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Effect of Amantadine Therapy on Neurological and Laboratory Outcomes in Post-Cardiac Arrest Intensive Care Patients: A Retrospective Analysis

Kardiyak Arrest Sonrası Yoğun Bakım Hastalarında Amantadin Tedavisinin Nörolojik ve Laboratuvar Sonuçlar Üzerine Etkisi: Retrospektif Bir Analiz

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Abstract

Background: Cardiopulmonary arrest (CPA) is a major public health issue due to its high mortality and risk of severe neurological impairment. This retrospective study investigated the impact of amantadine on neurological recovery, mortality, and inflammatory biomarkers in patients who achieved return of spontaneous circulation (ROSC) after CPA and were admitted to the intensive care unit (ICU).

Materials and Methods: This retrospective observational study included patients aged 18-85 years who were admitted to the ICU after ROSC and stayed for at least six days between January 1, 2016, and December 31, 2020. Patients were divided into two groups: amantadine group (Group A, n=31) and control group (Group C, n=47). Demographics, GCS, CPC, and laboratory parameters (lactate, neutrophil, lymphocyte, NLR) were recorded on days 1, 2, 4, and 6. Statistical analysis was performed using SPSS 22.0.

Results: No significant differences were found between the groups in terms of age, sex, or CPR duration. Targeted temperature management was more common in Group A. While GCS, CPC, and inflammatory markers did not significantly differ between groups, lactate levels on day 6 were significantly lower in survivors. In non-survivors, day 2 neutrophil levels and day 4 NLR were significantly lower.

Conclusions: Amantadine may offer neuroprotective benefits, though statistical significance was not reached. Larger prospective studies are needed. Lactate, neutrophil, and NLR may be valuable prognostic indicators in post-CPA patients.

Keywords: Amantadine, Cardiopulmonary resuscitation (CPR), Glasgow Coma Scale (GCS), Neutrophil/lymphocyte ratio (NLR), Cerebral Performance Category (CPC), Neuroprotection

Öz

Amaç: Kardiyopulmoner arrest (KPA), yüksek mortalite ve ciddi nörolojik hasar riski nedeniyle önemli bir halk sağlığı sorunudur. Bu retrospektif çalışma, KPA sonrası spontan dolaşımın geri dönüşünü (ROSC) sağlayan ve yoğun bakım ünitesine (YBÜ) yatırılan hastalarda amantadin'in nörolojik iyileşme, mortalite ve inflamatuar biyomarkerlar üzerindeki etkisini araştırmıştır.

Materyal ve metod: Bu retrospektif gözlemsel çalışma, 1 Ocak 2016 ile 31 Aralık 2020 tarihleri arasında ROSC sonra yoğun bakım ünitesine yatırılan ve en az altı gün kalan 18-85 yaş arası hastaları içermiştir. Hastalar iki gruba ayrılmıştır: amantadin grubu (Grup A, n=31) ve kontrol grubu (Grup C, n=47). Demografik bilgiler, GCS, CPC ve laboratuvar parametreleri (laktat, nötrofil, lenfosit, NLR) 1., 2., 4. ve 6. günlerde kaydedilmiştir. İstatistiksel analiz SPSS 22.0 kullanılarak yapılmıştır.

Bulgular: Gruplar arasında yaş, cinsiyet veya KPR süresi açısından anlamlı bir fark bulunmadı. Hedeflenen sıcaklık yönetimi A grubunda daha yaygındı. GKS, CPC ve inflamatuar belirteçler gruplar arasında anlamlı farklılık göstermezken, 6. günde laktat seviyeleri hayatta kalanlarda anlamlı derecede daha düşüktü. Hayatta kalamayanlarda ise 2. gün nötrofil seviyeleri ve 4. gün NLR anlamlı derecede daha düşüktü.

Sonuç: Amantadin nöroprotektif faydalar sağlayabilir, ancak istatistiksel anlamlılığa ulaşılamamıştır. Daha büyük prospektif çalışmalara ihtiyaç vardır. Laktat, nötrofil ve NLO, KPA sonrası hastalarda değerli prognostik göstergeler olabilir.

Anahtar Kelimeler: Amantadin, Kardiyopulmoner resüsitasyon (CPR), Glasgow Koma Skalası (GKS), Nötrofil/lenfosit oranı (NLR), Serebral performans kategorisi (SPK), Nöroproteksiyon

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Introduction

Cardiopulmonary arrest (CPA) is a devastating clinical event associated with high mortality and significant neurological morbidity, posing a substantial burden on public health (1,2). Survival rates for out-of-hospital cardiac arrest remain low, with only about 10% surviving to hospital discharge, while in-hospital CPA cases show slightly higher rates of 22-25% (3-5). Ischemic cardiovascular diseases are the predominant cause of CPA in adults (6-8).

The period following Return of spontaneous circulation (ROSC) is characterized by systemic ischemic-reperfusion (IR) injury, a complex pathophysiological process involving hypoxia, global ischemia, and subsequent reperfusion. This leads to severe biochemical dysfunction and an exacerbated systemic inflammatory response, with pro-inflammatory mediators and the migration of immune cells like macrophages, neutrophils, and lymphocytes contributing to tissue damage (9).

Neurological injury, primarily hypoxic-ischemic encephalopathy and secondary inflammatory processes, is the leading cause of death and long-term disability in post-resuscitation intensive care patients (10). Current management strategies aim to mitigate this damage, with targeted temperature management (TTM) being a cornerstone neuroprotective intervention (11). TTM works by suppressing free oxygen radicals and cytotoxic inflammatory products associated with IR injury, thereby preventing neurological sequelae (10).

Neuroprotective agents are increasingly recognized for their potential role in treating brain injury. Amantadine, an NMDA receptor antagonist with dopaminergic properties, is frequently used in patients with acquired brain injury to enhance dopamine release and inhibit its reuptake in the central nervous system (12,13). Its multifaceted actions suggest a potential to accelerate neurological recovery and improve functional outcomes (14). Recent research continues to explore amantadine's neuroprotective potential across various neurological conditions (15,16).

Despite its theoretical benefits, the clinical efficacy of amantadine in the post-CPR period remains underexplored and not sufficiently proven. This study hypothesizes that amantadine treatment may improve neurological recovery and reduce mortality rates in post-CPR intensive care patients. By comparing patients who received amantadine with those who did not, this retrospective study aims to contribute to the understanding of amantadine's impact on clinical outcomes in this critical population. The primary outcome was neurological recovery (GCS, neurological status at discharge), and secondary outcomes included 28-day mortality and laboratory parameters (lactate, neutrophil, etc.). The findings are expected to inform future neuroprotective strategies and improve care standards for cardiac arrest survivors.

Materials and Methods

Ethical Approval and Study Design

This retrospective observational study was approved by the Interventional Clinical Research Ethics Committee of Harran University (approval no: HRU/21.13.13, date: July 05, 2021). Patient records from the anesthesia intensive care unit (ICU) of our hospital, admitted after CPR between January 1, 2016, and December 31, 2020, were reviewed via the hospital automation system.

Patient Selection

Inclusion criteria were:

- Adult patients aged 18-85 years.
- Confirmed ROSC after cardiopulmonary resuscitation.
- Monitored in intensive care for a minimum of 6 days.
- Patients both receiving and not receiving amantadine treatment.

Exclusion criteria were:

- Patients monitored in intensive care for less than 6 days.
- Cases of mortality within the first 6 days.
- Patients with incomplete laboratory data.

Data Collection and Grouping

A total of 155 patient records were retrospectively reviewed for eligibility. Following the application of predefined exclusion criteria, 77 patients were excluded from the analysis. The remaining 78 patients who met all inclusion criteria were allocated into two groups: the Amantadine Group (Group A, n=31) and the Control Group (Group C, n=47). The process of patient screening, exclusion, and final group assignment is summarized in the CONSORT flow diagram (Figure 1), which provides a visual representation of the enrollment and grouping methodology applied in this study.

Demographic data (age, gender), comorbidities, CPR duration, ICU length of stay, application of TTM, amantadine treatment status, neurological assessment scores [Glasgow Coma Scale (GCS), Cerebral Performance Category (CPC)], and laboratory findings [lactate, neutrophil, lymphocyte, neutrophil-lymphocyte ratio (NLR)] were collected for all patients.

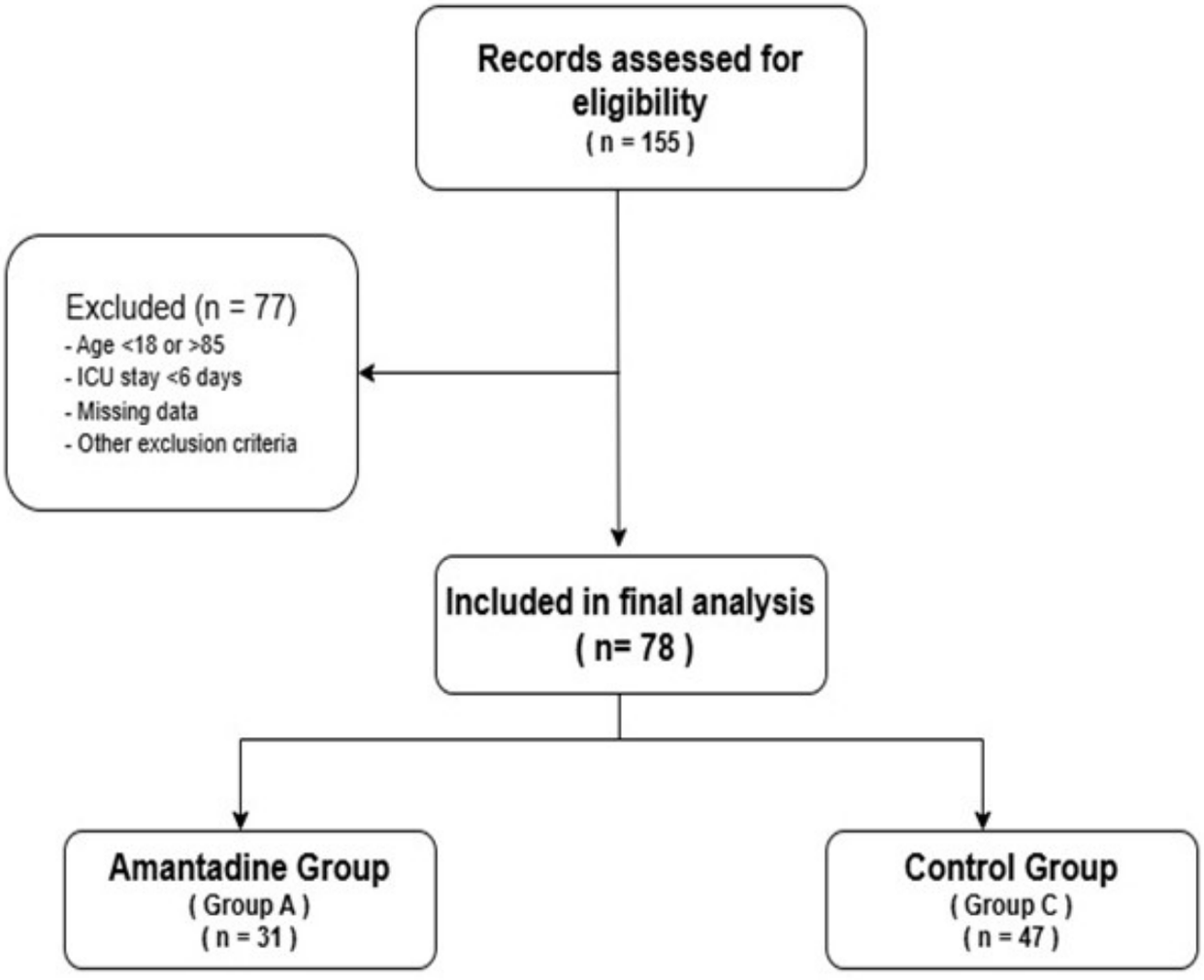

Figure 1. CONSORT flow diagram showing patient enrollment, exclusion criteria, and final grouping into the Amantadine (Group A) and Control (Group C) arms

Amantadine Treatment Protocol

Patients in Group A received intravenous amantadine sulfate (PK-MERZ, Merz Pharmaceuticals GmbH, Frankfurt, Germany) at a dose of 200 mg, twice daily, for five consecutive days (17). Doses remained constant throughout the treatment period.

Lactate, neutrophil, lymphocyte, NLR values, and GCS were recorded for both groups at specific time points: day 1, day 2, day 4, and day 6.

Statistical Analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences) 22.0. The Shapiro-Wilk test assessed the normality of continuous numerical variables. Data were presented as mean ± standard deviation, number, and percentage (%). The non-parametric chi-square test was used for comparing percentages of categorical variables between groups. Independent Sample T-test was applied for normally

distributed measurements, while the Mann-Whitney U test was used for non-normally distributed measurements. Repeated Measures ANOVA with Bonferroni correction was utilized for comparing repeated measurements within the same group. A p-value <0.05 was considered statistically significant.

Results

Demographic Characteristics of Patients

A total of 78 patients were included (Group A: n=31, Group C: n=47). Mean age was 57.6±20.8 years in Group A and 63.8±16.4 years in Group C, with no significant age difference (p= 0.234). Gender distribution was also similar (p=0.488). TTM was applied significantly more often in Group A (51.6%) compared to Group C (27.7%) (p=0.032), suggesting a potential neuroprotective advantage for Group A.

No significant differences were observed between the groups regarding CPR duration, ICU length of stay, discharge status, and CPC scores (p>0.05). The mean time to amantadine treatment initiation in Group A was 3.36±2.60 days. Table 1 summarizes these findings.

Table 1. Comparison of demographic information of patients between groups

Variables	**Grup A (n=31)**	**Grup C (n=47)**	**P değeri**
Age (years) (mean ± SD)	57.61±20.80	63.81±16.42	0.234*
Gender (number/%) Female Male	 14 (45.2) 17 (54.8)	 25 (53.2) 22 (46.8)	0.488**
TTM (number/%) Applied Not applied	 16 (51.6) 15 (48.4)	 13 (27.7) 34 (72.3)	**0.032****
CPR duration (min) (mean ± SD)	18.29±10.61	17.72±7.90	0.937*
Length of stay (days) (mean ± SD)	32.32±33.85	30.68±31.51	0.992*
Outcome (number /%) Ward transfer Deceased	 4 (12.9) 27 (87.1)	 5 (10.6) 42 (89.4)	 0.759**
CPC (number/%) Score 1 - 2 Score 3 - 5	 4 (12.9) 27 (87.1)	 3 (6.4) 44 (93.6)	 0.324**

n: Number of patients, SD: Standard deviation, CPC: Cerebral performance category, *Mann-Whitney U test, ** Chi-square test

Neurological Recovery and Laboratory Parameters

No statistically significant differences were observed in GCS scores between Group A and Group C on days 1, 2, 4, and 6 (p>0.05). Similarly, within-group comparisons did not reveal significant temporal changes in GCS values across time points (p>0.05). At discharge, the number of patients with a favorable neurological outcome (CPC 1-2) was 4 (12.9%) in Group A and 3 (6.4%) in Group C, with no statistically significant difference between the groups (p=0.324) (Table 2).

Table 2. Comparison of Glasgow Coma Scale between groups			
	GCS (mean ± SD)		**p***
	Amantadine (+) (n=31)	**Amantadine (-) (n=47)**	
GCS day 1	3.96±1.25	4.00±1.35	0.916
GCS day 2	4.64±2.07	4.14±1.36	0.206
GCS day 4	4.90±2.18	4.31±1.49	0.164
GCS day 6	5.19±2.56	4.44±1.93	0.147
p**	0.074	0.135	
n: Number of patients, SD: Standard deviation, GCS: Glasgow Coma Scale, * Independent Sample T-test, **Repeated measures ANOVA			

Regarding laboratory parameters, no significant intergroup differences were found in lactate, neutrophil, lymphocyte, or NLR levels on any of the recorded days (p>0.05). As shown in Table 3, inflammatory markers were comparable between groups at each time point.

Comparison of Surviving and Deceased Patients

A total of 9 patients (11.5%) were discharged alive, while 69 patients (88.5%) died. As shown in Table 3, comparisons between surviving and deceased patients revealed the following statistically significant findings:

- **Lactate level on day 6** was significantly lower in surviving patients (p=0.024).
- **Neutrophil level on day 2** was significantly lower in deceased patients (p<0.001).
- **Neutrophil-to-lymphocyte ratio (NLR) on day 4** was significantly lower in deceased patients (p=0.003).

These results suggest that lactate clearance and inflammatory markers such as neutrophil count and NLR may serve as useful prognostic indicators in post-cardiac arrest patients.

Table 3. Comparison of lactate, neutrophil, lymphocyte, and NLR values by mortality			
	Surviving (n=9) (mean ± SD)	**Deceased (n=69) (mean ± SD)**	**p***
Lactate (mmol/L)			
Lactate day 1	2.92±1.74	2.62±1.49	0.579
Lactate day 2	1.63±0.75	1.88±0.94	0.457
Lactate day 4	1.13±0.32	1.58±0.78	0.094
Lactate day 6	1.07±0.48	1.68±0.76	**0.024**
Neutrophil (10^3/mcL)			
Neutrophil day 1	17.88±9.15	14.99±7.73	0.305

Table 3. Continued			
Neutrophil day 2	21.08±12.83	12.31±5.11	**0.000**
Neutrophil day 4	13.82±5.59	10.69±6.23	0.157
Neutrophil day 6	11.60±4.41	10.66±5.94	0.652
Lymphocyte (10^3/mcL)			
Lymphocyte day 1	2.11±1.34	1.46±1.47	0.213
Lymphocyte day 2	1.31±0.52	1.13±0.71	0.486
Lymphocyte day 4	0.90±0.60	1.17±0.76	0.312
Lymphocyte day 6	1.56±0.62	1.26±0.76	0.261
NLR			
NLR day 1	14.33±14.42	16.95±15.69	0.636
NLR day 2	18.08±13.40	14.51±9.86	0.331
NLR day 4	22.52±17.24	11.85±8.28	**0.003**
NLR day 6	9.43±7.51	12.00±11.72	0.526
n: Number of patients, Mean: Mean, SD: Standard deviation, NLR: Neutrophil lymphocyte ratio, * Independent Sample T-test			

Discussion

This retrospective study aimed to evaluate the impact of amantadine treatment on neurological recovery and mortality in patients who achieved ROSC after CPR and were admitted to our intensive care unit. We compared laboratory parameters, GCS values, and clinical outcomes between patients receiving amantadine and those who did not. Our findings, while hinting at amantadine's potential to improve neurological outcomes, did not demonstrate statistically significant differences in GCS or CPC scores.

A notable finding was the significantly higher rate of TTM application in the amantadine group. Given TTM's established neuroprotective benefits, this represents a significant confounding factor, making it challenging to isolate the independent effect of amantadine. This highlights a critical limitation of retrospective designs and underscores the importance of controlling for such variables in future prospective studies (18).

In the broader literature, the most significant cause of mortality in ROSC patients post-CPR is hypoxic-ischemic encephalopathy, emphasizing the need for effective early neuroprotective strategies (10,19). Amantadine, with its dopaminergic and NMDA receptor antagonist properties, has been investigated for its wide-ranging effects in various conditions, including post-cardiac arrest syndrome (19). However, evidence regarding neurostimulant agents in the post-CPR period remains limited (20). A 2013 retrospective study by Reynolds et al. similarly explored methylphenidate and amantadine for stimulating reawakening in comatose post-cardiac arrest patients, concluding that prospective trials are needed (20). More recent studies continue to investigate amantadine's role, with some suggesting its potential in improving awakening in comatose patients resuscitated from cardiac arrest (17,21). However, a 2024 review indicated insufficient evidence to recommend specific drug therapy for comatose survivors of cardiac arrest (22).

While our study, consistent with some previous findings, did not find a statistically significant difference in neurological outcomes with amantadine, this could be attributed to the small sample size and the retrospective nature of the study. Previous research has shown amantadine to improve cognitive function and arousal in patients with traumatic brain injury and other disorders of consciousness (12,13,23,24). However, its specific

role in post-cardiac arrest patients requires further elucidation through robust clinical trials (25).

The observed differences in lactate, neutrophil, and NLR levels between surviving and deceased patients are particularly insightful. Lower lactate levels on day 6 in survivors, along with distinct patterns in neutrophil and NLR levels, reinforce their utility as prognostic indicators in this patient population (26-30). These biomarkers can aid in early risk stratification and guide clinical decision-making.

Limitations

This study is subject to several limitations. Firstly, its retrospective design inherently restricts the ability to establish definitive causality and fully control for all potential confounding variables. Secondly, the relatively small sample size and the imbalance between the amantadine and control groups (31 vs. 47) may have reduced statistical power, potentially leading to Type II errors (failure to detect a true effect). Thirdly, the lack of standardization in the timing of amantadine initiation and duration across all patients could introduce variability and bias. Finally, the significantly higher application rate of TTM in the amantadine group acts as a major confounding factor, making it challenging to attribute observed trends solely to amantadine. Future research should address these limitations through larger, prospective, and randomized controlled trials.

Conclusion

In conclusion, this retrospective study suggests a potential, albeit statistically non-significant, role for amantadine treatment in neurological recovery following cardiopulmonary resuscitation. The study reinforces the importance of prognostic biomarkers such as lactate, neutrophil, and NLR in post-cardiac arrest patients. Given the inherent limitations of a retrospective design and a small sample size, further large-scale, prospective, and randomized controlled trials are imperative to definitively ascertain the efficacy and safety of amantadine in this critical patient population. Such future studies must meticulously control for confounding factors like TTM to provide clearer and more conclusive insights into amantadine's neuroprotective potential.

Ethical Approval: *This retrospective observational study was approved by the Interventional Clinical Research Ethics Committee of Harran University (approval no: HRU/21.13.13, date: July 05, 2021).*

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Critical revision of manuscript: M.D.T., B.P., V.F.P., E.D.
Conflict of Interest: *The authors have no conflicts of interest to declare.*
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References

1. Graham R, McCoy MA SA. Strategies to Improve Cardiac Arrest Survival; Committee on the Treatment of Cardiac Arrest: Current Status and Future Directions; Board on Health Sciences Policy; Institute of Medicine. 1st ed. Washington, D.C.: National Academies Press; 2015.
2. Lynge TH, Risgaard B, Banner J, Nielsen JL, Jespersen T, Stampe NK, et al. Nationwide burden of sudden cardiac death: A study of 54,028 deaths in Denmark. Heart Rhythm 2021;18:1657-65.
3. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation 2017;135.
4. Meaney PA, Bobrow BJ, Mancini ME, Christenson J, de Caen AR, Bhanji F, et al. Cardiopulmonary Resuscitation Quality: Improving Cardiac Resuscitation Outcomes Both Inside and Outside the Hospital. Circulation 2013;128:417-35.
5. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart Disease and Stroke Statistics—2015 Update. Circulation 2015;131.
6. Love G, Haines C. Predicting Survival from In - Hospital CPR: An Update. Med Res Arch 2020;8. https://doi.org/10.18103/mra.v8i3.2038.
7. Joundi RA, Rabinstein AA, Nikneshan D, Tu J V., Fang J, Holloway R, et al. Cardiac Arrest in Acute Ischemic Stroke: Incidence, Predisposing Factors, and Clinical Outcomes. Journal of Stroke and Cerebrovascular Diseases 2016;25:1644-52.
8. Nolan JP, Sandroni C, Böttiger BW, Cariou A, Cronberg T, Friberg H, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med 2021;47:369-421.
9. Sorini Dini C, Geraci G, Valente S, Tizzani E, Sacco A, Grimaldi M, et al. [Post-cardiac arrest syndrome: definition, pathophysiology, and management]. G Ital Cardiol (Rome) 2025;26:488-99.
10. Hong DK, Park YS, Woo JS, Kim JH, Beom JH, Chung SP, et al. Transient Global Ischemia-Induced Brain Inflammatory Cascades Attenuated by Targeted Temperature Management. Int J Mol Sci 2021;22:5114.
11. Michels G, Pöss J, Thiele H. ERC-Leitlinien 2021 zur kardiopulmonalen Reanimation. Herz 2022;47:4-11.

12. Loggini A, Tangonan R, El Ammar F, Mansour A, Goldenberg FD, Kramer CL, et al. The role of amantadine in cognitive recovery early after traumatic brain injury: A systematic review. Clin Neurol Neurosurg 2020;194:105815.
13. Ghalaenovi H, Fattahi A, Koohpayehzadeh J, Khodadost M, Fatahi N, Taheri M, et al. The effects of amantadine on traumatic brain injury outcome: a double-blind, randomized, controlled, clinical trial. Brain Inj 2018;32:1050-5.
14. Heran M, Lindsay P, Gubitz G, Yu A, Ganesh A, Lund R, et al. Canadian Stroke Best Practice Recommendations: Acute Stroke Management, 7th Edition Practice Guidelines Update, 2022. Can J Neurol Sci 2024;51:1-31.
15. Öner Ö, Hanci V, Gürkok MÇ, Ergan B, Yaka E, Gökmen AN. The effect of amantadine treatment on neurological outcome and mortality in mechanically ventilated severe head trauma patients in intensive care unit. Medicine 2024;103:e38172.
16. Zhao Q, Li H, Li H, Zhang J. Research progress on pleiotropic neuroprotective drugs for traumatic brain injury. Front Pharmacol 2023;14.
17. Sahin F, Peksen S, Kocayigit H, Kaya B, Erdem AF. Effect of amantadine in comatose patients: Traumatic brain injury versus post-cardiac resuscitation syndrome. Neurol Asia 2025;30:603-8.
18. Plaitano EG, Scharf RA, Aboutaleb PE, Glennon AL, Melkumova E, Green-LaRoche DM. Informing future randomized controlled trials of amantadine hydrochloride in neurocritical care and post-neurocritical care stroke patients through a retrospective study. BMC Neurol 2024;24:338.
19. Danysz W, Dekundy A, Scheschonka A, Riederer P. Amantadine: reappraisal of the timeless diamond—target updates and novel therapeutic potentials. J Neural Transm 2021;128:127-69.
20. Reynolds JC, Rittenberger JC, Callaway CW. Methylphenidate and amantadine to stimulate reawakening in comatose patients resuscitated from cardiac arrest. Resuscitation 2013;84:818-24.
21. Coppler PJ, Gagnon DJ, Flickinger KL, Elmer J, Callaway CW, Guyette FX, et al. A multicenter, randomized, doubleblind, placebo-controlled trial of amantadine to stimulate awakening in comatose patients resuscitated from cardiac arrest. Clin Exp Emerg Med 2024;11:205-12.
22. McGuigan PJ, Pauley E, Eastwood G, Hays LMC, Jakobsen JC, Moseby-Knappe M, et al. Drug therapy versus placebo or usual care for comatose survivors of cardiac arrest; a systematic review with meta-analysis. Resuscitation 2024;205:110431.
23. Węgrzyn D, Kutwin-Chojnacka A, Bilski J, Mroszczyk K, Węgrzyn K. Neurotrophic Factors in the Treatment of Acute Brain Hypoxia Secondary to Cardiac Arrest: a Case Report. J Med Life 2019;12:233-5.
24. Dekundy A, Pichler G, El Badry R, Scheschonka A, Danysz W. Amantadine for Traumatic Brain Injury—Supporting Evidence and Mode of Action. Biomedicines 2024;12:1558.
25. Grüdtner DOM, Rocha JP, Monteiro MD, Mazon J, Silveira GSB, Koerbel A. Efficacy and safety of amantadine for functional recovery in adults with traumatic brain injuries: A comprehensive systematic review and meta-analysis. Clin Neurol Neurosurg 2025;257:109084.
26. Zhou B-C, Zhang Z, Zhu J-J, Liu L-J, Liu C-F. Blood Lactate or Lactate Clearance: Which Is Robust to Predict the Neurological Outcomes after Cardiac Arrest? A Systematic Review and Meta-Analysis. Biomed Res Int 2018;2018:1-11.
27. Patel VH, Vendittelli P, Garg R, Szpunar S, LaLonde T, Lee J, et al. Neutrophil-lymphocyte ratio: A prognostic tool in patients with in-hospital cardiac arrest. World J Crit Care Med 2019;8:9-17.
28. Altaş ÖF, Kızılkaya M. The Effects of Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio and Prognostic Markers in Determining the Mortality in Patients Diagnosed With Pneumonia in Intensive Care. Medeni Med J 2021.
29. Forget P, Khalifa C, Defour J-P, Latinne D, Van Pel M-C, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes 2017;10:12.
30. Weiser C, Schwameis M, Sterz F, Herkner H, Lang IM, Schwarzinger I, et al. Mortality in patients resuscitated from out-of-hospital cardiac arrest based on automated blood cell count and neutrophil lymphocyte ratio at admission. Resuscitation 2017;116:49-55.