±s.d.	**Median % (min-max)**
Neurosedation during the procedure	No	124	(91.18)
	Yes	12	(8.82)
Procedure-related complications	No	134	(98.53)
	Vascular dissections	1	(.74)
	Vascular perforations	1	(.74)
Symptomatic intracranial hemorrhage	No	119	(87.50)
	Yes	17	(12.50)
Admission NIHSS		14.07 ±3.93	15 (5-26)
24th hour NIHSS		8.88 ± 6.36	8 (0-31)
Admission ASPECT		8.82 ± 1.15	9 (6-10)
Onset to admission time		183.54 ± 138.28	168 (10-780)
Admission to imaging time		17.78 ± 9.16	16 (0-69)
Imaging to puncture time		48.23 ± 29.98	39 (10-171)
Puncture to recanalization time		49.57 ± 25.79	43.5 (15-143)
Symptom onset to recanalization time		299.12 ± 136.05	279 (110-960)
Admission to puncture time		66.74 ± 33.79	56.5 (14-235)
Imaging to recanalization time		94.75 ± 42.87	90 (3-217)

mRS: Modified Rankin Scale; TICI: Thrombolysis in cerebral infarction; IV r-tPA: Intravenous recombinant tissue plasminogen activator; MCA M1: M1 segment of Middle Cerebral Artery; MCA M2: M2 segment of Middle Cerebral Artery; Distal ICA: Distal Segment of İnternal Carotid Artery; NIHSS: National Institutes of Health Scale Score.

litus (n=49). The rate of CAD was higher in those with mRS scores of 3-6 than in those with scores of 0-2 (n=23, 38.33%, n=13, 17.11% $p=0.005$).

The most common occlusion site was the mean cerebral artery (MCA) M1 segment (n=86). Depending on the operator's preference, the most frequently used technique was a combination of aspiration and a stent retriever (n=107). The anesthesia procedure most commonly employed was local anesthesia (n=110). Two procedure-related complications were observed: vascular dissection in one patient and vascular perforation in another patient. Seventeen patients (12.5%) developed symptomatic intracranial hemorrhage following the procedure. While the admission NIHSS score was 14.07±3.93, the NIHSS score decreased to 8.88±6.36 24 hours after treatment.

When the age, admission NIHSS and 24th-hour NIHSS scores were compared between the mRS groups, the admission NIHSS and 24th-hour NIHSS averages were found to be higher in the mRS 3-6 group than in the mRS 0-2 group (admission NIHSS 13.38±4.17 and 14, 95±3.45 $p=0.039$; 24th-hour NIHSS 7.07±5.19 and 11.17±6.98 $p=0.001$).

The ASPECT score was 8.82±1.15. The onset to admission time was 183.54±138.28 min (n/mean±s.d), the admission to CT time was 17.78±9.16 min, the imaging to puncture time was 48.23±29.98 min, and the onset to recanalization time was 299.12±136.05 min. Admission, preoperative, and perioperative mean arterial pressure values were compared. No significant difference was found between the mRS 0-2 and mRS 3-6 groups.

To compare the effects of preoperative and postoperative blood gas parameters on morbidity and mortality they were grouped as mRS 0-2 and mRS 3-5 and 6. No significant difference was detected between the groups in preoperative blood gas parameters ($p>0.05$). The postoperative 5th-hour $PaCO_2$ of patients with mRS 0-2 (36.28±5.68 mmHg) in blood gas was significantly higher than that of patients with mRS 3-5 (36.1±6.46 mmHg) and mRS 6 (32.33±5.52 mmHg) ($p=0.046$). In the same blood gas, the lactate levels of those with mRS 6 (1.95±0.96) were significantly higher than those of those with mRS 0-2 (1.34±0.76) and mRS 3-5 (1.6±0.94) ($p=0.039$).

The mRS 0-2 and mRS 3-6 groups were compared to observe the effect of blood gas parameters before and after endovascular treatment on poor outcomes (Table II).

No significant difference was detected between the groups in preoperative blood gas parameters. SaO_2 in postoperative 1st-hour blood gas was lower in those with mRS 3-6 than in those with mRS 0-2 ($p=0.038$). Additionally, the postoperative 5th-hour lactate and pH values of those with mRS 3-6 were higher than those with mRS 0-2 ($p=0.034$ and $p=0.018$, respectively).

Regression analysis was performed on variables affecting the status of mRS 3-6. A one-unit increase in postoperative 3rd-hour blood gas lactate value increased mRS 3-6 by 1.632 times (*p*=0.024) (Table III).

Effect of Blood Gas Parameters on Early Neurological Improvement

We examined whether there was a relationship between the ENI and preoperative and postoperative blood gas parameters. There was no significant difference between the groups in preoperative blood gas parameters. However, when looking at the relationship between postoperative blood gas values and ENI, the postoperative 5th-hour blood gas lactate was lower than the others (without ENI 1.79±1.09, with ENI 1.3±0.61, *p*=0.014).

Regression analysis was performed on variables affecting early recovery status. Accordingly, a one-unit increase in the postoperative 3rd-hour lactate value reduced early improvement by 0.50 times (*p*=0.003).

Effect of Blood Gas Parameters on Symptomatic Intracranial Hemorrhage

The effect of preoperative and postoperative blood gas parameters on symptomatic intracranial hemorrhage was examined. No significance was detected between the groups (*p*>0.005). However, when the mean postoperative 5th-hour blood gas analysis was taken, the mean PaO_2 was significantly higher than in those without symptomatic intracranial hemorrhage (without symptomatic hemorrhage: 96.39±25.77, with symptomatic hemorrhage 111.49±30.66 *p*=0.044).

Regression analysis was performed on variables affecting symptomatic intracranial hemorrhage. A one-unit increase in the mean postoperative PaO_2 value increases the risk of bleeding by 1.018 times (*p*=0.038). The key findings of the study are demonstrated in Figure 1.

Table II. Results of preoperative and postoperative blood gas parameters according to mRS 0-2 and 3-6 groups.

	mRS		
	0-2 n/mean ± s.d.	**3-6 n/mean ± s.d.**	***p***
Preoperative pH	7,39 ± 0.05	7.39 ± 0.06	0.901
Preoperative HCO_3 (mmol/L)	23.42 ± 2.83	23.38 ± 2.85	0.828
Preoperative Lactate (mmol/L)	1.64 ± 0.78	1.72 ± 1.05	0.982
Preoperative SaO_2 (%)	94.97 ± 6.03	94.92 ± 3.81	0.550
Preoperative PaO_2 (mmHg)	92.74 ± 36.08	95.47 ± 46.76	0.823
Preoperative $PaCO_2$ (mmHg)	37.23 ± 5.95	37.81 ± 6.59	0.278
Postop 1st pH	7.47 ± 0.39	7.4 ± 0.08	0.964
Postop 1st HCO_3 (mmol/L)	23.34 ± 5.01	22.92 ± 3.08	0.969
Postop 1st Lactate (mmol/L)	1.57 ± 0.83	1.62 ± 0.95	0.809
Postop 1st SaO_2 (%)	95.91 ± 6.26	95.43 ± 3.31	**0.038***
Postop1st PaO_2 (mmHg)	90.35 ± 24.28	98.96 ± 44.59	0.808
Postop 1st $PaCO_2$ (mmHg)	36.03 ± 5.69	37.68 ± 6.4	0.054
Postop 3rd pH	7.39 ± 0.05	7.39 ± 0.06	0.309
Postop 3rd HCO_3 (mmol/L)	22.8 ± 3.24	23.34 ± 2.49	0.292
Postop 3rd Lactate (mmol/L)	1.4 ± 0.7	1.75 ± 0.95	0.056
Postop 3rd SaO_2 (%)	96.88 ± 2.88	95.99 ± 3.32	0.054
Postop 3rd PaO_2 (mmHg)	100.23 ± 28.97	94.37 ± 32.93	0.104
Postop 3rd $PaCO_2$ (mmHg)	37.35 ± 9.47	36.39 ± 5.8	0.943
Postop 5th pH	7.38 ± 0.04	7.4 ± 0.07	**0.034***
Postop 5th HCO_3 (mmol/L)	22.92 ± 3.05	23.34 ± 3.05	0.154
Postop 5th Lactate (mmol/L)	1.34 ± 0.76	1.69 ± 0.95	**0.018***
Postop 5th SaO_2 (%)	97.28 ± 2.31	96.86 ± 2.69	0.406
Postop 5th PaO_2 (mmHg)	100.53 ± 25.48	106.3 ± 56.75	0.539
Postop 5th $PaCO_2$ (mmHg)	36.28 ± 5.68	35.15 ± 6.41	0.217

*Mann Whitney-U test. mRS: Modified Rankin Scale, HCO_3: Bicarbonate, SaO_2: Oxygen Saturation, PaO_2: Parsiel Oxygen Pressure, $PaCO_2$: Parsiel Carbondioxide Pressure, SO_2: Oxygen saturation, Postop 1st: Postoperatively measured in blood gas immediately after recanalization, Postop 3th: Postoperatively measured in blood gas at 3 hours after recanalization, Postop 5th: Postoperatively measured in blood gas at 5 hours after recanalization.

Table III. Logistic regression analysis to determine the variables that influence the likelihood of having a modified Rankin Scale (mRS) score of 3-6.

MRS 3-6	B	Sig.	Exp (B)	95% C.I. for Exp (B)	
				Lower	Upper
Postop 1st SaO_2 (%)	-0.018	0.596	0.982	0.918	1.051
Postop 5th pH	6.381	0.050	590.570	0.993	351,082.445
Postop 5th lactate (mmol/L)	0.490	**0.024***	1.632	1.065	2.502

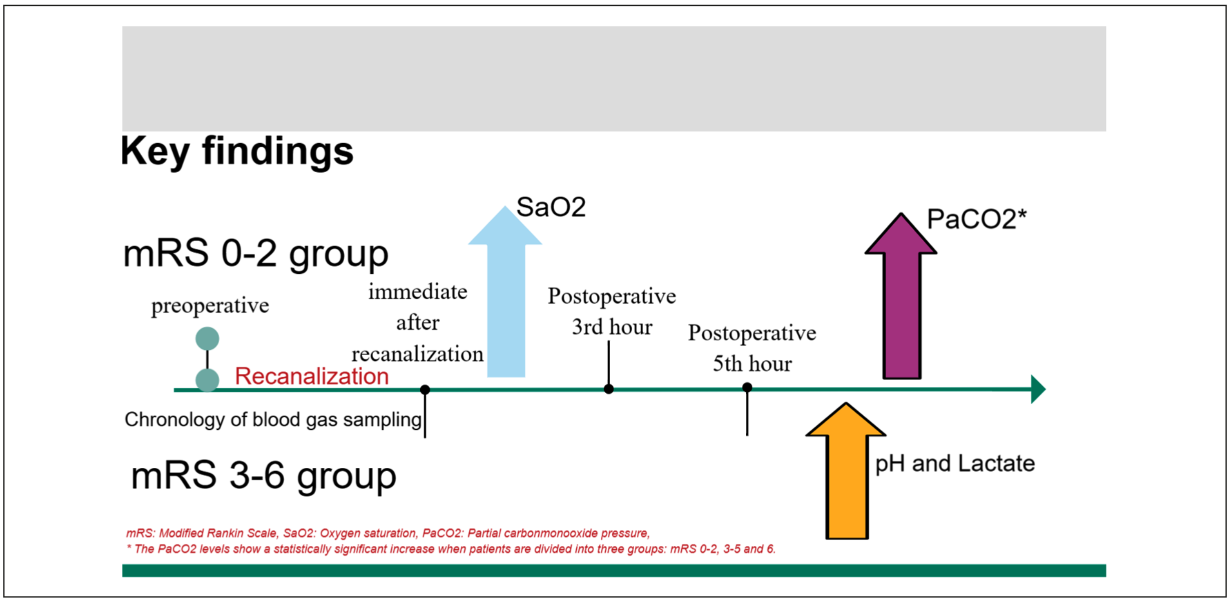
*Logistic regression. Postop 1st SaO_2: Oxygen saturation measured in blood gas immediately after recanalization, Postop 5th pH: pH level measured in blood gas at 5 hours after recanalization, Postop 5th lactate: lactate level measured in blood gas at 5 hours after recanalization.

Discussion

The key findings of our study are as follows: patients with a score of 6 on the modified Rankin Scale (mRS) had significantly higher postoperative 5th-hour lactate levels than those with scores of 0-2 and 3-5 (*p*=0.039). Additionally, patients with scores of 0-2 on the mRS had significantly higher postoperative 5th-hour $PaCO_2$ levels in blood gas than those with scores of 3-5 and 6 (*p*=0.046).

When comparing the mRS 0-2 group with the mRS 3-6 group to examine the impact of blood gas parameters on poor outcomes, it was found that patients with mRS 3-6 had lower immediate postoperative 1st-hour SaO_2 values (*p*=0.038). Furthermore, the pH levels and lactate levels at the 5th hour after recanalization were significantly increased in the mRS 3-6 group. A 0.50-fold reduction in early recovery was observed for each one-unit increase in the postoperative 5th-hour lactate value (*p*=0.003). Conversely, a 1.018-fold increase in the risk of symptomatic intracranial hemorrhage was associated with each one-unit increase in the postoperative PaO_2 mean value (average of postoperative, postoperative 3rd-, and 5th-hour PaO_2) (*p*=0.038).

After cerebral ischemia, limited oxygen promotes anaerobic glycolysis, and pyruvate is reduced to lactate, causing lactic acidosis. The resulting lactate is transmitted from astrocytes to neurons and used as an effective energy source. Thus, it serves as an alternative energy substrate in place of glucose under



mRS: Modified Rankin Scale, SaO2: Oxygen saturation, PaCO2: Partial carbonmonooxide pressure,
* The PaCO2 levels show a statistically significant increase when patients are divided into three groups: mRS 0-2, 3-5 and 6.

Figure 1. Key findings of the study.

various conditions[17]. A study[18] was conducted on patients with acute ischemic stroke and transient ischemic attack to examine the relationship between blood lactate levels measured at baseline, the 24th-hour, the 72nd-hour, and the 7th-day and the 3rd-month modified Rankin Scale (mRS). The study found no correlation between these blood lactate levels and the 3rd-month mRS. Similarly, there was no correlation observed between cerebrospinal fluid measurements and the 3rd-month mRS. In another study[19], it was shown that increased lactate was correlated with increased infarct volume in measurements made using measurement of intracranial pressure (ICP) and micro dialysis in large middle cerebral artery infarction. Using magnetic resonance spectroscopy, Graham et al[20] demonstrated lactate accumulation in ischemic lesions in acute stroke patients. In a study[21] aiming to show the relationship between venous blood lactate level and prognosis, an admission blood lactate value above 2 mmol/L was accepted as hyperlactatemia. This has been shown to correlate with 3-month mortality and poor prognosis. In our blood gas samples, the average lactate level was higher in the postoperative 3rd- and postoperative 5th-hour in patients with mRS 6 (p=0.039). At the same time, when regression analysis was performed with variables affecting early recovery, it was seen that a one-unit increase in the postoperative 5th-hour lactate value reduced early recovery by 0.50 times (p=0.003).

Although the co-occurrence of lactate accumulation and acidic pH levels is common, it has been shown, especially in experimental studies[22,23], that physiological pH values and even alkaline pH changes can also be detected. After reversible cerebral ischemia and in experimental brain tumors, an increase in lactate may be accompanied by a physiological tissue pH or even an alkaline pH shift[18]. Zhao et al[23] showed in their study that the proximal/femoral pH ratio before EVT was associated with early recovery of neurological function after endovascular treatment. In our study, the postoperative 5th-hour pH value of patients with poor functional outcomes after reperfusion was higher than the postoperative 3rd-hour pH value of patients of functionally independent patients.

During acute ischemia, glucose transport decreases, and lactate production and carbon dioxide levels increase, causing acidosis. As a result, these disorders lead to excitotoxicity and the release of reactive oxygen species, resulting in cytogenic edema and permanent cellular death[24]. Changes in arterial $PaCO_2$ can affect cerebrovascular tone, thereby affecting cerebral blood flow (CBF) and cerebral blood volume (CBV) by altering extravascular pH. On the one hand, hypercapnia can help deliver oxygen and nutrients to brain tissue by increasing blood flow to the brain during ischemia when blood flow is reduced or blocked. This may aid in limiting the extent of damage caused by the ischemic event. On the other hand, excessive carbon dioxide elevation can increase intracranial hemorrhage[25]. However, studies in literature have generally been conducted on the effect of CO_2 on acute brain injury. There is no study that evaluates the effect of CO_2 in pretreatment and post-treatment reperfusion processes in acute ischemic stroke. Focusing on oxygenation and carbon dioxide (CO_2), Scudellari et al[26] aimed to identify ventilation strategies with better neurological outcomes in AIS patients undergoing MT. In 6 articles that met the inclusion criteria, the correlation between CO_2 targets and neurological outcomes was examined, and it was stated that there was a potential relationship between intraoperative hypocapnia during MT and worse neurological outcomes. It was mentioned that hypocapnia negatively affects prognosis in all completed studies, and it was criticized that all of them were retrospective and single-centered[26-28]. Consistent with the literature, the postoperative 5th-hour $paCO_2$ average of those with mRS 0-2 was higher than that of those with mRS 6 (p=0.046).

It is known that hypoxia increases morbidity and mortality in stroke patients and causes areas with insufficient blood supply, such as the penumbra, to progress toward infarction. As stated in the AHA/ASA guidelines[29], the target SaO_2 should not be below 94%. In the study of Cheng et al[30], after MT received high-flow NBO by a Venturi mask (FiO_2 50%, flow 15 L/min) or routine low-flow oxygen supplementation by nasal cannula (flow 3 L/min) after vessel recanalization for 6 h, patients were compared. As a result, it was stated that NBO treatment was effective in improving 3-month functional results, reducing mortality, and reducing infarct volumes[31]. In our study, when we looked at the patients with poor functional results (mRS 3-6 group), it was seen that their postoperative SaO_2 values were lower (p=0.038).

Hyperoxia, on the other hand, is seen to have both beneficial and harmful results by triggering pro-inflammatory and anti-inflammatory reactions, especially in the predominant organs, such as the lung, brain, and eye[32] . After a successful mechanical thrombectomy, reperfusion is ensured, and adequate blood flow and oxygen are carried out. However, excess oxygen stimulates the formation of free radicals and increases hypoperfusion caused by vasoconstriction, potentially exacerbating brain damage[31,33]. The Normobaric Oxygen Therapy Study in Acute Ischemic Stroke conducted by Parr et al[28] was terminated early after 85 out of 240 patients were admitted due to the reported increase in mortality in the high-flow oxygen group. To understand the effect of hyperoxia on functional recovery, López et al[32] divided the patients into 2 groups: $PaO_2 \leq 120$ mmHg and $PaO_2 > 120$ mmHg after mechanical thrombectomy. mRS and mortality rates were higher in the hyperoxia group than in the $PaO_2 \leq 120$ mmHg group. However, the limitations of this study were that it was an observational study, supplemental oxygen applied until the beginning of MT was not homogeneous, and there was only a single ICU admission blood gas analysis in the study[32].

The occurrence of symptomatic intracranial hemorrhage (SICH) presents a significant safety issue in endovascular therapy for acute ischemic stroke. This indicates that the incidence of post-reperfusion HT in patients recanalized with IV-TPA and/or MT therapy is 10 times higher than that in spontaneous recanalization[33,34]. Many factors, such as cardioembolic stroke, poor collateral circulation, long procedure time, multiple passes with a stent retriever device, high initial neutrophil rate, and low ASPECT score, are risk factors for HT. Therefore, the incidence of symptomatic HT varies between 0.6 and 20%[35]. In our study, when the postoperative average PaO_2 was examined, the PaO_2 of patients with bleeding was higher (No: 96.39±25.77, Yes: 111.49±30.66, $p=0.044$). When regression analysis was performed on the variables affecting the occurrence of bleeding, it was determined that a one-unit increase in the mean postoperative PaO_2 (mean 1-2-3) value increased the occurrence of symptomatic intracranial hemorrhage by 1.018 times ($p=0.038$).

Limitations

One of the limitations of our study is that blood gases were taken from the femoral artery, and their levels in the ischemic tissue after thrombus are unknown. In a study conducted by Spears et al[25], systemic blood and cerebral blood parameters were compared during thrombectomy, and it was observed that PaO_2, $PaCO_2$, and bicarbonate levels in systemic blood were significantly higher. Apart from this, our study was a retrospective, multicenter study with a small sample size. Additionally, our cohort represents stroke patients who were successfully recanalized with MT therapy, and our results may not be extrapolated to the entire stroke patient population. To confirm our results, a larger number of patients with AIS should be evaluated.

Futile recanalization is a term used to describe an unsuccessful restoration of blood flow following mechanical thrombectomy. Through this identification, patients can receive more structured and purposeful treatment following MT. Predicting the occurrence of ineffective restoration of blood flow can be advantageous for both patients and neuroscientists. Blood gas analysis is a simple, rapid, cost-effective, minimally invasive, and readily available method for predicting futile recanalization.

Conclusions

Serial blood gas analysis measurements can be used to identify futile recanalization. Comparing blood gas analysis initially and after 3 and 5 hours of mechanical thrombectomy can be particularly advantageous. Clinicians may derive advantages from observing the crucial factors for predicting futile recanalization, especially the levels of lactate and pH at the 5th hour, as indicated by our findings. Through this methodology, clinicians are able to anticipate the requirements of patients at an early stage, enabling them to administer treatment that is more targeted toward specific goals.

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Informed Consent

Not applicable, due to the retrospective nature of the study.

Ethics Approval

The study was approved by the Kartal Dr. Lutfi Kırdar City Hospital Clinical Research Ethics Committee (Decision No.: 2023/514/254/29, Date: 19/07/2023).

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Conflict of Interest

The authors declare no conflict of interest.

Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Aysenur Onalan, Erdem Gurkas, Cetin Kursad Akpinar, Turkan Acar and Ozlem Aykac. The first draft of the manuscript was written by Aysenur Onalan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of Data and Materials

The datasets provided in this study are available upon request by the corresponding author.

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