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The journal aims to publish scientifically high quality articles which can contribute to the literature and written in the emergency medicine field and other related fields. Review articles, case reports, editorial comments, letters to the editor, scientific letters, education articles, original images and articles on history and publication ethics which can contribute to readers and medical education are also published.

The journal's target audience includes Emergency Medicine experts, School members who conduct scientific studies and work in the Emergency Medicine field, researchers, experts, assistants, practicing physicians and other health sector professionals.

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Manuscript Types

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Review Article	5000	200	50	6	10 or total of 20 images
Case Report	1500	200	10	No tables	10 or total of 20 images
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Book Section: Sherry S. Detection of thrombi. In: Strauss HE, Pitt B, James AE, editors. Cardiovascular Medicine. St Louis: Mosby; 1974.p.273-85.

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The reviewers review the manuscript.

The editor makes a final decision based on editorial priorities, manuscript quality, and reviewer recommendations.

The decision letter is sent to the author.

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Is it well presented?

What is the length of the manuscript?

2. Publication timing, quality, and priority

How important is the manuscript in this field?

Does it present original data?

Does it carry priority in publishing?

3. Specific questions regarding the quality of the manuscript

Does the title describe the study accurately?

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Do the authors state the study question in the introduction?

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Are ethical guidelines met?

Are statistical analyses appropriate?

Are the results presented clearly?

Does the discussion cover all of the findings?

Are the references appropriate for the manuscript?

4. Remarks to the editor

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Accepted after modest revisions

Reconsidered for acceptance after major changes

Rejected

5. Remarks to the author

What would be your recommendations to the author?

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Editorial
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What is New in Eurasian Journal of Emergency Medicine-Long-term Cardiac Effect of Carbon Monoxide Poisoning

İsa Kılıçaslan

Gazi University Faculty of Medicine, Department of Emergeny Medicine, Ankara, Turkey

Keywords: Carbon monoxide poisoning, cardiac injury, myocardial infarction

Carbon monoxide (CO) poisoning is the second most common cause of fatal poisoning in the United States (1). It can be likened to the tip of an iceberg. It is suspected to be the most common cause of fatal poisoning worldwide, especially given the underreported cases in Asia and Europe (2-4).

The primary target tissues for CO poisoning are the brain and the myocardium. The major morbidity and mortality related to CO poisoning are mainly due to cardiac and neurological dysfunctions.

The long-term neurological effects of CO poisoning are well reported as delayed neurological sequelae in the literature and can occur 4 days to 5 weeks after CO exposure. The reported incidence varies widely, from 3% to 40% of patients (5). Reported neurological effects include cognitive impairment and affective disorders (6).

Besides neurological sequelae, the long-term effects of CO poisoning in the myocardium remain an important issue, and long-term mortality is known to increase, particularly if myocardial injury occurs in severely intoxicated cases. The cardiovascular complications of CO poisoning include acute myocardial ischemia, cardiomyopathy, left ventricular dysfunction, pulmonary edema, and arrhythmia.

A cohort of patients who suffered an acute myocardial injury caused by moderate to severe CO poisoning and followed long-term follow-up (median 7.6 years) had a mortality rate of 24% (7). The mortality rate among poisoned patients with myocardial injury was more than twice that of poisoned patients without signs of cardiac injury, and it is projected to be three times that of a comparable, unpoisoned cohort. With a mean age of 47 years, the study population was young and had a low incidence of identified cardiac diseases or risk factors associated with them, except for smoking (7).

Based on initial ED results, Cha et al. (8) found that the incidence of cardiomyopathy was as high as 74.4% (32 of 43 patients) in CO-poisoned patients with cardiac injury. They also reported the incidence and patterns of CO-induced cardiomyopathy as global left ventricular dysfunctions (51.2%), non-cardiomyopathy (25.6%, and Takotsubo-like cardiomyopathy (23.2%).

The risk of myocardial infarction after CO poisoning is another concern related to moderate-to-severe CO poisoning. Acute myocardial infarction has been reported from increased thrombogenicity due to CO poisoning (9).

In a cohort study with a population-based design conducted across the country, Huang et al. (3) found that after adjusting for other independent predictors involving older age, male sex, and underlying comorbidity of hypertension, diabetes, and renal disease, CO-poisoned patients had an increased risk of myocardial infarction, with an incidence rate of 1.45 compared to the non-CO-poisoned patients. However, another study that evaluated the relationship between coronary artery health and the development of cardiomyopathy in CO-poisoned patients with myocardial injury showed that not all patients with CO-induced cardiomyopathy require coronary artery evaluation

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(10). In general, patients with underlying coronary artery disease (CAD), persistent LV dysfunction, or risk factors for CAD may benefit from additional testing, such as angiography and revascularization (11).

In summary, the rates of cardiac disease-related complications and mortality were 2 to 3 times higher in CO poisoning patients who experienced acute phase cardiac injury over the course of a long-term (7-8 years) follow-up than in patients without cardiac injury (7). Early detection of cardiac damage in CO poisoning patients is crucial for determining whether to proceed with additional therapy or to forecast mortality and morbidity (12).

In this regard, the prospective cross-sectional cohort study entitled "Comparison of Myocardial Infarction Frequency in Normal Population and Population of Late Period after Carbon Monoxide Poisoning" published in this issue of the Eurasian Journal of Emergency Medicine is interesting and provides additional information for myocardial infarction due to CO poisoning compared to the normal population (13). The follow-up period was approximately 5 years. Their observations also demonstrated the myocardial infarction types and mortality in patients with CO poisoning.

In our country, where CO poisoning is frequently observed and related deaths often occur, acute complications and long-term cardiac/neurologic effects due to CO should be well known, and follow-up and treatment should be performed accordingly in cases of CO poisoning.

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ResQvent: A Practical Solution for Addressing the Needs of Mechanical Ventilation in Low Resource and Income Healthcare Settings

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Abstract

Respiratory emergencies are common and can require intensive management with complex medical equipment. Experiences from global pandemics such as Coronavirus disease-2019 have shown collapse of healthcare infrastructure and spikes in mortality because of shortage of critical equipment, such as mechanical ventilators, especially in under resourced settings. In this article, we present a brief review of medical literature regarding established and readily available blueprints for ventilator systems. We also present our design relevant to under resourced areas called the ResQvent, which is a portable artificial manual breathing unit add-on device that can be automated to allow cyclical compression of the bag to provide adequate ventilation according to standard recommendations for infants, children and adults. Powered by 220-240 V electrical supply, this 18x8x8 inches, extremely portable device can prove to be a game changer in providing temporary automated ventilation at a reasonable cost. ResQvent has been successfully bench tested for accuracy on simulation software. With the continued motivation arising from the pandemic, we assume similar projects will attract attention; however, efforts are still required to design policies and arrange dependable financial resources for the creation and evaluation of open-source ventilators.

Keywords: COVID-19, respiratory emergencies, prototype, ventilator

Introduction

Coronavirus disease-2019 (COVID-19), which is caused by infection from Severe acute respiratory syndrome-Coronavirus-2, is very dangerous as it threatens to overpower the existing medical healthcare system, resulting in increased mortality rates (1,2). Within the medical infrastructure, there is a limited inventory of equipment, and it lacks the overall capacity to cope with an overwhelming influx of patients during pandemics. As a result, people suffer globally due to a combination of COVID-19 illness and limited accessibility to specific equipment (3). Mechanical ventilators are an important example that has now been proven to be in a critical short supply in the odds of such circumstances (4).

Previous research has shown that intensive care units are insufficiently equipped to handle the majority of patients in need of ventilator support during pandemics (5,6). While certain countries, such as the United States, possess ventilator stockpiles (7), it is widely agreed upon that the existing supply is inadequate for significant pandemics (8). Consequently, ethical rationing may be required to allocate ventilators rather than relying on a first-come first-served basis (9).

The prevailing healthcare system relies on widely manufactured ventilators sourced from a small group of providers. This model falters when confronted with an abrupt surge in demand for intricate devices such as mechanical ventilators during a pandemic. The bulk of medical equipment is tightly patented by a few medical corporations. Furthermore, entities that do not actively practice medicine continue to obstruct the implementation of medical treatments, even in the midst of the present COVID-19 pandemic (10).

With the recent progress and incremental adoption of small-scale open-source manufacturing technologies (11), a different

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methodology called mass-distributed manufacturing has surfaced. Under this framework, designs are generated and openly shared through the internet with open-source licenses, enabling others to replicate the designs using their own equipment (12). Open-source scientific hardware has achieved tremendous triumph (13), presenting custom equipment that is comparatively inexpensive and exhibits superior performance compared to proprietary scientific tools (14). In the current scenario, this approach would, to some extent, address the shortages of medical supplies (15), especially in relation to ventilators (16).

Brief Literature Review

In the realm of peer-reviewed literature, most ventilator devices use a standard artificial manual breathing unit (AMBU) bag, which undergoes rhythmic compression using either a mechanical or pneumatic design. These compression are controlled by a microcontroller. The controls, which represent the most complex element of these designs, rely on Arduino technology that can be programmed or activated using existing source codes. It is noteworthy that a significant number of low-cost designs employ the bag approach, while commercial mechanical ventilators do not incorporate bags, bellows, or pistons due to concerns surrounding performance. Now, we will delve into the discussion of three distinct categories of cost-effective ventilators.

Both continuous positive airway pressure (CPAP) and bilevel positive airway pressure machines have been converted into ventilators by including an oxygen concentrator and viral high-efficiency particle air (HEPA) filter (17). Sleep apnea machines, specifically CPAP devices, come with a high price tag and can present obstacles regarding availability in settings lacking sufficient resources. This restriction impedes the swift deployment of these devices.

Researchers have also constructed conventional ventilators using readily available components from nonclinical supply chains. A number of these devices have acquired Emergency Use Authorization from the Food and Drug Administration, including the ventilator intervention technology accessible locally produced by the Jet Propulsion Laboratory of the National Aeronautics and Space Administration (18), and the Mechanical Ventilator Milano developed by Elemaster S.P.A. Tecnologie Elettroniche (19). These prototypes rely on several components that may not be suitable for efficient mass production and rapid deployment within a condensed timeframe.

Several universities have been actively pursuing simplified solutions by automating the operations of a standard manual AMBU bag. Table 1 provides a compilation of open-source ventilator projects based on the AMBU system, accompanied by relevant specifications. AMBU-based ventilators possess certain advantages, including easy accessibility, a basic mechanism with a minimal number of components, cost-effectiveness, and the ability for swift deployment. Most of the currently available designs heavily rely on a 3D printing for the assembly process. However, the production of such components on a large scale can become challenging during lockdowns, and they may also have a limited lifespan, potentially leading to device malfunction (20-24).

Innovation

As described, the AMBU bag remains a portable, simple, and easily accessible airway device under resourced settings; however,

Table 1. List of open source AMBU-based ventilator projects

Name	Developers	Characteristics	Source
AmboVent (20)	Innovators in Israel	Open sourceobot arm for compression has a backup battery and a cutoff for high resistance/ pressure	https://github.com/AmboVent-1690-108/ AmboVent
ApolloBVM (21)	Rice University	Open source, rack and pinion based, adult and child settings, 24 hour operational	http://oedk.rice.edu/apollobvm
Emergency Ventilator/ E-Vent (22)	MIT	Open source motor-driven cam mechanism for squeezing AMBU bag has assist control mode to detect pressure	https://e-vent.mit.edu/
OpenVent-Bristol (23)	Innovators in the UK	Open source, motorized arm to enable squeezing, referenced from existing open source	https://openventbristol.co.uk/
AmbuBox (24)	University of California, Davis	Open source, no moving parts, lightweight	https://www.ucdavis.edu/coronavirus/news/ uc-davis-engineers-clinician-develop-low-cost-portable-ventilator

BVM: Bag Valve Mask, MIT: Massachusetts Institute of Technology, UK: United Kingdom, AMBU: Artificial manual breathing unit

if used manually, it can be highly dependent on interprovider variability and fatigue; making it less effective than a mechanical ventilator (25-28).

Our team aimed at combining the positive aspects of ventilation systems and ensuring that the resulting product remains accessible and affordable without compromising on the effectiveness of the proposed ventilator. The need for this innovation arose especially in the setting of decreased mechanical ventilators available for COVID-19 patients, especially in the setting of a resource-limited country such as Pakistan.

Keeping the above considerations in mind, we invented "Rapid Rescue Ventilator" (ResQvent) (Figure 1). Our overall goal was to create an automated, reliable, and long-lasting attachment that could fit onto a standard AMBU bag and automate compression and air supply. As seen with other similar models (20-24), the attachment had to function smoothly with relatively little human interference as the intent is to free up medical care providers from the AMBU bag operation. We aimed to target total expenses at approximately USD 150, which is far less compared to other low-cost pandemic portable ventilators (21,29,30).

The time our device can run without human intervention is around 6 h without power supply. We believe that this time should be sufficient while trying to find a reliable power supply source. When connected to a power supply, the device will work indefinitely while using a standard voltage between 220 and 240 V with no special requirement. During this, the device can accurately supply properly timed breaths with a margin of error less than 10%. The device can act as potentially life-saving ventilation equipment until a mechanical ventilator is arranged, saving lives that may be lost due to lack of medical and human resources.

The time the device takes from start to the first compression cycle values set according to standard recommendations (30-32) is approximately 45 seconds. Measuring 18x8x8 inches with a weight of around three kilograms, ResQvent is easy to position and carry around device. We believe that ensuring compactibility and portability for such device is important so it can be easy to maneuver across different environments.

The functioning of ResQvent is divided into five components:

1) Securing the AMBU bag

This is done via properly securing the device to the patient for ventilation. We designed the device to be used for noninvasive and invasive ventilation. The noninvasive mode of the device requires the AMBU bag to be connected via tubing to an appropriate-sized mask secured to the conscious patient to make an effective seal. This mode enables the device to serve as a conduit for continuous oxygen delivery while being able to provide continuous positive pressure ventilation through manual control of positive end expiratory pressure (PEEP) valve. For the invasive mode, the patient would have to be intubated and connected to the AMBU bag. In addition, the automation device must be properly secured with the AMBU to ensure proper ventilation and no errors during cyclical compression via metallic sliders fixed on the base of the assembly. A HEPA filter can be

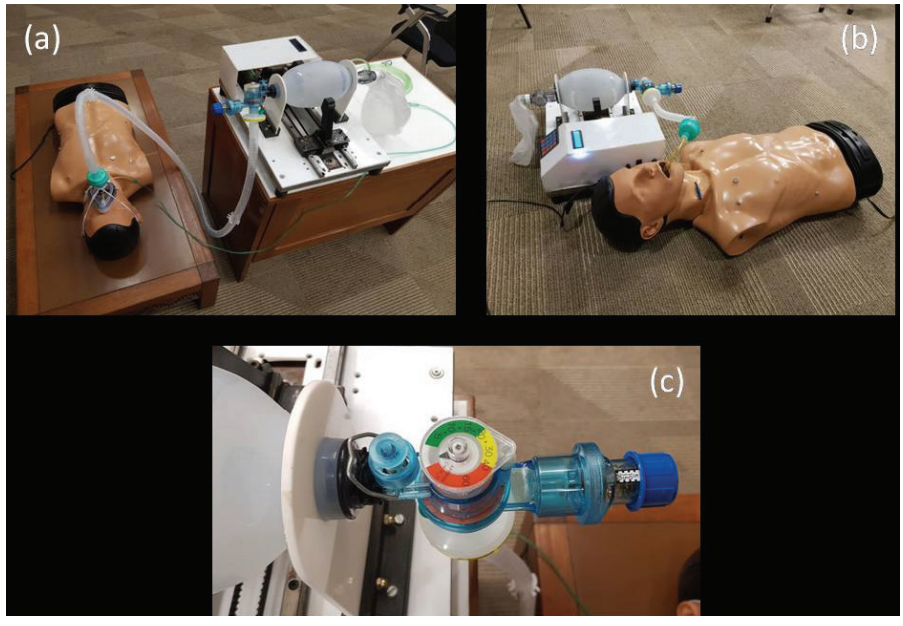

Figure 1. Rapid rescue ventilator (ResQvent). Panel (a): A screenshot demonstrating the noninvasive mode of ventilation. Panel (b): A screenshot demonstrating the invasive mode of ventilation. Panel (c): A screenshot of the manometer for safe tidal-volume delivery and the positive end-expiratory pressure valve

placed on the ventilator circuit near the patient to reduce the risk of aerosolization of viral particles. The device is well secured when stationary to prevent excessive movements of the entire structure

2) Powering the device

ResQvent is powered using a standard 220-240 V energy supply. This is needed for proper functioning of the compression mechanism and the display unit, aiding in the monitoring of the device.

3) Controlling/adjusting the device

Using Arduino software that operates the microcontroller, ResQvent provides the user with the ability to independently adjust the amount and rate of compression.

4) Compressing the bag

A "level controller" is used to control and monitor the amount and rate of compression. These variables can be adjusted manually courtesy of the Arduino microcontroller, which provides input to the stepper motor. The stepper monitor then controls the input of the desired compression level data to provide sufficient amount and rate of ventilation to the patient by consistently controlling the compression of the AMBU bag while considering preliminary factors such as speed and power. All of this compression metadata can be entered using a basic keypad.

5) Monitoring outcomes

The compression-level data, respiratory rate, and other important ventilation variables are displayed on a laser color display monitor for easy user operability.

A portable breathing circuit on one limb was constructed and tested by engineers and doctors on a test lung using Arduino software. It was connected to the test lung for device reading. Using simulation software such as MatLab/Simulink and LabVIEW, we helped develop system design platforms and development environments, enabling better visualization and accuracy in predicting research and project outcomes. We used the Hamilton ventilation website simulation software to confirm the results. There, we mimicked the conditions and looked at how a portable ventilator responds. Figure 2 graphically demonstrates the various ventilation and volume-pressure loops generated by our device. The model was calibrated to our prototype in two steps. If the lung port was blocked, the parameters of the PEEP and pop-off pressure relief valves were first calibrated by comparing the model output with the measured output. In this series of studies, when the solenoid valve was opened and closed, the pressure at the inlet to the solenoid control valve was monitored as a function of the total inlet gas flow rate. The experiments used PEEP values of 2, 5, and 10 cm H_2O. The set pressure difference and maximum valve-opening area for each pressure relief valve in the model were modified to best suit the measured data. The Simscape logging mechanism is used to find

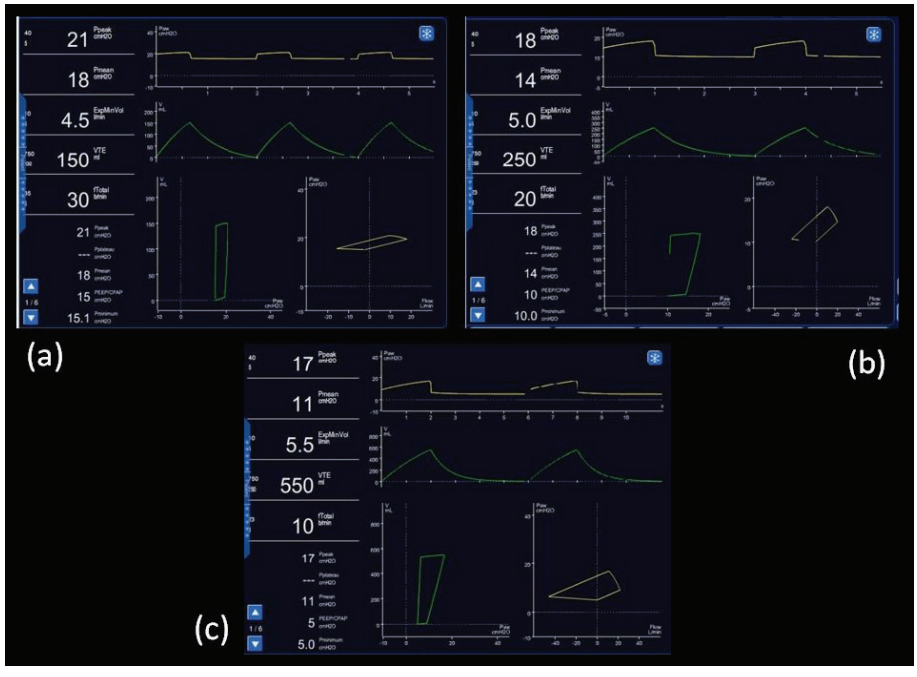

Figure 2. Graphical user interface (GUI) for different patient categories. Panel (a): GUI of infant setting using the compression 150 mL set at a rate of 30 compression per minute. Panel (b): GUI of child setting using the compression 250 mL set at a rate of 20 compression per minute. Panel (c): GUI of adult setting using the compression 550 mL set at a rate of 10 compression per minute

the simulation results. The temperature and relative humidity of the air flowing through the inspiratory and expiratory tubes are displayed. We used an Arduino Nano 3 microcontroller (ATmega328 microcontroller) to develop an electronic pulse train signal responsible for regulating the respiratory rate and inspiratory time. In the pneumatic signal circuit, the microcontroller triggers a solenoid valve connected to the exhalation manifold. Two potentiometer microcontrollers were employed to accept user input for controlling the respiratory rate and inspiratory time. Additionally, two push buttons have been incorporated, enabling the user to select a positive airway pressure and either lock or unlock the potentiometer button. The respiratory rate can be adjusted while the inspiratory time is governed through a pneumatic signal, which in turn controls the input of the electronic microcontroller. To assess the performance of the portable ventilator, we conducted evaluations using the ASL5000 breathing simulator. This simulator incorporates a realistic lung model capable of autonomous breathing and is calibrated to match the ventilator prototype, thereby accurately simulating ventilator behavior.

ResQvent's present design can secure the AMBU bag and provide therapeutic-specific ventilation to infants, children, and adults through a simple user interface. However, we believe that the device can be made more robust by installing an external protective casing to make it more durable in harsher surroundings. Cooling mechanisms such as a miniaturized fan can be installed in the assembly for managing device overheating. In terms of testing, ResQvent needs to be tested thoroughly for accuracy of volume and frequency over a wide range of conditions and over longer periods of time so that it can be used confidently in life saving situations.

Conclusion

Although promising but with further refinements, ResQvent can prove to be a game changer with an excellent potential of being utilized in low resource setting hospitals, clinics as well as the austere pre-hospital environment.

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Ethics

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: M.A.B., Design: M.A.B., A.S.A., Data Collection or Processing: M.A.B., A.S.A., Analysis or Interpretation: M.A.B., A.S.A., Literature Search: M.A.B., Writing: M.A.B.

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Determining Prevalence and Risk Factors of Seizure Recurrence in the Early Period in Patients Who Present to the Emergency Department with Epileptic Seizures

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Abstract

Aim: Although the basic principles of acute epileptic seizure management in the emergency department (ED) are well known, there is no consensus on the optimal discharge time from the ED for patients who return to a normal-basal state of consciousness after an epileptic seizure. The main concern for physicians in terms of the optimal discharge time from the ED is the possibility of acute recurrent seizures (ARS) in the early postdischarge period. Such concerns can lead to extended monitoring of patients, resulting in overcrowding in the ED and higher hospital charges. The aim of this study was to determine the frequency of ARSs and risk factors for recurrence within the first 6 and 24 h after presentation to the ED with an acute seizure in patients with a confirmed diagnosis of epilepsy.

Materials and Methods: This prospective observational study was conducted with patients aged older than 18 year old with a diagnosis of epilepsy who presented with convulsive seizures to the ED between October 2018 and October 2019. The primary outcome was the frequency of ARS within the early period (6 and 24 hours). The second outcome was the potential risk factor for ARS, which was seizure recurrence within the first 6 or 24 h after admission to the ED with the complaint of a seizure.

Results: In to patients with epilepsy with seizure attacks were included during the study period. The prevalence of ARS within the first 6 and 24 h was found to be 21.8% and 27.4%, respectively. Risk factors for ARS within 6 h were found to be non-adherent to antiepileptic drug (AED) therapy, active seizures/postictal period on admission, and white blood cells, while risk factors for ARS within 24 h were found to be non-adherent to AED therapy, AED polytherapy, a history of weekly seizures, duration of the postictal period, and white blood cells.

Conclusion: ARS are not rare in the early period after admission to the ED, with an incidence of 21.8% in the first 6 h and 27.4% in the first 24 h. Potential risk factors of ARS seem to be non-adherent to AED therapy, AED polytherapy, a history of weekly seizures, duration of the postictal period, and white blood cell.

Keywords: Acute recurrent seizure, acute repetitive seizure, seizure cluster, epilepsy, emergency department

Introduction

Patients with a history of epilepsy often experience acute seizures and m, andof these patients are admitted to the emergency department (ED) for treatment (1). Although the basic principles of acute epileptic seizure management in the ED are well known, there is no consensus on the optimal discharge time from the ED for patients who return to a normal-basal state of consciousness after an epileptic seizure (2,3). The main concern for physicians in terms of the optimal discharge time from the ED is the possibility of acute recurrent seizures (ARS) in the early post-discharge period (i.e., within the first 24 hr), as ARS in the early post-discharge period may be associated with an increased risk of status epilepticus, morbidity, mortality, and re-admission to the ED (4-7). Such concerns can lead to extended monitoring of patients, resulting in overcrowding in the ED and higher hospital

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charges. Determining the risk factors for ARS can shed light on patients who require long-term monitoring. Such information is crucial for both physicians and patients.

Although several studies have determined the prevalence of ARS and associated risk factors, there is no clear consensus in the literature on this issue. The use of different terminologies for ARS is one of the main reasons for the lack of consensus (4,8). Although seizure cluster (SC) is generally used to identify ARS, it is not listed in the International League against Epilepsy (ILAE) Commission on Classification and Terminology (9). Similarly, there are different clinical definitions for SC, with some studies defining it as three or more seizures in 24 h (10-12), and others defining it as two to four seizures in less than 48 h (13), two or more seizures in 6 h (14), or two or more seizures in 24 h (15). Due to these diverse definitions of SC in the literature, different studies have reported different risk factors and prevalences. Consequently, no clear clinical consensus has been established.

The aim of this study was to determine the frequency of ARS and risk factors for recurrence within the first 6 and 24 h after presentation to the ED with an acute seizure in patients with a confirmed diagnosis of epilepsy.

Materials and Methods

Study Type and Design

This single-center prospective study was conducted in the ED of a Ankara Keçiören Training and Research Hospital between 15 October 2018 and 15 October 2019 after receiving approval from the Local Ethics Committee (protocol id and date: 48865165-020/07.10.2018). The research was conducted in accordance with the tenets of the Declaration of Helsinki, and written informed consent was obtained from all patients or their legally authorized relatives.

Subjects

During the study period, all consecutive patients aged older than 18 year old with a diagnosis of epilepsy who presented with convulsive seizures (generalized type according to the ILAE 2017 classification) to the ED were included in the study. Patients who were pregnant, who were diagnosed with status epilepticus at the time of admission, and who had a lack of basic laboratory results (hemogram, biochemistry panel, venous blood gases) or clinical/demographic data were excluded from this study.

Study Protocol

All patients included in the study were evaluated and examined by emergency physicians in a critical care room of the ED at the time of admission. Patients' demographic and clinical data, vital signs, physical/neurological examination findings, bedside blood sugar, and main laboratory findings, including those of a hemogram, biochemistry panel, and venous blood gases, and pregnancy tests were obtained and recorded by the emergency physicians. Toxicology screening and radiological examination were performed if clinically indicated. Details on each patient's epilepsy history and previous and most recent seizure attacks were obtained from patients, their relatives, and other eyewitnesses. These data included a history of epilepsy in the patient's family, patients' sleep patterns/sleep disorders, type and frequency of previous seizures, epilepsy patterns and seizure recovery times, signs and symptoms during the postictal period, seizure-triggering clinical conditions, and whether antiepileptic drug (AED) use is regular or not (adherent or non-adherent therapy) - non-adherent to AED therapy was defined as non-use of three or more days in the last month based on the anamnesis of the patient.

After initial supportive care and resuscitative procedures when required, all patients were observed for at least 6 h in the ED according to routine clinical practice in our hospital. After this observation period, patients without repeated seizures or clinical conditions requiring hospitalization and did not require specific treatment were discharged from the ED. All these patients were asked to return to the ED within a 24-h period from the time of discharge from the ED to undergo screening by a neurologist in the neurology clinic. If clinically indicated, the neurologist performed electroencephalographic testing. At the same time, the patient was asked about recurrent seizures in the 24-h period since their first admission to the ED. Finally, the neurologist categorized the epileptic seizure according to the ILAE 2017 classification. Patients with seizures other than generalized seizures (focal and unknown) and those who were not followed up were excluded.

Outcomes of Interest

Two outcomes were defined in this study. The first outcome was the frequency of ARS in patients with a confirmed diagnosis of epilepsy who presented to the ED with acute seizures in the early period (i.e., within the first 6 h and 24 hr). The second outcome was the potential risk factors for ARS. In this study, ARS was defined as seizure recurrence within the first 6 or 24 h after admission to the ED with the complaint of a seizure (14,16).

Statistical Analysis

All data were analyzed using Statistical Package for the Social Sciences (SPSS) v25.0 for Mac OS X (SPSS Inc., Chicago, IL, USA). The normality of the data distribution was determined by the Shapiro-Wilk test, histograms, and Q-Q plots. The categorical variables of the patients were expressed as numbers and percentages and analyzed using a chi-square test. Continued variables were

presented as the mean standard deviation or median values and interquartile range (IQR) of 25-75%. Non-parametric values were analyzed using the Mann-Whitney U test, and parametric values were analyzed using the Student's t-test. To determine the predictive value of the variables, those with a p value of <0.1 in the univariate analysis were entered into a multivariate regression model using the blockwise entry method. Correlations among these variables were analyzed using Spearman's test. In each pair, the variable that detected a correlation with the other variable was excluded from the regression model. To assess the model's goodness of fit, the Hosmer-Lemeshow test was performed. The 95% confidence intervals (95% CIs) were calculated whenever appropriate, and a two-tailed p value of <0.05 was considered statistically significant.

Results

In to patients with epilepsy with seizure attacks were included during the study period. The median age of the patients was 31.5 years (IQR: 25-75%: 24-43), and 72 (50.7%) of the patients were males. At the time of admission to the ED, 54 (38%) of the patients were in the postictal period/active seizure and the remaining 88 (62%) patients were fully conscious. According to the history taken from the patients' relatives, the postictal period was prolonged in 35 (24.6%) of the patients as compared to the usual duration. The baseline characteristics of the patients are shown in Table 1.

Thirty-one (21.8%) of the 142 patients experienced ARS within the first 6 h of follow-up in the ED. When the demographic and clinical characteristics of these patients were compared with those without ARS during this period, the following factors were more common in the ARS group: cerebral palsy, a weekly history of seizures, active seizures or postictal period on admission to the ED, psychotropic drug use in the last 24 h, and intravenous AED administration in the ED. In addition, the duration of the postictal period and lactate and white blood cell values on admission was higher in patients with ARS than in those without ARS. The GCS and pH values of patients with ARS were lower than those without ARS. In the multivariate regression model created to assess the factors predicting ARS within the first 6 h of follow-up in the ED, nonadherent to AED therapy [odds ratio (OR): 2.5, 95% CI: 1.01 to 6.4], active seizures/postictal period on admission (OR: 4.3, 95% CI: 1.7 to 11), and white blood cell (OR: 1.2, 95% CI: 1.08 to 1.3) were predictive factors for ARS within the first 6 h of follow-up in the ED (Table 2).

In terms of the prevalence of ARS and associated risk factors within the first 24 h after admission to the ED, 39 of the 142 (27.4%) patients experienced ARS within this period. When the demographic and clinical characteristics of the patients with and without ARS within the first 24 h after admission to the ED were compared, the following factors were more common in the ARS group: cerebral palsy, a history of cluster epilepsy, non-adherent to AED therapy, AED polytherapy, a history of weekly seizures, active seizures or postictal period on admission to the ED, psychotropic drug use in the previous 24 hr, and intravenous AED administration in the ED. In addition, the duration of the postictal period, pulse rate, length of stay in the ED, and lactate and white blood cell values on admission were higher in patients with ARS than in those without ARS. The GCS and pH values of the patients with ARS were lower than those without ARS. In the multivariate regression model created to assess the factors predicting ARS within the first 24 h after admission to the ED, non-adherent to AED therapy (OR: 2.5, 95% CI: 1.09 to 6.5), AED polytherapy (OR: 2.9, 95% CI: 1.08 to 8.1), a history of weekly seizures (OR: 3.9, 95% CI: 1.2 to 12), duration of the postictal period (OR: 1.01, 95% CI: 1.001 to 1.026), and white blood cell (OR: 1.18, 95% CI: 1.06 to 1.3) were predictive of ARS within the first 24 h after admission to the ED (Table 3).

Discussion

The pThisy investigated prevathe prevalence and factors for ARS or SC in patients with epilepsy who were admitted to the ED with the complaint of seizures. In this study, the prevalence of ARS after admission to the ED was 21.8% in the first 6 h and 27.4% in the first 24 h. Previous studies on the prevalence of ARS or SC reported figures ranging from 3% to 57% (9,16-18). The difference in the reported seizure prevalence may be due mainly to the lack of consensus on the definitions of SC and ARS, both of which are used to describe repetitive seizures in the early period. Among the various definitions of ARS, in this study, ARS was defined as having two or more seizures in the first 6 h (14) and two or more seizures in the first 24 h (16). We considered this definition more appropriate in emergency medicine practice in our study. In terms of ED practice and the first 6 h after an acute seizure, although there is no clear evidence, the general view is that all patients should be monitored during this period and that those without seizure recurrence during this time, as well as those who not have any significant clinical problems requiring specific treatment, can be discharged. Similarly, during this 6-h period, despite the lack of a high level of evidence, patients who have seizures again are considered to have a high risk of status epilepticus (7). Because of concerns about ARS, many patients are monitored for long periods in the ED. To address this issue, it is important to define the main risk factors for ARS in the first 6 to 24 h.

In this study, although several variables were identified as potential risk factors for ARS within the first 6 h in the univariate analysis,

Table 1. Demographical and clinical characteristics of all patients	
Gender n (%)	
Male	72 (50.7)
Female	70 (49.3)
Age median (IQR 25-75%)	31.5 (24-43)
Comorbidities n (%)	
Chronic hypertension	10 (7)
Coroner artery disease	6 (4.2)
Diabetes mellitus	6 (4.2)
Cerebral palsy	5 (3.5)
Cerebra-vascular event	8 (5.6)
Psychiatric disorders	16 (11.3)
Chronic alcohol use	11 (7.7)
Others	23 (16.2)
The history of epilepsy n (%)	
Epilepsy history in family	28 (19.7)
Previously meningitis history	6 (4.2)
Febrile convulsion history	41 (28.9)
Difficult birth history	25 (17.6)
Severe head trauma history*	35 (24.6)
Previously status epilepticus history	21 (14.8)
Hospital admission history due to epilepsy	48 (33.8)
ICU admission history due to epilepsy	17 (12)
Intubation history due to epilepsy	3 (2.1)
Epileptic surgery history	1 (0.7)
Cluster-type epilepsy history**	75 (52.8)
Drug history n (%)	
AED use	132 (93)
Nonadherent to AED therapy	48 (33.8)
Unused last of AED dosage	70 (49.3)
Polytherapy AED use	47 (33.1)
Third-generation AED use	91 (64.1)
Age of when diagnosed epilepsy median (IQR 25-75%)	20 (12-30)
Duration time since diagnosed epilepsy/year median (IQR 25-75%)	10 (3-20)
The presence of weekly routine seizures in history n (%)	22 (15.5)
The presence of monthly routine seizures in history n (%)	55 (38.7)
Epilepsy etiology n (%)	
Symptomatic#	93 (65.5)
Idiopathic##	49 (33.1)
The state of consciousness on admission to ED n (%)	
Active seizure/postictal period	54 (38)
Conscious	88 (62)
Duration of postictal period (minute) median (IQR 25-75%)	20 (10-40)
Seizure features n (%)	
Presence aura in the pre-seizure period	46 (32.4)
Prolonged postictal period***	35 (24.6)
Seizure period	
06:00-12:00	55 (38.7)
12:00-20:00	39 (27.5)
20:00-06:00	48 (33,8)
Relationship of seizure to sleep	
On sleeping	31 (21.8)
Awake	111 (78.2)
Clinical features n (%)	
Fever higher than 38 °C in last 24 h	23 (16.2)
Disturbed sleep in the last 48 h	79 (55.6)
Alcohol intake in the last 24 h	5 (3.5)
Acute traumatic injury	57 (40.1)
Psychotropic drug use in the last 24 h	7 (4.9)
Acute psychological stress in the last week	87 (61.3)
Changing AED dosage	21 (14.8)
Use of herbal medicine	4 (2.8)

Table 1. Continued	
Cerebral localization of epilepsy**** n (%)	
Frontal	9 (6.3)
Temporal	22 (15.5)
Parietal	49 (34.5)
Occipital	12 (8.5)
Limbic	5 (3.5)
Unknown	45 (31.7)
Vital signs on admission median (IQR 25-75%)	
Systolic blood pressure: mmHg	120 (110-133)
Diastolic blood pressure: mmHg	70 (65-78.25)
Pulse-beat/min	91.5 (79.75-102)
Fever -°C	36.4 (36.1-36.8)
Blood sugar: mg/dL	105 (91.75-121)
Oxygen saturation -%	96 (94-98)
Glasgow-coma scale	15 (11-15)
Laboratory findings median (IQR 25-75%)	
pH	7.38 (7.31-7.41)
PCO_2 - mmHg	40.5 (35-46)
Bicarbonate - mmol/L	23 (20-26)
Lactate - mEq/L	3.2 (1.9-6.3)
White blood cell - $x10^3/\mu L$	8.7 (6.8-11.5)
Neutrophil - $x10^3/\mu L$	4.95 (3.9-7.2)
Lymphocyte - $x10^3/\mu L$	2.4 (1.6-3.3)
Hemoglobin - g/dL	14.05 (12.8-15.5)
Platelet - $x10^3/\mu L$	239.5 (185.7-291)
Creatinine	0.7 (0.8-0.9)
Urea - mg/dL	24 (19-30)
BUN - mg/dL	10 (8-14)
ALT - IU/L	14 (11-22)
AST - IU/L	21 (17-27)
GGT - IU/L	24 (14.7-41.5)
Total bilirubin: mg/dL	0.3 (0.1-0.4)
Direct bilirubin - mg/dL	0.08 (0.05-0.1)
Sodium - mEq/L	138 (137-140)
Potassium - mEq/L	4 (3.8-4.3)
Calcium - mg/dL	9.55 (9.1-9.9)
Length of stay ED median (IQR 25-75%)	4 (4-6)
IV AED needing in ED n (%)	27 (19)

*Severe head trauma history: Presence of head trauma requiring hospitalization or surgical intervention and accompanying altered mental status in history.
**Cluster-type seizure: Two or more seizures in 24 h.
***Prolonged postictal period: Prolonged postictal period compared to the previous postictal period based on the anamnesis taken from relatives.
****Location detected on EEG that performed after the last seizure attack.
#Epilepsy disease secondary to organic lesion (intracranial hemorrhage, ischemic stroke, etc.).
##Epilepsy that starts unrelated to any organic lesion.

only the white blood cell count, non-adherent to AED therapy, and active seizures/postictal period on admission were significant risk factors in the multivariate logistic regression analysis. Similarly, when we assessed the risk of ARS within the first 24 h, a history of weekly seizures, AED polytherapy, non-adherence to AED therapy, white blood cell count, and postictal period duration were significant risk factors in the multivariate logistic regression analysis. Although small in number, several studies are focused on ARS prevalence and its potential risk factors in the literature. However, the main findings of these studies differ from each other. One possible reason for the discord be differences in the composition of the study populations.

In a prospective cohort study on 163 epilepsy patients older than 18 years, Haut et al. (12) aimed to determine the potential risk factors for SC, which they defined as the occurrence of three or more seizures within a 24 h period. In their study, in which generalized seizures were excluded, the authors reported that the prevalence of SC was 29% and that a history of head trauma with loss of consciousness before epilepsy onset and extratemporal lobe epilepsy were risk factors for SC. In another prospective cohort study on 300 epilepsy patients older than 12 years, Detyniecki et al. (14) reported that the number of AEDs used during a patient's lifetime was a risk factor for SC, which they defined as two or more seizures in a 6 h period. In their study, extratemporal lobe epilepsy was not a risk factor for SC (14). Another important finding of the study by Detyniecki et al. (14) was that the occurrence of SC in the previous year was a risk factor for the recurrence of SC the following year (OR:

Table 2. Demographical and clinical characteristics of patients according to the presence of recurrence seizure within first 6 h					
	Presence seizure (n=31)	**Absence seizures (n=111)**	**p value**	**Unadjusted odds ratio 95% CI**	**Adjusted odds ratio 95% CI**
Gender n (%) Male Female	 14 (45.2) 17 (54.8)	 58 (52.3) 53 (47.7)	 0.4	 0.75 (0.33 to 1.6)	 -
Age median (IQR 25-75%)	35 (20 to 43)	31 (24 to 43)	0.59	0.9 (0.96 to 1.025)	-
Comorbidities n (%) Chronic hypertension Coronary artery diseases Diabetes mellitus Cerebral palsy Cerebra-vascular event Psychiatric disorders Chronic alcohol use Others	 1 (3.2) 0 (0) 1 (3.2) 4 (12.9) 2 (6.5) 3 (9.7) 4 (12.9) 7 (22.6)	 9 (8.1) 6 (5.4) 5 (4.5) 1 (0.9) 6 (5.4) 13 (11.7) 7 (6.3) 16 (14.4)	 0.6 0.3 1 **0.008** 1 1 0.2 0.2	 0.3 (0.04 to 3.1) N/A 0.7 (0.79 to 6.2) 16.2 (1.7 to 151) 1.2 (0.2 to 6.2) 0.8 (0.2 to 3.1) 2.2 (0.6 to 8.01) 1.7 (0.6 to 4.6)	 - - - N/A[a] - - - -
The history of epilepsy n (%) Epilepsy history in family Previously meningitis history Febrile convulsion history Difficult birth history Severe head trauma history* Previously status epilepticus history Hospital admission history due to epilepsy ICU admission history due to epilepsy Intubation history due to epilepsy Epileptic surgery history Cluster-type epilepsy history**	 4 (12.9) 2 (6.5) 6 (19.4) 6 (19.4) 8 (25.8) 6 (19.4) 11 (35.5) 5 (16.1) 1 (3.2) 0 20 (64.5)	 24 (21.6) 4 (3.6) 35 (31.5) 19 (17.1) 27 (24.3) 15 (13.5) 37 (33.3) 12 (10.8) 2 (1.8) 1 (0.9) 55 (49.5)	 0.2 0.6 0.1 0.7 0.8 0.4 0.8 0.5 0.5 1 0.1	 0.5 (0.1 to 1.6) 1.8 (0.3 to 10.5) 0.5 (0.1 to 1.3) 1.1 (0.4 to 3.2) 1.08 (0.4 to 2.6) 1.5 (0.5 to 4.3) 1.1 (0.4 to 2.5) 1.5 (0.5 to 4.9) 1.8 (0.1 to 20) N/A 1.8 (0.8 to 4.2)	 - - - - - - - - - N/A[a] -
Drug history n (%) AED use Nonadherent to AED therapy Unused last of AED dosage Polytherapy AED use Third-generation AED using	 30 (96.8) 15 (48.4) 15 (48.4) 11 (35) 21 (67.7)	 102 (91.9) 33 (29.7) 55 (49.5) 36 (32) 70 (63.1)	 0.3 0.052 0.9 0.7 0.6	 2.6 (0.3 to 22) 2.2 (0.9 to 4.9) 1.04 (0.4 to 2.3) 1.1 (0.4 to 2.6) 1.2 (0.5 to 2.8)	 - **2.5 (1.01 to 6.4)** - - -
Age of when diagnosed epilepsy median (IQR 25-75%)	14 (7-21)	19 (13.5-28.5)	0.3	0.98 (0.95 to 1.01)	-
Duration time since diagnosed epilepsy/year median (IQR 25-75%)	22 (1-38)	8 (2.75-16)	0.1	1.02 (0.9 to 1.05)	-
The presence of weekly routine seizures in history n (%)	9 (29)	13 (11.7)	**0.02**	**3.08 (1.1 to 8.1)**	2.7 (0.8 to 8.8)
The presence of monthly routine seizures in history n (%)	11 (35.5)	44 (39.6)	0.6	0.8 (0.3 to 1.9)	-
Epilepsy etiology n (%) Symptomatic[#] Idiopathic[##]	 20 (64.5) 11 (35.5)	 73 (65.8) 38 (34.2)	 0.8	 1.07 (0.4 to 2.4)	 -
The state of consciousness on admission to ED n (%) Active seizure/postictal period Conscious	 21 (67.8) 10 (32.2)	 33 (29.7) 78 (70.3)	 **<0.001**	 **4.9 (2.1 to 11.6)**	 **4.3 (1.7 to 11)**
Duration of postictal period (minute) median (IQR 25-75%)	30 (20-60)	20 (10-40)	**0.03**	**1.012 (1.002 to 1.02)**	1.007 (0.99 to 1.01)
Seizure features n (%) Presence aura in the pre-seizure period Prolonged postictal period*** Seizure period 06:00-12:00 12:00-20:00 20:00-06:00 Relationship of seizure to sleep On sleeping Awake	 9 (29) 10 (32.3) 7 (22.6) 9 (29) 15 (48.4) 9 (29) 22 (19.8)	 37 (33.3) 25 (22.5) 48 (43.2) 30 (27) 33 (29.7) 22 (71) 89 (80.2)	 0.6 0.2 0.07 0.2	 0.8 (0.3 to 1.9) 1.6 (0.6 to 3.9) N/A 0.6 (0.2 to 1.4)	 - - - -

Table 2. Continued

	Presence seizure (n=31)	Absence seizures (n=111)	p value	Unadjusted odds ratio 95% CI	Adjusted odds ratio 95% CI
Clinical features n (%)					
Fever higher than 38 °C in last 24 h	8 (25.8)	15 (13.5)	0.1	2.2 (0.8 to 5.8)	-
Disturbed sleep in the last 48 h	21 (67.7)	58 (52.3)	0.1	1.9 (0.8 to 4.4)	-
Alcohol intake in the last 24 h	0 (0)	5 (4.5)	N/A	N/A	N/A[a]
Acute traumatic injury	12 (38.7)	45 (40.5)	0.8	0.9 (0.4 to 2.0)	-
Psychotropic drug use in the last 24 h	4 (12.9)	3 (2.7)	**0.04**	**5.3 (1.12 to 25.2)**	N/A[a]
Acute psychological stress in the last week	18 (58.1)	69 (62.2)	0.6	0.8 (0.3 to 1.8)	-
Changing AED dosage	7 (22.6)	14 (12.)	0.2	2.02 (0.7 to 5.5)	-
Use of herbal medicine	0 (0)	4 (3.6)	N/A	N/A	N/A[a]
Cerebral localization of epilepsy**** n (%)					
Frontal	2 (6.5)	7 (6.3)			
Temporal	6 (19.4)	16 (14.4)			
Parietal	9 (29)	40 (36)	0.8	N/A	-
Occipital	3 (9.7)	9 (8.1)			
Limbic	0 (0)	5 (4.5)			
Unknown	11 (35.5)	34 (30.6)			
Vital signs on admission median (IQR 25-75%)					
Systolic blood pressure: mmHg	120 (109 to 140)	120 (110-132)	0.9	0.99 (0.97 to 1.02)	-
Diastolic blood pressure: mmHg	70 (65 to 80)	70 (65-80)	0.9	1.02 (0.9 to 1.04)	-
Pulse - beat/min	100 (82 to 116)	90 (79-100)	**0.009**	**1.039 (1.012 to 1.066)**	1.027 (0.99 to 1.05)
Fever - °C	36.4 (36 to 37.8)	36.3 (36.1 to 36.7)	0.1	2.06 (0.8 to 3.5)	-
Blood sugar: mg/dL	109 (96 to 131)	104 (91 to 120)	0.1	1.02 (0.9 to 1.02)	-
Oxygen saturation - %	95 (92 to 97)	96 (94 to 98)	0.3	0.9 (0.7 to 1.07)	-
Glasgow-coma scale	11 (9 to 15)	15 (13 to 15)	**<0.001**	0.7 (0.6 to 0.9)	-
Laboratory findings median (IQR 25-75%)					
pH	7.30 (7.20-7.40)	7.39 (7.34-7.42)	**<0.001**	**0.002 (0.001 to 0.08)**	Not included[b]
PCO_2 - mmHg	41 (35-47)	40 (35-46)	0.5	1.03 (0.9 to 1.08)	-
Bicarbonate - mmol/L	22 (16-26)	23 (20-26)	0.3	0.9 (0.8 to 1.03)	-
Lactate - mEq/L	6.2 (3.2-9.2)	2.8 (1.8-4.8)	**<0.001**	**1.2 (1.08 to 1.3)**	1.09 (0.96 to 1.2)
White blood cell - $x10^3/\mu L$	12.7 (8.8-15.2)	7.9 (6.7-10.1)	**<0.001**	**1.2 (1.1 to 1.3)**	**1.2 (1.08 to 1.3)**
Neutrophil - $x10^3/\mu L$	8.9 (4.6-11.7)	4.7 (3.9-6.6)	**<0.001**	**1.2 (1.1 to 1.3)**	Not included[c]
Lymphocyte - $x10^3/\mu L$	2.4 (1.2-4.5)	2.3 (1.69-3.2)	0.8	1.01 (0.9 to 1.1)	-
Hemoglobin - g/dL	14 (12.8-15.5)	14.1 (12.8-15.5)	0.8	1.01 (0.8 to 1.2)	-
Platelet - $x10^3/\mu L$	223 (182-299)	240 (191-287)	0.8	0.99 (0.97 to 1.003)	-
Creatinine	0.8 (0.7-1)	0.8 (0.7-0.9)	0.7	1.12 (0.1 to 6.8)	-
ALT - IU/L	16 (10-25)	14 (11-21)	0.6	0.99 (0.97 to 1.01)	-
Total bilirubin: mg/dL	0.3 (0.2-0.36)	0.3 (0.15-0.4)	0.7	0.4 (0.1 to 2)	-
Sodium - mEq/L	138 (137-140)	138 (137-140)	0.9	1.01 (0.9 to 1.1)	-
Potassium - mEq/L	3.9 (3.7-4.1)	4.1 (3.8-4.3)	0.06	0.3 (0.1 to 1.02)	-
Calcium - mg/dL	9.5 (9-10)	9.6 (9.2-9.9)	0.06	0.8 (0.4 to 1.5)	-
Length of stay ED median (IQR 25-75%)	8 (6-12)	4 (4-6)	0.1		-
IV AED needing in ED n (%)	23 (74.2)	4 (3.6)	**<0.001**		Not included[d]

*Severe head trauma history: Presence of head trauma requiring hospitalization or surgical intervention and accompanying altered mental status in history.
**Cluster-type seizure: Two or more seizures in 24 h.
***Prolonged postictal period: Prolonged postictal period compared to the previous postictal period based on the anamnesis taken from relatives.
****Location detected on EEG that performed after the last seizure attack.
#Epilepsy disease secondary to organic lesion (intracranial hemorrhage, ischemic stroke, etc.).
##Epilepsy that starts unrelated to any organic lesion.
[a]: Insufficient sample size in cells to perform regression analysis.
[b]: pH variable was found to be highly correlated with lactate values. Therefore, it was excluded in the regression model.
[c]: Neutrophil variable was found to be highly correlated with white blood cell values. Therefore, it was excluded in the regression model.
[d]: It was considered as an alternative outcome.
AED: Anti-epileptic drug, ED: Emergency department, N/A: Not applicable

Table 3. Demographical and clinical characteristics of patients according to the presence of recurrence seizure within first 24 h					
	Presence seizures (n=39)	**Absence seizures (n=103)**	**p value**	**Unadjusted odds ratio 95% CI**	**Adjusted odds ratio 95% CI**
Gender n (%)					
Male	17 (43.6)	55 (53.4)	0.2	0.64 (0.3 to 1.4)	-
Female	22 (56.4)	48 (46.6)			
Age median (IQR 25-75%)	34 (22 to 41)	31 (25 to 44)	0.4	0.99 (0.96 to 1.019)	-
Comorbidities n (%)					
Chronic hypertension	1 (2.6)	9 (8.7)	0.2	0.27 (0.03 to 2.4)	-
Coronary artery diseases	0 (0)	6 (5.8)	N/A	N/A	-
Diabetes mellitus	1 (2.6)	5 (4.9)	1	0.5 (0.05 to 4.5)	-
Cerebral palsy	4 (10.3)	1 (1)	**0.02**	**11 (1.2 to 107)**	N/A[a]
Cerebra-vascular event	2 (5.1)	6 (5.8)	1	0.8 (0.1 to 4.5)	-
Psychiatric disorders	5 (12.8)	11 (10.7)	0.7	1.2 (0.3 to 3.8)	-
Chronic alcohol use	9 (23.1)	14 (13.6)	0.1	1.5 (0.4 to 5.6)	-
Others	4 (10.3)	7 (6.8)	0.4	1.9 (0.7 to 4.8)	-
The history of epilepsy n (%)					
Epilepsy history in family	6 (15.4)	22 (21.4)	0.4	0.6 (0.2 to 1.8)	-
Previously meningitis history	2 (5.1)	4 (3.9)	0.6	1.3 (0.2 to 7.6)	-
Febrile convulsion history	11 (28.2)	30 (29.1)	0.9	0.9 (0.4 to 2.1)	-
Difficult birth history	7 (17.9)	18 (17.5)	0.9	1.03 (0.39 to 2.7)	-
Severe head trauma history*	11 (28.2)	24 (23.3)	0.5	1.2 (0.5 to 2.9)	-
Previously status epilepticus history	7 (17.9)	14 (13.6)	0.5	1.3 (0.5 to 3.7)	-
Hospital admission history due to epilepsy	16 (41)	32 (31.1)	0.2	1.5 (0.7 to 3.3)	-
ICU admission history due to epilepsy	6 (15.4)	11(10.7)	0.5	1.5 (0.5 to 4.4)	-
Intubation history due to epilepsy	1 (2.6)	2 (1.9)	1	1.3 (0.1 to 15)	-
Epileptic surgery history	0	1 (1)	-	N/A	N/A[a]
Cluster-type epilepsy history**	28 (71.8)	47 (45.6)	**0.005**	**3.03 (1.3 to 6.7)**	2.1 (0.8 to 5.8)
Drug history n (%)					
AED using	38 (97.4)	94 (91.3)	0.2	3.6 (0.4 to 29)	-
Nonadherent to AED therapy	18 (46.2)	30 (29.1)	0.056	2.08 (0.9 to 4.4)	**2.5 (1.09 to 6.5)**
Unused last of AED dosage	19 (48.7)	51 (49.5)	0.9	1.03 (0.4 to 2.1)	-
Polytherapy AE use	16 (41)	30 (29.1)	0.07	1.8 (0.8 to 4.03)	**2.9 (1.08 to 8.1)**
Third-generation AED using	28 (71.8)	63 (61.2)	0.2	1.6 (0.7 to 3.6)	-
Age of when diagnosed epilepsy median (IQR 25-75%)	17 (12 to 26)	22 (12 to 30)	0.1	0.98 (0.95 to 1.04)	-
Duration time since diagnosed epilepsy/year median (IQR 25-75%)	13 (4 to 23)	8 (2 to 18)	0.1	1.02 (0.9 to 1.05)	-
The presence of weekly routine seizures in history n (%)	11 (28.2)	11 (10.7)	**0.01**	**3.2 (1.2 to 8.3)**	**3.9 (1.2 to 12)**
The presence of monthly routine seizures in history n (%)	14 (35.9)	41 (39.8)	0.6	0.8 (0.3 to 1.8)	-
Epilepsy etiology n (%)					
Symptomatic[#]	26 (66.7)	67 (65)	0.8	0.9 (0.4 to 2.02)	-
Idiopathic[##]	13 (33.3)	36 (35)			
The state of consciousness on admission to ED n (%)					
Active seizure/postictal period	23 (59)	31 (30.1)	**0.002**	**3.3 (1.5 to 7.1)**	1.5 (0.5 to 4.5)
Conscious	16 (41)	72 (69.9)			
Duration of postictal period (minute) median (IQR 25-75%)	30 (20-60)	20 (10-30)	**0.009**	**1.014 (1.003 to 1.025)**	**1.01 (1.001 to 1.026)**
Seizure features n (%)					
Presence aura in the pre-seizure period	13 (33.3)	33 (32)	0.8	1.06 (0.4 to 2.3)	-
Prolonged postictal period***	13 (33.3)	22 (21.4)	0.1	1.8 (0.8 to 4)	-
Seizure period					
06:00-12:00	11 (28.2)	44 (42.7)			
12:00-20:00	10 (25.6)	29 (28.2)	0.1	N/A	-
20:00-06:00	18 (46.2)	30 (29.1)			
Relationship of seizure to sleep					
On sleeping	11 (28.2)	20 (19.4)	0.2	0.6 (0.2 to 1.4)	-
Awake	28 (71.8)	83 (80.6)			

Table 3. Continued

	Presence seizures (n=39)	Absence seizures (n=103)	p value	Unadjusted odds ratio 95% CI	Adjusted odds ratio 95% CI
Clinical features n (%)					
Fever higher than 38 °C in last 24 h	8 (20.5)	15 (14.6)	0.3	1.5 (0.5 to 3.9)	-
Disturbed sleep in the last 48 h	24 (61.5)	55 (53.4)	0.3	1.3 (0.6 to 2.9)	-
Alcohol intake in the last 24 h	0 (0)	5 (4.9)	-	N/A	N/A[a]
Acute traumatic injury	14 (35.9)	43 (41.7)	0.5	0.7 (0.3 to 1.6)	-
Psychotropic drug use in the last 24 h	5 (12.8)	2 (1.9)	**0.01**	**7.4 (1.3 to 25.2)**	N/A[a]
Acute psychological stress in the last week	24 (61.5)	63 (61.2)	0.9	1.01 (0.4 to 2.1)	-
Changing AED dosage	7 (17.9)	14 (13.6)	0.5	1.3 (0.5 to 3.7)	-
Use of herbal medicine	0 (0)	4 (3.9)	N/A	N/A	N/A[a]
Cerebral localization of epilepsy**** n (%)					
Frontal	2 (5.1)	7 (6.8)			
Temporal	7 (17.9)	15 (14.6)			
Parietal	14 (35.9)	35 (34)	0.2	N/A	-
Occipital	3 (7.7)	9 (8.7)			
Limbic	0 (0)	5 (4.9)			
Unknown	13 (34)	32 (31.1)			
Vital signs on admission Median (IQR 25-75%)					
Systolic blood pressure: mmHg	120 (110 to 140)	120 (110 to 132)	0.8	0.99 (0.97 to 1.02)	-
Diastolic blood pressure: mmHg	70 (64 to 75)	70 (65 to 80)	0.4	1.02 (0.9 to 1.04)	-
Pulse - beat/min	95 (82 to 110)	90 (78 to 100)	**0.02**	**1.039 (1.012 to 1.066)**	1.009 (0.9 to 1.04)
Fever - C°	36.4 (36.1 to 37)	36.4 (36 to 36.7)	0.3	2.06 (0.8 to 3.5)	-
Blood sugar: mg/dL	105 (92 to 122)	105 (91 to 120)	0.5	1.02 (0.9 to 1.02)	-
Oxygen saturation - %	95 (93 to 97)	96 (94 to 98)	0.1	0.9 (0.7 to 1.07)	-
Glasgow-coma scale	13 (10 to 15)	15 (13 to 15)	**0.003**	0.83 (0.72 to 0.95)	Not included[b]
Laboratory findings median (IQR 25-75%)					
pH	7.35 (7.25-7.4)	7.39 (7.34-7.42)	**<0.006**	**0.001 (0.0001 to 0.2)**	Not included[c]
PCO_2 - mmHg	41 (36-48)	40 (35-45)	0.4	1.03 (0.9 to 1.08)	-
Bicarbonate - mmol/L	24 (17-26)	23 (23-26)	0.6	0.97 (0.91 to 1.03)	-
Lactate - mEq/L	5.4 (2.8-8.5)	2.7 (1.8-5.2)	**<0.001**	**1.15 (1.04 to 1.2)**	1.12 (0.99 to 1.2)
White blood cell - $x10^3/\mu L$	11.6 (7.7-14.4)	7.9 (6.6-10.1)	**<0.001**	**1.2 (1.1 to 1.3)**	**1.18 (1.06 to 1.3)**
Neutrophil - $x10^3/\mu L$	7.2 (4.5-10.8)	4.7 (3.8-6.5)	**<0.001**	**1.2 (1.1 to 1.38)**	Not included[d]
Lymphocyte - $x10^3/\mu L$	2.4 (1.3-4.1)	2.3 (1.7-3.1)	0.8	0.99 (0.8 to 1.1)	-
Hemoglobin - g/dL	14.1 (13-15.5)	14 (12.7-15.5)	0.5	1.06 (0.8 to 1.2)	-
Platelet - $x10^3/\mu L$	241 (182-296)	234 (187-290)	0.9	0.99 (0.98 to 1.003)	-
Creatinine	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.8	0.6 (0.1 to 3.6)	-
ALT - IU/L	14 (10-23)	14 (11-21)	0.9	0.99 (0.97 to 1.01)	-
Total Bilirubin: mg/dL	0.3 (0.2-0.3)	0.3 (0.1-0.4)	0.4	0.3 (0.08 to 1.4)	-
Sodium - mEq/L	138 (137-141)	138 (137-140)	0.8	1.03 (0.9 to 1.1)	-
Potassium - mEq/L	4 (3.8-4.1)	4.1 (3.8-4.3)	0.1	0.4 (0.1 to 1.1)	-
Calcium - mg/dL	9.7 (9-9.9)	9.5 (9.2-9.8)	0.4	0.99 (0.93 to 1.05)	-
The length of stay ED median (IQR 25-75%)	6 (5 to 12)	4 (4 to 6)	**<0.001**	**1.6 (1.3 to 2.02)**	Not included[e]
IV AED needing in ED n (%)	23 (59)	4 (3.9)	**<0.001**	**35 (10 to 116)**	Not included[e]

*Severe head trauma history: Presence of head trauma requiring hospitalization or surgical intervention and accompanying altered mental status in history.
**Cluster-type seizure: two or more seizures in 24 h.
***Prolonged postictal period: Prolonged postictal period compared to the previous postictal period based on the anamnesis taken from relatives.
****Location detected on EEG that performed after the last seizure attack.
#Epilepsy disease secondary to organic lesion (Intracranial hemorrhage, ischemic stroke, etc.).
##Epilepsy that starts unrelated to any organic lesion.
[a]: Insufficient sample size in cells to perform regression analysis.
[b]: Glasgow coma scale was found to be highly correlated with "State of Consciousness on admission to ED" variable. Therefore, it was excluded in the regression model.
[c]: pH variable was found to be highly correlated with lactate values. Therefore, it was excluded in the regression model.
[d]: Neutrophil variable was found to be highly correlated with white blood cell values. Therefore, it was excluded in the regression model.
[e]: It was considered as an alternative outcome.
AE: Antiepileptic, ED: Emergency department, N/A: Not applicable

11.02). Similarly, in a retrospective study by Chen et al. (17) on epilepsy patients older than 16 years, symptomatic generalized epilepsy, a history of status epilepticus, and AED treatment failure (two or more AEDs' failure) were risk factors for the occurrence of SC. In the same study, Chen et al. (17) reported that patients who experienced SC were significantly less likely to be seizure-free for 1 year (27.8%) compared with patients who did not experience SC (50.9%). The main difference between these studies and our study is that they focused on SC that can be experienced in any period, whereas our study focused on ARSs within the early period after the last seizure attack. The studies by Detyniecki et al. (14) and Chen et al. (17) appear to point to two primary risk factors for SC or ARS: a history of SC in the previous year and AED treatment failure. In our study, although a history of cluster-type epilepsy was not a significant predictor for ARS in the multivariate analysis, the ratio of cluster-type epilepsy in the ARS group was higher than that in the non-ARS group (71.8% vs 45.6%) in the univariate analysis. We believe that the number of AEDs used during a lifetime, a risk factor for SC in the study by Detyniecki et al. (14), treatment failure with two or more AEDs, a risk factor for SC in the study by Chen et al. (17), and AED polytherapy, which was a risk factor for ARS in our study, may be related to AED resistance. We conclude that a history of AED resistance is a crucial risk factor for SC and ARS.

Similar to our study, Choquet et al. (18) conducted a prospective study aimed at determining the frequency and predictors of ARS in the early period (at least one ARS within the first 24 hr) after admission to the ED. This study included not only patients with a confirmed diagnosis of epilepsy but also patients with new-onset seizures. The frequency of ARS in their study was 18.4%, and the GCS of the patients was lower than 15 points on admission. Age (i.e., older than 40 y) and a history of alcoholism were risk factors for ARS within the first 24 h after admission with a seizure. In our study, although alcoholism and older age were not predictive factors, a low GCS score seemed to be an important predictor of ARS. However, we did not include a low GCS score as a variable in the regression model because of its high correlation with state of consciousness on admission to the ED. We reported the presence of active seizures/postictal period on admission as predictors instead of a low GCS score.

Finally, in a study on 94 epilepsy patients older than 14 years, Kılıc et al. (19) evaluated the diagnostic performance of venous blood gases for ARS within the follow-up period in the ED in patients who were admitted to the ED with seizures. The authors reported that lactate, pH, base excess, and bicarbonate values in venous blood gases measured within 1 h after the last epileptic seizure episode appeared to be helpful in predicting ARS in the early period with high accuracy. Similarly, in our study, lactate and pH values seemed to be potential predictors of ARS in the univariate analysis, although they were not significant predictors of the risk of ARS in the multivariate analysis. Unlike previous studies, WBC count was identified as a predictor factor for ARS in our study. It has been reported that increase in WBC count in seizures can be related to increasing muscle activity and prolonged muscle activity can cause more increasing WBC count by several studies (20,21). Therefore, we think that prolonged seizures (mean prolonged muscle activity and more increasing WBC count) can be related to recurrence seizures. We believe that prognostic values of WBC count for recurrence seizures is not sufficiently studied in the literature.

Study Limitations

This study has some limitations. First, we think that our sample size could be limited to determine most factors predicting the risk of ARS in the multivariate regression analysis. Second, although we tried to include as many demographic and clinical variables as possible in our model, some risk factors may have been overlooked. Finally, the definition of ARS in our study may be a limitation. There is no standard definition of SC or ARS, with the definitions for both varying in the literature. Therefore, it is not easy to generalize and compare our findings with those of previous studies, which may have employed different SC and ARS definitions.

Conclusion

Despite the limitations of the present study, it showed that after a first seizure, ARS is not rare in the early period after admission to the ED, with an incidence of 21.8% in the first 6 h and 27.4% in the first 24 h. In our study, nonadherent to AED therapy, active seizures/postictal period on admission, and white blood cell count seemed to be related to an increase in ARS within the first 6 h and that nonadherent to AED therapy, AED polytherapy, a history of weekly seizures, and the postictal period duration appeared to be associated with an increase in ARS within the first 24 h.

As a result, we think that physicians should be aware of the need to follow up patients with 24-h ARS risk factors in the EDs for a longer time or to inform their relatives about the risk of ARS in case of a decision to be discharged.

Ethics

Ethics Committee Approval: The study was approved by the Ankara Keçiören Training and Research Hospital of Local Ethics Committee (protocol id and date: 48865165-020/07.10.2018).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.Ş.Ç., D.Y.C., Concept: H.Ş.Ç., Ş.K.Ç., D.Y.C., E.E., Y.Ç., Design: H.Ş.Ç., Ş.K.Ç., D.Y.C., E.E., Y.Ç., Data Collection or Processing: H.Ş.Ç., D.Y.C., Y.Ç., Analysis or Interpretation: Ş.K.Ç., E.E., Y.Ç., Literature Search: H.Ş.Ç., Ş.K.Ç., E.E., Writing: H.Ş.Ç., Ş.K.Ç., D.Y.C., E.E.

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Comparison of the Effects of COVID-19 Pandemic on Acute Appendicitis Treatment and Its Clinical Outcomes with the Pre-COVID-19 Pandemic Period

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Abstract

Aim: We aimed to compare the rate of admission to the hospital, duration of symptoms, prior admission to an external center, laboratory values, risk of complication development, and length of hospitalization of patients diagnosed with acute appendicitis and undergoing appendectomy during the pre- and Coronavirus disease-2019 (COVID-19) pandemic periods.

Materials and Methods: A total of 464 patients, male and female, over the age of 18 years who were operated on with the diagnosis of acute appendicitis in Gaziantep University Medical Faculty Hospital General Surgery Clinic were included in our retrospective study. All patients underwent an open appendectomy with the diagnosis of acute appendicitis. Periods are pre-COVID-19 pandemic (March 11, 2019-March 10, 2020) and COVID-19 pandemic period (March 11, 2020-March 10, 2021).

Results: Of the cases included in the study, 254 (54.7%) were admitted before the pandemic and 210 (45.3%) were admitted during the pandemic period. Of the patients, 238 (51.3%) were female and 226 (48.7%) were male. The mean duration of symptoms of the patients was 2.41±2.38 days. In our study, it was found that only the duration of symptoms was prolonged during the pandemic period.

Conclusion: Because of our study, patients applied to our health center later due to limitations in social life and fear of contamination during the pandemic period. The pandemic period did not increase the complication risk of acute appendicitis cases.

Keywords: Acute appendicitis, pandemic, COVID-19, acute abdomen, duration of symptoms

Introduction

The most common cause of emergency surgery in the world is acute appendicitis (1,2). Acute appendicitis is the clinical picture that occurs due to inflammation in the appendix. Fecalitis and lymphoid tissue proliferation are the most common causes of acute appendicitis (3). Diagnosis is made by physical examination and supported using laboratory and imaging methods. It is most commonly seen in the second and third decades (4). Its incidence is 233/100,000 people in the world. It is more common in men (1). Each year, appendectomy is performed on 700000 people in Europe and 250000-300000 people in the USA. Currently, there are many different views and approaches in the management of acute appendicitis. But the gold standard in treatment is surgery. In late intervention, the clinic of simple appendicitis leaves its place to perforation, and mortality increases in morbidity (5). The probability of the perforation of the appendix within 36 h after the onset of abdominal pain is between 16-36%. The longer the time, the higher the rate (6).

At the end of 2019, cases of pneumonia of unknown cause were reported in the city of Wuhan in the Hubei region of China. On January 7, 2020, it was reported that the cause of these pneumonia cases was an unprecedented new type of coronavirus (2019-nCoV). The World Health Organization (WHO) declared an emergency that threatens the health of the international community on January 30, 2020 and was declared a "pandemic" on March 11, 2020 by WHO (7). Coronavirus disease-2019 (COVID-19) studies started in Turkey on January 10, 2020 and the first scientific advisory board meeting was held on January 22, 2020. The first COVID-19

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case in Turkey was seen on March 11, 2020 (8). Since this date, changes have been made in surgical services in hospitals with the COVID-19 pandemic. Elective cases have been postponed, and there have been changes in treatment protocols for emergencies.

Our aim in this study was to compare the treatment and clinical outcomes of patients hospitalized with the diagnosis of acute appendicitis in the general surgery clinic of Gaziantep University Medical Faculty Hospital between the 1-year period from the beginning of the COVID-19 pandemic (March 11, 2020-March 10, 2021) and the 1-year period before the COVID-19 pandemic (March 11, 2019-March 10, 2020).

Materials and Methods

Gaziantep University Faculty of Medicine Clinical Research Ethics Committee approval was obtained for the study with protocol number 2021/255 dated August 5, 2021. A total of 464 patients, male and female, over the age of 18 years who were operated on with the diagnosis of acute appendicitis in Gaziantep University Medical Faculty Hospital General Surgery Clinic were included in our study. All patients underwent an open appendectomy with the diagnosis of acute appendicitis. The recorded data of the patients in the archive of Gaziantep University Faculty of Medicine, Department of General Surgery, and in the hospital database were analyzed retrospectively. Patients 1 year before the onset of the COVID-19 pandemic (March 11, 2019-March 10, 2020) and 1 year after the onset of the COVID-19 pandemic (March 11, 2020-March 10, 2021) were included in the study. In both periods, such as age, gender, admission status (admission to an external center), duration of pain, delayed admission (more than 3 days), appendix diameter, C-reactive protein (CRP) value, white blood cells (WBC) value, type of incision, perforated appendicitis, presence of abscess, complication, and length of hospitalization parameters were compared.

Statistical Analysis

Data were evaluated by statistical analysis with IBM Statistical Package for the Social Sciences 23 (IBM Inc., Chicago, IL, USA) program. Median 25% and 75% values were used in the descriptive statistics of continuous variables, while the number of people (n) and percentage (%) values were given in the definition of categorical variables. Relationships between categorical variables were examined by chi-square test analysis. Whether the continuous variables showed normal distribution was checked with Shapiro-Wilk's test of normality, and homogeneity of variance was checked with Levene's test. Bi-level comparisons were made with the independent sample median test in cases where normal distribution was not observed. A value of $p<0.05$ was set as the significance in all analysis (n: number of people, p: p value).

Results

In our study, appendectomy was performed in 464 patients with the diagnosis of acute appendicitis, 254 (54.7%) before the pandemic and 210 (45.3%) during the pandemic period.

Of the patients included in the study, 238 (51.3%) were female and 226 (48.7%) were male. The youngest of the patients was 18 years old, the oldest was 90 years old, and the mean age was 35.34±14.89 years (Table 1).

Of the patients included in the study, 114 (24.6%) were patients who had previously applied to an external center. The mean duration of symptoms of the patients was 2.41±2.38 days, and there were 90 (19.4%) patients with symptom duration more than 3 days and 374 (80.6%) patients with symptom duration less than 3 days. The mean appendix diameter of the patients was 9.77±2.44 mm, mean CRP value was 51.90±68.81 mg/L, mean WBC value was 13.78 103/L. McBurney incision was present in 389 (83.8%) patients, and midline incision was found in 75 (16.2%) patients. Perforation was observed in 79 (17.0%) patients, and periappendicular abscess was observed in 38 (8.2%) patients. Appendicitis was complicated in 90 (19.4%) patients. The mean hospital stay of the patients was 3.54±2.61 days, and the patients were hospitalized for the shortest 1 day and the longest 25 days (Table 2).

The median age of the patients was 30 years before the pandemic and 31 years during the pandemic period. It was found that the median age of the patients did not have a statistically significant relationship with the pre-pandemic period ($p>0.05$) (Table 1).

Before the pandemic, 115 (45.3%) of the patients were male and 139 (54.7%) were female; During the pandemic period, 111 (52.9%) were male and 99 (47.1%) were female. No statistically significant relationship was found between the gender and pandemic periods ($p>0.05$) (Table 1).

It was found that there was no statistically significant relationship between the pandemic period and the patients' previous admission to an external center and their delayed admission ($p>0.05$). There was no statistically significant difference in the median values of appendix diameter, CRP, and WBC of the patients before and during the pandemic period. It was found that there was no statistically significant difference ($p>0.05$). While the median symptom duration of the patients before the pandemic was 1 day, it was obtained as 2 days for the patients in the pandemic period. It was observed that the median symptom duration was statistically significantly higher in patients in the pandemic period ($p=0.008$) (Figure 1).

Before the pandemic, 210 (82.7%) patients had McBurney incision and 44 (17.3%) had midline incision; During the pandemic period, McBurney incision was observed in 179 (85.2%) patients and midline incision was observed in 31 (14.8%) patients. While there were perforation in 42 (16.5%) patients before the pandemic, it was seen in 37 (17.6%) patients during the pandemic period. Periappendicular abscess was observed in 24 (9.4%) of the patients before the pandemic and in 14 (6.7%) during the pandemic period. Complicated appendicitis was detected in 42 (20%) patients during the pandemic period and 48 (18.9%) before the pandemic. There was no statistically significant relationship between the pandemic period and the presence of incisions, perforations, periappendicular abscesses, or complicated appendicitis ($p>0.05$). There was no statistically significant difference in the median length of hospital stay of the patients before and during the pandemic ($p>0.05$) (Table 3).

Discussion

The COVID-19 pandemic has affected Turkey and other countries. WHO has determined rules to stop the transmission of the virus (9). Many measures have been taken, such as a curfew, interruption of face-to-face education, application to hospital, and visit restrictions unless there is an emergency. During the pandemic period, emergency and noncancer surgeries were postponed or canceled (10,11). During this period, there was a significant decrease in the hospital admissions. Some hospitals in cities have been accepted as pandemic hospitals, and only COVID-19 diagnosis and treatment have been given. Our center was not a pandemic hospital; elective surgeries were canceledwhen the pandemic peaked, and emergency and cancer surgeries continued. In our study, it was determined that 254 (54.7%) of 464 patients applied before the pandemic and 210 (45.3%) applied after the pandemic. In the study of Antakia et al. (12), 116 (56.03%)

Table 1. Comparison of general demographic characteristics of patients in pre- and post-pandemic groups

	Period				
	Prepandemic (n=254)		**Pandemic (n=210)**		
	Median (25-75%)		**Median (25-75%)**		**p**
Age	30 [24-45]		31 [24 -41]		0.929
	n	**%**	**n**	**%**	**p**
Gender					0.104
Male	115	45.3	111	52.9	
Female	139	54.7	99	47.1	

*A p value less than 0.05 (typically ≤0.05) is statistically significant

Table 2. Comparison of the pre-op characteristics of the patients in the pre- and post-pandemic groups

	Period				
	Prepandemic (n=254)		**Pandemic (n=210)**		
	Median (25-75%)		**Median (25-75%)**		**p**
External center application					0.100
Yes	70	27.6	44	21.0	
No	184	72.4	166	79.0	
Delayed application					0.314
Yes	45	17.7	45	21.4	
No	209	82.3	165	78.6	
	Median (25-75%)		**Median (25-75%)**		**p**
The duration of symptoms (day)	1 [1-3]		2 [1-3]		0.008*
Appendix diameter (Mm)	10 [8-11]		10 [8-11]		0.567
CRP (mg/L)	19.57 [5.8-66.58]		22.46 [6.1-81.56]		0.641
WBC (10^3/μL)	12.79 [9.52-16.84]		13 [10.11-16]		0.463

*A p value less than 0.05 (typically ≤0.05) is statistically significant.
CRP: C-reactive protein, WBC: White blood cells

of 207 patients applied before the pandemic and 91 (44.97%) during the pandemic period. He attributed this to isolation during the pandemic period. However, the number of patients did not significantly decrease in our study. The reason for this is that other state hospitals in our province do not receive surgical cases due to the pandemic, and these emergency cases are taken in our center.

While the median duration of symptoms was 1 day before the pandemic, it was 2 days during the pandemic period. In our study, the duration of symptoms was significantly higher during the pandemic period than before the pandemic. During the pandemic period, patients applied later than in the previous period. The reason for this is the fear of COVID-19 contamination,

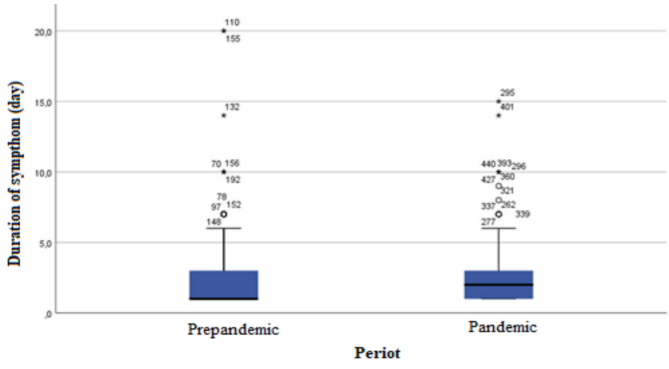

Figure 1. Comparison of symptom duration of patients during and before the pandemic

curfew, and transportation difficulties during the pandemic period. In the study of Tankel et al. (13), the median duration of symptoms was found to be 1.8 before the pandemic and 1.5 during the pandemic period. The reason why there was no significant difference in this study is that the study was conducted in an early period and in a short time.

In our study, 114 (24.6%) patients had previously applied to an external center. The rate of application to an external center was 27.6% before the pandemic and 21% during the pandemic period. The reason for this decrease is that patients apply directly to our center because other hospitals in the city center are pandemic hospitals.

Extending the length of stay increases the cost, the risk of infection, mortality, and morbidity. In our study, the duration of hospitalization of all patients was calculated as days, with an average of 3.54±2.61 days. The patients were hospitalized for the shortest 1 day and the longest 25 days. The median length of stay in the pre-pandemic period was 3 days, and the pandemic period was 3 days. No significant difference was observed between the duration of hospitalization during and before the pandemic period (p=0.978). In the study of Tankel et al. (13), the average hospital stay was found to be 2.4 days, 2.5 days before the pandemic, and 2.3 days during the pandemic. No significant difference was found (p=0.139). Our study supports similar studies.

Table 3. Comparison of per- and post-op values of patients in the pre- and post-pandemic groups

	Period				
	Prepandemic (n=254)		**Pandemic (n=210)**		
	n	**%**	**n**	**%**	**p**
Incision					0.456
McBurney	210	82.7	179	85.2	
Midline	44	17.3	31	14.8	
Perforation					0.757
Yes	42	16.5	37	17.6	
No	212	83.5	173	82.4	
Periappendicular abscess					0.277
Yes	24	9.4	14	6.7	
No	230	90.6	196	93.3	
Complicated appendicitis					0.765
No	206	81.1	168	80.0	
Yes	48	18.9	42	20.0	
	Median (25-75%)		Median (25-75%)		p
The length of stay (days)	3 [2-4]		3 [2-4]		0.978

*A p value less than 0.05 (typically ≤0.05) is statistically significant

In our study, appendectomy was performed on all patients. No medical treatment was given. In the study of Ganesh et al. (14), 100% of them had appendectomy before the pandemic, while 56.3% of them underwent appendectomy during the pandemic period and a significant difference was observed ($p<0.001$). In the study of Köhler et al. (15), surgical percentages did not change (91%) during and before the pandemic period, and no significant difference was found. In the study of Antakia et al. (12), the duration of medical treatment and hospitalization increased during the pandemic period compared with the pre-pandemic period, but it did not gain significance due to the short study period and the low number of patients included in the study. Medical treatment resulted in a longer length of stay and hospitalization with acute appendicitis clinic This extended the length of the hospital stay. The cost of a longer hospital stay increases the risk of hospital-acquired infection, mortality, morbidity, and most importantly, the risk of COVID-19 infection during the pandemic period. Therefore, we did not change our treatment during the pandemic period, as in the pre-pandemic period, and surgical treatment was applied to all patients with acute appendicitis.

In our study, perforated appendicitis was detected in 79 (17%) of all patients. Perforated appendicitis was detected in 42 (16.5%) patients before the pandemic and in 37 (37%) patients during the pandemic period. There was no significant difference in the incidence of perforated appendicitis during and before the pandemic ($p>0.05$). In the study of Orthopoulos et al. (16), a 21% increase in the number of perforated appendicitis was observed during the pandemic period and it was found to be significant. In our study, there was an increase in perforated appendicitis, but it did not reach a significant value.

In our study, periappendicular abscess was found in 38 (8.2%) of all patients. Periappendicular abscess was detected in 24 (9.4%) patients before the pandemic and in 14 (6.7%) patients during the pandemic period. No significant difference was found in the occurrence of periappendicular abscess during and before the pandemic period ($p>0.05$). In the study of Orthopoulos et al. (16), an increase in the number of periappendicular abscesses was observed during the pandemic period and it was found to be significant. In our study, a decrease was found in the number of periappendicular abscesses.

Complicated appendicitis was detected in 90 (19.4%) patients in all patients, while noncomplicated appendicitis was detected in 374 (80.6%) patients. Complicated appendicitis was detected in 48 (18.9%) patients before the pandemic and in 42 (20%) patients during the pandemic period. The rate of complicated appendicitis during and before the pandemic was high, but no significant increase was found. In the study of Tankel et al. (13), the rates of complicated appendicitis were 15.9%, 13.1% before the pandemic, and 20.6% after the pandemic, and no significant difference was found in all patients. In the study of Bonilla et al. (17), the rates of complicated appendicitis were 35% before the pandemic and 33% during the pandemic, and no significant difference was found ($p=0.870$). In our study, like these studies, there was no significant increase in the number of complicated appendicitis. The first goal for treating acute appendicitis is to treat the patient before complications develop. Because we did not change our treatment method in our study, there was no significant increase in the number of complicated appendicitis.

Study Limitations

The first limitation of our study is that it was conducted in a single center and in a single city. Larger populations should be studied to validate our data. The second limitation is that while other hospitals in the city are pandemic hospitals, our hospital continues to serve in a similar way to the pre-pandemic period. Therefore, no significant differences were detected.

Conclusion

We recommend not changing the treatment protocol for acute appendicitis during pandemic periods. In our study, using the same treatment protocol, it was observed that there was no increase in the incidence of complicated appendicitis and duration of hospitalization during the pandemic period. This shows that additional resources cannon be spent on acute surgical services during pandemic periods and can be diverted.

Ethics

Ethics Committee Approval: Gaziantep University Faculty of Medicine Clinical Research Ethics Committee approval was obtained for the study with protocol number 2021/255 dated August 5, 2021.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.K., L.Y., A.A., Concept: M.K., L.Y., Design: M.K., L.Y., Data Collection or Processing: M.K., L.Y., A.A., Analysis or Interpretation: M.K., L.Y., Literature Search: M.K., L.Y., A.A., Writing: M.K., L.Y.

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Decision to Close a Factory in the COVID-19 Pandemic: Only One Hour of Work

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Abstract

Aim: Accurate and rapid screening with polymerase chain reaction (PCR) is important for epidemic management. In our study, samples taken at a local factory were evaluated to report cases of Coronavirus disease-2019 (COVID-19). In this study, we show the importance of the pooling method.

Materials and Methods: In this study, samples were taken from 840 people with suspected COVID-19 in a textile factory in Turkey. COVID-19 RT-qPCR Detection Kit (Bio-Speedy®) performing one-step reverse transcription (RT) and real-time PCR (qPCR) (RT-qPCR) targeting the RNA-dependent RNA polymerase (RdRp) gene Severe acute respiratory syndrome (SARS)-CoV-2 The specific region was used. Non-sigmoid curves and curves below the threshold level were considered negative. The result was interpreted as SARS-CoV-2 (2019-nCoV) positive if RdRp was positive and as SARS-CoV-2 (2019-nCoV) negative if RdRp was negative.

Results: Among the pooled samples, 20 (23%) were found to be positive, and when the samples were studied individually, 102 (12%) were positive. Since all the samples fit on a single test plate with the aid of pooling method, it was possible to work at once and the results were obtained 1 h after the samples arrived at the laboratory. Thus, the separation of positive and negative persons was carried out in 1 h by pooling and it was 12 times shorter.

Conclusion: In cases where large screening groups need a rapid diagnosis, pooling is thought to be beneficial in terms of preventive medicine and social and economic aspects.

Keywords: COVID-19, pandemic, polymerase chain reaction, pooling

Introduction

Coronavirus disease-2019 (COVID-19) is an infectious disease that appeared in December 2019 in Wuhan, China, which emerged as pneumonia of unknown etiology and caused a pandemic in a short time. The disease primarily affects the respiratory system, and non-specific symptoms such as fever, cough, myalgia, headache, hemoptysis, diarrhea, and dyspnea can also be seen. Coronaviruses (CoV) as a member of the Coronaviridae family can progress to different clinical situations, from flu to lower respiratory tract and lung infections, depending on the patient's immune system (1,2). Although lung computed tomography, high C-reactive protein level, and low leukocyte count are helpful in the diagnosis of the disease, they are not sufficient to distinguish it from other pneumonia forms (3). Also, the symptoms observed in the patients are nonspecific and other respiratory system infections may present with a similar clinical picture.

Molecular tests are the most widely used method to prove the presence of the virus, and many nucleic acid and antibody detection kits have been approved. Today, reverse transcriptase-polymerase chain reaction (RT-PCR) is the most frequently used method for detecting the agent in respiratory tract samples (4). RT-PCR tests have some limitations, test results can be obtained for a long time, and they are expensive and technically difficult.

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In addition, the risk of contamination is high and the process requires specialized equipment and experienced personnel. In addition to methodological handicaps, it is possible to obtain false-negative results depending on the characteristics of the agent and infection. The results are affected by the timing of the sample (being taken in the early or late period of the disease), sample quality, transportation conditions, and test technique (eg virus mutation, inhibition in the test) (5). When the first case is detected in crowded communities in social life and workplaces, studies should be carried out for RT-PCR in the form of rapid and collective screenings so that work and social life are not affected. However, when this sudden workload is far beyond the capacity of the laboratory, the diagnostic time becomes longer.

In cases of limitation, closure, and mass quarantine, determination of how much of the scanned community is infected is important in terms of limiting transmission. In the diagnostic process, the isolation rules and the increasing restrictions on both business and social life made it necessary to detect patients immediately. Samples can be examined one by one or by the pooling method, which is simple, practical, and valuable in that it uses minimal research resources (6).

In our study, we used samples taken for the decision to close a local factory with suspicion of disseminated disease. The results of the RT-PCR performed with the pooling method and the studies performed for each patient were compared later on, and we aimed to reveal the importance of the pooling method.

Materials and Methods

In this study, samples taken upon the detection of COVID-19 cases in a textile factory in Mardin city were evaluated. Samples were taken from 840 factory workers to close the factory due to the epidemic or to take the quarantine decision of the contacts. Before starting the study, the necessary permission was obtained from the Ethics Committee of the Ankara City Hospital no. 2 with the decision dated 02.03.2022 and numbered E2-22-2493. After evaluating the RT-PCR results performed using the pooling method in the first hour, the results were verified by working the samples one by one.

Samples were taken along with the same test strip, first as an oropharyngeal swab and then as a nasopharyngeal swab. After visualizing the posterior wall of the oropharynx, the tip of the test stick was rubbed against the posterior pharyngeal wall with a rolling motion without touching the tongue, base of the tongue, tonsils, or soft palate. After it was observed that the tip of the swab was wetted with secretion, the swab was then taken out without touching the surroundings, and the nasopharyngeal sampling phase was started. The test stick was passed through the nostril and advanced parallel to the palate from the inferior meatus under the inferior concha, and the tip of the test stick was wetted by secretion. The test rod was advanced to the distance from the nostrils to the level of the external auditory canal (8-10 cm) and it was ensured to reach the nasopharynx. The test strip was held in this area for a few seconds to absorb the secretions and then slowly removed. After the samples were taken, the swab was placed in the transport container and the excess part was broken off and discarded. The samples were placed in a VNAT (viral nucleic acid buffer) (Bioeksen, Turkey) solution and delivered to the microbiology laboratory without breaking the cold chain.

After the samples reached the microbiology laboratory, necessary sorting and recording procedures were performed. In the isolation room, 100 µL was withdrawn from each of the 10 samples and transferred to the same tube and this was accepted as a new sample. All 84 samples were studied in single cycle.

The samples were taken into class 2 biosafety cabinet. The COVID-19 RT-qPCR Detection Kit targeting the SARS-CoV-2-specific RdRp (RNA-dependent RNA polymerase) gene region was used for nucleic acid isolates obtained in the medium. The kit was run with the Biorad CFX96 system, and the detection limit for the RdRp gene was based on 3.8 copies-RNA/reaction. The number of thermal cycles was determined as 40. Non-sigmoid curves and subthreshold curves were considered negative. The RNase P gene in the kit was used as the internal control of the test. If the result was RdRp positive, it was interpreted as SARS-CoV-2 (2019-nCoV) positive, and if the result was RdRp negative, it was interpreted as SARS-CoV-2 (2019-nCoV) negative. If the target gene and internal control amplification were invalid, the test was repeated. After the results were obtained, the relevant authorities were notified and a preliminary report was prepared in terms of the factory's decision to continue to work. The final results were reported to the relevant administrative units.

Statistical Analysis

This study was designed retrospectively. Data were analyzed using the Statistical Package for Social Sciences (SPSS) 20.0 for Windows (SPSS Inc., Chicago, IL). The results of the samples studied one by one and the data obtained because of pooling method were evaluated with descriptive statistical methods.

Results

In this study, samples were taken from 840 people working in a textile factory for COVID-19 screening. The samples taken from 840 people were examined by pooling method and 20 (23%) of the pools were found to be positive. Later on samples were studied individually and 102 (12%) were positive. When the

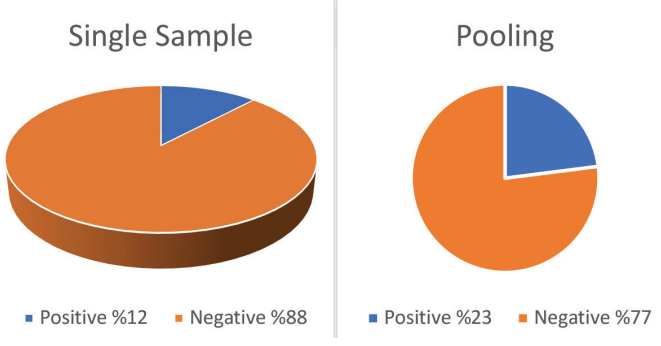
negative pools were opened and studied one by one, no positive samples were detected (Graphic 1).

When working with pooling method, the results were obtained 1 h after the samples reached the laboratory. All samples were studied in one run because they fit on one test plate. A preliminary report was prepared in 1 h for 840 samples. When the samples were run individually, 840 samples were run in 9 runs and the results were reported after approximately 12 h (Table 1).

Discussion

With the provisional guide published on March 2, 2020, the World Health Organization has determined an algorithm on how diagnostic tests can be applied in different transmission scenarios in the COVID-19 outbreak. Accordingly, in countries where the virus is rare, two steps are required to confirm the diagnosis of the first case. In the first stage, a positive result should be obtained with the NAAT test targeting at least two different regions in the virus genome, and then partial or whole genome sequencing of the virus should be performed. In countries where SARS-CoV-2 is common, screening with RT-PCR using a single distinctive target region has been recommended. However, one or more negative results will not exclude the possibility of infection (7).

Loeffelholz and Tang (8) (2020) evaluated the literature data and presented general information about the usage of COVID-19 tests. In the study, it was stated that although the nasopharyngeal swab usually the collection method, it may miss some cases. To prevent this, they suggest taking deeper samples, for example, by bronchoscopy. Alternatively, repeated testing may be used to increase the possibility of SARS-CoV-2 demonstration. It was emphasized in the study that various integrated, random access, point-of-care molecular devices have been developed for the rapid and accurate diagnosis of SARS-CoV-2 infection. It was suggested that these assays are simple, fast, and safe and can be used in local hospitals and clinics that carry the burden of identifying and treating patients.



Graphic 1. Positive rate of samples in the case of pooling and a single sample study

Indeed, RT-PCR tests have many limitations such as the delay in results, technical time-consuming, need for special equipment-experienced personnel, expensiveness, and risk of contamination. Negative results are obtained depending on the pathogenesis of the agent infection and the methodological handicaps. The nature of the material in the sample, sample collection time, improper transportation, and technical problems (e.g., virus mutation, inhibition in the test) affect the test result (9).

Yan et al. (9), point out the importance of nucleic acid tests (NAT) in the diagnosis of COVID-19 and stated that the most important and first key to responding to epidemics is early diagnosis and that laboratory tests play a major role in the early detection of infected people, enabling the identification of the source of infection and cutting the transmission route. It has been emphasized that RT-PCR is the preferred and most widely used method for NAT due to its easy methodology and extensively validated standard operating procedure (10). The pooling of PCR test samples is simple, practical, and valuable because it uses minimal research resources (6). In our study, the COVID-19 RT-q PCR detection kit was used; only 840 people working in the specified factory were included and no additional samples were taken from other applications.

Because clinical studies used different RNA extraction methods and different RT-PCR kits, it would be difficult to compare their results. Virtually, it will be necessary to conduct experiments to validate the current kit and extraction method before pooling the samples. In addition, the possibility of catching positivity by pooling may vary according to the country, region, and even the specific group tested. Therefore, the size of the pooled tests and the positivity rates of the specific groups tested should be regional at the laboratory level. Pooling should not be done in groups with high probability of positive results and in such circumstances samples should be studied one by one.

Table 1. Comparison of pooling method and single sample studies

	Pooling	Single sample run
Result time	1 hour	12 hour
Positivity rate	23%	12%
Consumable usage	1 time	9 times
Positivity	20 wells x 10 pools: 200	102 original case

In mathematical modeling, it shows that the sample pooling strategy will work better in environments with low prevalence and in asymptomatic individuals (11-13).

When large numbers of individuals should be evaluated, pooling of 5 samples is better than pooling of 10 samples to reduce false negativity and false positivity. Similar to our study, samples of 10 patients were pooled in the USA, Spain, and Chile studies (14-16). Another factor affecting our pooling plan is that factory workers are considered to have a low prevalence.

In particular, samples with a cq value greater than 33 cycles are more unsuitable for pooling (14-16). In the USA, Spain, and Chile studies, it was observed that positive samples above 30 cq were found to be false negatives, especially when clinicians pooled 10 samples (14-16) (Table 2). In our study, 10 samples were collected in 1 pool and sigmoid curves below 33 cq, which passed internal controls, were considered positive. When the negative pools were studied one by one, no positive cases were found. After we studied 840 samples in our study, a preliminary report was prepared and 102 positive cases were detected.

By using the pooling method, positive and negative people were separated in as little as 1 h, and the contact time was 12 times shorter than the individual study.

Patients infected with SARS-CoV-2 are the main source of infection. These patients should either be isolated at home or kept in the hospital according to the severity of the disease, in line with the recommendations of the health personnel. When isolation is preferred at home, patients should be kept in a single room and contact with those living at home should be minimized. The items used should be disinfected, and the room should be kept clean and ventilated appropriately (17).

Conclusion

An accurate and rapid diagnosis of COVID-19 is important for correct epidemic management. Scanning with PCR at factories, soccer matches, or concerts are key to the continuation of these activities. In such cases it takes days to run thousands of samples. Hence, individuals should be evaluated by pooling first, and samples should be studied one by one after the decision to continue the activity is made. When the factory population in our study was evaluated, no new cases were detected in the following days, and it was seen that the spread of the virus was prevented.

We conclude that pooling will be beneficial in terms of preventive medicine and social and economic aspects in cases where large screening groups need a rapid diagnosis.

Table 2. Examples of different pooling strategies and pools from different countries

Different pooling strategies from different countries			
Country	**Pooling strategy**	**The number of samples pooled**	**Reference**
Israel	Pooling of extracted RNA	32 samples/1 pool	(14)
Israel	Combined pooling strategies	348 samples/48 pools	(16)
Germany	Pooling of extracted RNA	4-30 samples/1 pool	(13)
Germany	Pooling of swabs directly in a pooling container	5 samples/1 pool	(15)
United States of America	1 pool of 5 samples of 50 µL each	5 samples/1 pool	(10)
Chile	Pooling of nasopharyngeal specimens from the transport medium	5 samples/1 pool	(9)
Spain	Pooling of nasopharyngeal specimens in transport medium	5-10 samples/1 pool	(11)

Ethics

Ethics Committee Approval: Permission was obtained from the Ankara City Hospital Ethics Committee with the date 02.03.2022 and number E2-22-2493. All procedures in this study comply with the 1975 Declaration of Helsinki, updated in 2013.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.S., Concept: A.T., E.S., Design: A.T., E.S., H.C., A.B., Data Collection or Processing: A.T., Analysis or Interpretation: A.T., H.C., A.B., Literature Search: E.S., H.C., A.B., Writing: H.C., A.B.

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Cost Evaluation of Current Pulmonary MTB Diagnosis Process in a Hospital in Abu Dhabi and Proposal to Implement the World Health Organization MTB Clinical Pathway

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Abstract

Aim: Mycobacterium tuberculosis (MTB) is a leading cause of death worldwide. The World Health Organization (WHO) recommends X-pert MTB/RIF or X-pert Ultra as the initial test for pulmonary MTB diagnosis. While several studies have explored the cost-effectiveness of this technology, none have specifically looked at its use in the United Arab Emirates (UAE). To evaluate the average estimated cost and length of stay for suspected MTB patients admitted from the emergency department to the respiratory isolation rooms to rule out MTB using the MTB classic diagnosis pathway of 3 AFB smear and MTB cultures compared to the estimated cost if the WHO X-pert MTB/RIF outpatient pathway is implemented for suspected MTB.

Materials and Methods: A quality improvement project was conducted with a retrospective audit and data analysis of suspected pulmonary MTB infection at a secondary care hospital in Abu Dhabi, UAE. We report the true accrued costs of the current admission practice for management of suspected pulmonary MTB. We also report the estimated cost of working up these same patients with the WHO pathway using X-pert MTB/RIF testing.

Results: Data analysis demonstrated that 62% of the cost of working up suspected pulmonary MTB was accumulated during admissions for patients who ultimately proved to be MTB negative. Cost evaluation of study data suggests that using the WHO X-pert MTB/RIF clinical pathway would cost approximately one-tenth as much as the current practice.

Conclusion: This analysis presents evidence for cost savings associated with the use of the WHO X-pert MTB/RIF clinical pathway in a low MTB incidence area such as the UAE. Further analysis to assess how the pulmonary MTB diagnostic pathway was influenced by COVID-19 is needed.

Keywords: Pulmonary MTB, emergency department, cost evaluation, mycobacterium tuberculosis, WHO clinical pathway, X-pert MTB/RIF, AFB smear

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Introduction

Mycobacterium tuberculosis (MTB) is an infectious disease commonly affecting the lungs (pulmonary MTB), also it may involve other organs (1). Prompt diagnosis of active pulmonary MTB is a priority for TB control, both for treating the individual and for public health intervention to reduce further spread in the community (2). MTB is often a curable disease if it is detected early and effectively treated (3). In 2018, the United Arab Emirates (UAE) total population was 10 million. The World Health Organization (WHO) estimated UAE MTB incidence at 1 (0.88-1.2) per 100 000 signifying that UAE is a low MTB incidence and burden country (4).

Current practice in many hospitals in UAE involves admitting patients with suspected MTB to the respiratory isolation ward to confirm or rule out the MTB infection. Patients are subjected to multiple diagnostic tests, including chest X-ray (CXR) and acid-fast bacilli sputum smear microscopy (AFB smear). Adding to that, the gold standard MTB culture and at times additional diagnostic tests such as QuantiFERON Gold test or MTB rapid polymerase chain reaction (PCR) may be performed. This practice has an impact on the system, resulting in increasing hospital admission rates & prolonged hospital stay, and hospital overcrowding which then leads to emergency department (ED) exit block. these practices affect patients directly through increased total cost, and indirectly can impact the patient's and their family's social and mental health (5,6).

WHO recommends X-pert MTB/RIF or the X-pert Ultra, the newest version, as the initial test for MTB (7). This testing procedure is to replaces the current standard practice of the three AFB smear (8-12). X-pert MTB/RIF test has multiple advantages: it is an automated PCR test using the GeneXpert platform, it can detect both MTB complex and rifampicin resistance in a single test with high sensitivity and specificity profile on both culture positive and culture negative sputum samples, and it is a rapid test with results available in two hours with minimal hands-on technical time. The assay's sample reagent has tuberculocidal properties eliminating biosafety concerns during the test procedure (7,13-15). WHO in 2013 published a pathway utilizing X-pert MTB/RIF test to screen / work up suspected MTB as outpatient (16). To our knowledge, there is no published literature regarding the cost and hospital resource use for suspected MTB patients in the UAE. This quality improvement project evaluates the average estimated cost and length of stay for suspected MTB patients admitted from the ED to the respiratory isolation rooms using the current practice described above and estimated cost if the WHO X-pert MTB/RIF outpatient pathway is implemented for suspected MTB.

Materials and Methods

This was a quality improvement project where we conducted a retrospective audit and data analysis for suspected MTB patients admitted through our ED over a 1-year period. The hospital where the analysis was performed is a secondary care hospital in Abu-Dhabi with 380 beds. In 2017, the hospital had a bed occupancy rate of 84% with an average length of stay (LoS) of 6.2 days.

All patients admitted through the ED for suspicion of pulmonary MTB over the calendar year 2017 were included in this analysis, and there were no patients excluded for any reason. The primary goal of the audit was to evaluate the cost and LoS of patients who tested negative for pulmonary MTB. Secondary analysis included the cost and LoS of patients who tested positive for pulmonary MTB. We collected data from health information management, and cost data was requested and obtained from the revenue development management with the assistance of the patient service accountant. All data storage and an analysis were performed in Microsoft Excel.

Ethics committee approval was not required for quality improvement projects at our hospital when this project was planned. Clinical data can be used for research under the general consent that all patients sign on admission to the ED. Appropriate methods were used for the storage, security, and destruction of the excel data collection sheet.

Results

In 2017, 200 patients with suspected MTB were admitted from the ED, of which 123 were male and 77 were female. Thirteen patients were below 18 years of age and 31 patients were above 65 years of age. Thirty-one patients were UAE nationals and 169 patients were expatriates. 33% (66/200 patients) were diagnosed with pulmonary MTB and 67% (134/200 patients) did not have pulmonary MTB (Table 1).

One hundred thirty-four patients (67%) who did not have pulmonary MTB had an average LoS of 13 days. 62% of the total hospital cost was for these patients (around $1,216,119.88 USD) and the average cost per MTB negative patient was around $9,075.52 USD.

Sixty-six patients (33%) were diagnosed with pulmonary MTB with an average LoS 27 days. This accounted for 38% of the total cost. The overall cost for the pulmonary MTB-positive patients was $735,235.00 USD, and the average cost per person was $11,140.42 USD (Tables 2, 3).

Statistical Analysis

Cost Analysis

The total cost for evaluating 200 patients with suspected MTB as inpatients was $1,951,387.31 USD. Detailed analysis showed per night average cost of a respiratory isolation room at $375.71 USD, single AFB smear at $14.16 USD, QuantiFeRON test at $157.91 USD, MTB culture at $27.50 USD, and Gene X-pert MTB average per-test costs is $82.20 USD per test. The estimated cost of evaluating suspected MTB patient as out patient who presents to the ED and tests negative inclusive of a repeat Gene X-pert test when MTB is highly suspected or if first test is not conclusive in addition to a follow-up appointment in the Respiratory Clinic was calculated to be $996.31 USD (16). Figure 1 outlines the WHO X-pert MTB/RIF clinical pathway and Table 4 details the cost analysis and minimum cost per patient for MTB likely negative patients if managed as inpatients versus outpatients. On the other hand, the estimated minimum cost saving per patient applying the WHO X-pert MTB/RIF outpatient screening clinical pathway is estimated to be $3923.91 USD (see Table 5 for details).

Table 1. Baseline characteristics of study participants (n=200)

Age range	**2-91 year**
Male	123 (61.5%)
Female	77 (38.5%)
Pediatric ≤18 years	13 (6.5%)
Elderly >65	31 (15.5%)
UAE National	31 (15.5%)
MTB positive (TB culture)	66 (33%)
MTB negative (TB culture)	134 (67%)
Total cost	$1,951,387.31

MTB: Mycobacterial tuberculosis, TB: Tuberculosis, UAE: United Arab Emirates

Table 2. LoS for Suspected MTB patients

	MTB positive=66/200	**MTB negative=134/200**
Average LoS	27 days	13 days
Median LoS	13 days	10 days

MTB: Mycobacterial tuberculosis, LoS: Length of stay

Table 3. Cost review for suspected MTB patients as inpatients

	MTB positive=66/200	**MTB negative=134/200**
Cost	$735,235.00 (38% of total cost)	$1,216,119.88 (62% of the total cost)
Average cost per patient	$11,140.42	$9,075.52
Median cost per patient	$4,869.91	$4,212.36

MTB: Mycobacterial tuberculosis

Discussion

In 2010, WHO endorsed X-pert MTB/RIF as an initial diagnostic test for people thought to have MDR-TB or HIV-associated tuberculosis (15,17). In 2013, WHO extended its proposal that X-pert MTB/RIF can replace AFB smear as the initial diagnostic test for all adults and children patients with suspected MTB (10,15,18). Data showed that 67% of suspected pulmonary MTB tested negative and their average LoS was 13 days, which has a high impact on hospital admission rate, bed occupancy rate, and ED exist block. The average cost was $9,075.52 USD per patient, which includes the cost of diagnostics (about 10-20%) and admission and hospital stay expenses, which highlights multiple opportunities for cost saving. These patients also stay in a respiratory isolation room for days, which creates anxiety for the patients and their families (5).

Studies in patients with suspected MTB reported X-pert MTB/RIF sensitivity of 85% and a specificity of 98%. In a smear-positive with culture-positive, X-pert MTB/RIF sensitivity is about 98%, while in a smear-negative with culture-positive MTB, the sensitivity is 67% (19,20). when compared to X-pert MTB/RIF, X-pert Ultra yielded a sensitivity of 88% and a specificity of 96% (14). X-pert Ultra, when compared to X-pert MTB/RIF, for detection of smear-negative culture-positive MTB, yielded a higher sensitivity of 63% than X-pert MTB/RIF of 46%, and lower specificity of 96% than X-pert MTB/RIF 98% (14). In contrast, AFB smear is a low-cost test but with low sensitivity of between 50 and 60%, which can result in a large number of MTB cases that can go undiagnosed until culture results are obtained (21-28). Around 5000 to 10,000 CFU/mL must be present in the specimen for MTB bacteria to be visible by AFB smear by contrast, X-pert MTB/RIF can detect as low as 112.6 CFU/mL, and X-pert Ultra can detect as low as 15.6 CFU/mL (14,21-23).

Fifteen studies analyzed X-pert MTB/RIF cost-effectiveness, with most studies are taking place in sub-Saharan Africa. Twelve studies found that X-pert MTB/RIF is cost-effective in their setting and 3 studies (in India, Malawi, and South Africa) showed a neutral cost profile (24). One study quoted that X-pert MTB/RIF saved $2,278 USD per admission and $533,520 USD per year, and most cost savings arose from reductions in LoS in respiratory isolation (18).

Millman et al. (19) reported that X-pert MTB/RIF decreased isolation bed utilization from an average of 2.7 to 1.4 days per suspected MTB patient. Likewise, they showed a reduction in total annual isolation bed usage from 632 to 328 bed-days, directly bringing down bed occupancy rates, and potentially reducing ED exit block (19).

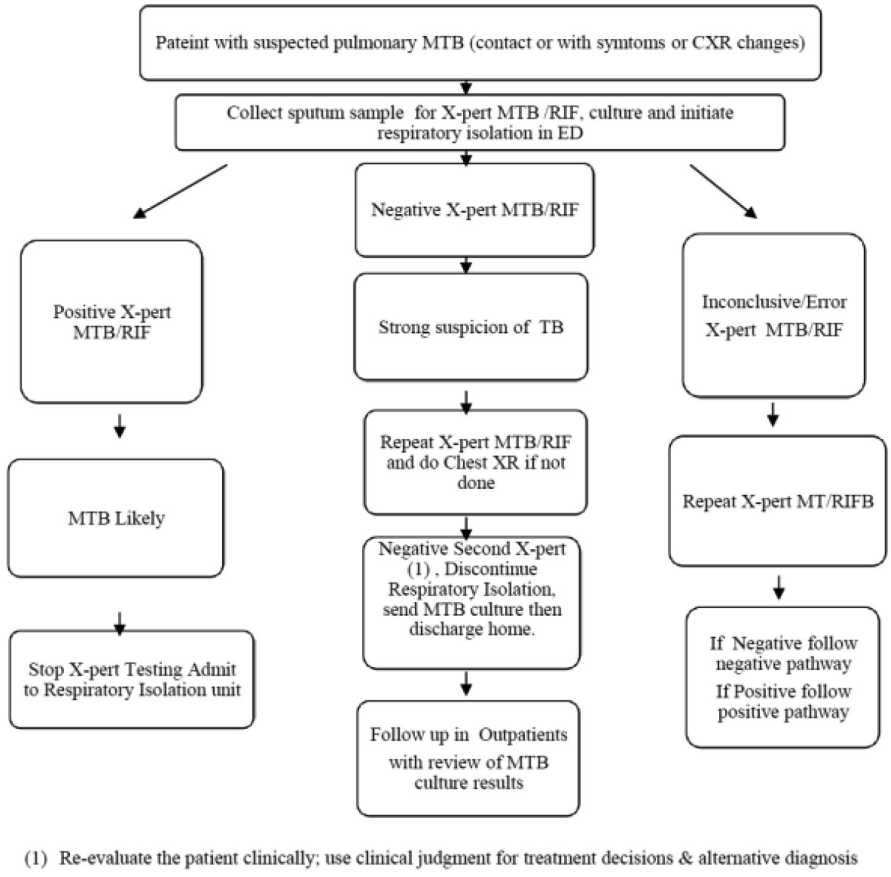

Figure 1. WHO X-pert MTB/RIF outpatient screening clinical pathway
WHO: World Health Organization, MTB: Mycobacterial tuberculosis, CXR: Chest X-ray

Table 4. Cost analysis of likely negative MTB when managed as in patient versus out patient

	Test	Cost per unit	Amount needed	Total cost
In patient track total **minimum** cost per patient: $5,112.12 USD	Per night average cost of a respiratory isolation room	$375.71 USD	Average loss 13 days	$4884.23 USD
	Single AFB smear	$14.16 USD	Average 3 AFB smear	$42.48 USD
	QuantiFeRON test	$157.91 USD	1	$157.91 USD
	MTB culture	$27.50 USD	1	$27.50 USD
Outpatient track **minimum** cost if negative $1,188.21 USD	Gene X-pert MTB average per-test costs	$82.20 USD	2	$164.4 USD
	MTB culture	$27.50 USD	1	$27.50 USD
	Follow-up appointment in the respiratory clinic	$996.31 USD	1	$996.31 USD

Note that we did not factor in other care variables such as symptomatic treatment or imaging such as CXR as both tracks will need to do CXR our comparison is focused on the microbiological testing being done as inpatient versus outpatient.
CXR: Chest X-ray, MTB: Mycobacterial tuberculosis

Table 5. Cost saving if applying WHO X-pert MTB/RIF outpatient screening clinical pathway

Hospital beds occupancy nights saved	**13x134=**	**1742 nights**
Care cost mimunum saved per patient	In patient track Total **minimum** cost per patient: $5,112.12 USD - Outpatient track **minimum** cost if negative $1188.21 USD=	$3,923.91 USD

WHO: World Health Organization, MTB: Mycobacterial tuberculosis

In 2015, the Food and Drug Administration approved the X-pert MTB/RIF test for pulmonary MTB detection as an initial diagnostic test replacing AFB smear, and this test has been widely implemented in 18 countries (17,19,25). Implementing the X-pert MTB/RIF in UAE and other low MTB incidence and burden countries will be cost-saving and cost-effective compared with the traditional admission for 3 AFP smears and culture. Data analysis showed that changing this practice could reduce the cost of MTB workup by about 90% while providing for safe practice. WHO pathway suggest that suspected MTB patients based on symptoms or abnormal CXR, or close contact with pulmonary MTB patients, should undergo X-pert MTB/RIF as an initial diagnostic test (Figure 1) (15,26,27).

To our knowledge, this is the first study evaluating the cost of the current pulmonary MTB diagnostic process in the UAE. It describes the effect of this diagnostic process on LoS and costs for patients with suspected pulmonary MTB. The current average cost of an inpatient-based MTB is almost 10 times higher at $9,075.52 USD versus the proposed outpatient X-pert MTB/RIF - based evaluation, which will cost about $996.31 USD.

Study Limitations

This is a single-center retrospective one-year audit in a low-incidence TB country, resulting in a small number of MTB-infected patients. In addition this study analysed 2017 data and was ready for publication before the Coronavirus disease-2019 (COVID-19) pandemic, which resulted in delayed submission; hence, there may be practice changes already due to COVID-19 and the demand on airborne isolation rooms in any system. A new audit to address the changes in the MTB diagnostic pathway and how it was influcned by COVID-19 in UAE will be needed.

Conclusion

Working up a patient with pulmonary MTB as an inpatient is costly and unjustified in the presence of an alternative cost-effective diagnostic pathway using X-pert MTB/RIF as an initial test to rule in/out pulmonary MTB within 2 hrs in an outpatient setting without the need for inpatient admission. Further analysis to assess how the pulmonary MTB diagnostic pathway was influenced by COVID-19 is needed.

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Ethics

Ethics Committee Approval: Ethics committee approval was not required for quality improvement projects at our hospital when this project was planned.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: W.G., Y.A., A.A., Design: W.G., Y.A., A.A., Data Collection or Processing: W.G., A.A., Analysis or Interpretation: W.G., Y.A., S.A., A.A., Literature Search: W.G., A.A., Writing: W.G., Y.A., S.A., A.A.

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Alternative Methods to Endtidal CO_2 Predicting the Outcome of Resuscitation: Glial Fibrillary Acidic Protein and Copeptin

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Abstract

Aim: Using the end-tide carbon dioxide ($ETCO_2$) level to predict the outcome of resuscitation may be misleading. This study investigated the usability of glial fibrillary acidic protein (GFAP) and copeptin levels measured at regular intervals during the resuscitation process as an alternative to the $ETCO_2$ level in the prediction of resuscitation outcome.

Materials and Methods: This study was prospectively conducted with patients who were resuscitated at the emergency department of a tertiary hospital. The sample included 31 patients, of whom 18 died and 23 had the return of spontaneous circulation (ROSC). $ETCO_2$, GFAP, and copeptin values were measured at the beginning (1), 20th minute (2), and end (3) of resuscitation and statistically analyzed.

Results: When calculated in percent units, the $ETCO_2$ 1-2 difference, $ETCO_2$ 2-3 difference, GFAP 1-2 difference, and copeptin 2-3 difference statistically significantly differed between the patients who died and those with ROSC ($p<0.05$).

Conclusion: We observed that the GFAP and copeptin levels were not sufficient to guide the decision to terminate resuscitation when examined at the beginning of resuscitation, but changes in these copeptin levels measured in series could predict mortality.

Keywords: Resuscitation, end-tidal carbon dioxide, glial fibrillary acidic protein, copeptin

Introduction

Currently, there is no specific time defined during resuscitation (1,2). This causes legal problems related to the duration or unnecessarily prolonged resuscitation. In guidelines published for the standardization of resuscitation, the most well-known parameter that can be used to terminate resuscitation is the end-tidal carbon dioxide ($ETCO_2$) level (1,3). $ETCO_2$ is the partial pressure of carbon dioxide in exhaled air measured at the end of expiration. $ETCO_2$ levels are affected by many factors during resuscitation; therefore, it is not recommended to use $ETCO_2$ levels as the only criterion for the termination of this process (4).

Damage caused by hypoxia to the central nervous system (CNS) before and during resuscitation is often irreversible and may be a determinant of mortality after resuscitation. Two new biomarkers used to predict post-resuscitative damage are glial fibrillary acidic protein (GFAP) and copeptin (5,6). GFAP is released from astrocytes in the CNS. Since astrocyte damage occurs under hypoxic conditions, the GFAP-level increases in the CNS (7). Considering this information, this parameter was used to predict mortality in patients with post-resuscitative return of spontaneous circulation (ROSC) and was found to be effective for this purpose (8-10).

Copeptin increases in circulation in the initial period of acute myocardial infarction and pathological conditions, such as pain, hypoglycemia, hypoxia, stroke, infections, and shock. high copeptin levels are associated with a poor prognosis in cases of pneumonia, myocardial infarction, diabetes, heart failure, and stroke (11,12). However, there are only few studies in the literature on the relationship between serum copeptin levels and prognosis in non-traumatic arrest patients undergoing resuscitation (6,11,13,14).

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Both GFAP and copeptin levels have been found to be effective in predicting mortality in post-resuscitative patients. However, there is no literature study on the success and usability of these levels during resuscitation in predicting ROSC success or mortality. This study investigated the usability of GFAP and copeptin levels measured at regular intervals during the resuscitation process as an alternative to the $ETCO_2$ level in the prediction of resuscitation outcome.

Materials and Methods

Study Design

This study was prospectively conducted at the emergency department of a tertiary hospital from January 1, 2022 through June 1, 2022. Ethical approval was obtained from the Atatürk University Local Clinical Research Ethics Committee (number: 41/09, date: 30/12/2021). The study was conducted in accordance with the tenets of the Declaration of Helsinki. Since resuscitation was applied to the patients to be included in the study, informed consent for participation was obtained from their legal representatives. Standard treatment methods were used for resuscitation in all patients.

Study Population

This study was conducted with patients who were referred to the emergency department by the 112 ambulance service or who had a cardiac arrest when in the department. Individuals aged <18 years, pregnant women, patients with traumatic cardiopulmonary arrest, stroke, hemorrhage, or a neurodegenerative disease that could affect the CNS, and those with an intracranial mass that could affect GFAP and copeptin levels were excluded from the study. The patients who underwent resuscitation and did not meet these inclusion criteria were included in the study. NCSS/PAS software was used to determine that 31 patients should be included in the study at the reference area under the curve (AUC) values of 0.60 and 0.87 in the receiver operating characteristic (ROC) analysis at 80% power and 95% confidence interval (CI).

During the study, 132 patients were resuscitated at the emergency department of the hospital where the study was conducted. After applying the exclusion and inclusion criteria, 31 patients were included in the study. A total of 101 patients were excluded (Figure 1). Of the 31 patients included in the study, 18 died and 13 achieved ROSC. Accordingly, the patients were divided into two groups: those that died (G1) and those with ROSC (G2).

Data Collection

It was noted whether each patient had an out-of-hospital cardiac arrest (OHCA) or an in-hospital cardiac arrest (IHCA). The time to reach the emergency department of the patients with OHCA was recorded according to the information obtained from the 112 ambulance service personnel. In the OHCA cases, the time when the 112 healthcare professionals diagnose cardiopulmonary arrest was considered as the onset of arrest. In addition, the patients' age, gender, and resuscitation times after admission to our hospital emergency department were recorded. The sum of both times was specified as the resuscitation time. Routine radiological CNS imaging was not performed in the patients during resuscitation; however, radiological imaging was performed to determine the cause of the arrest after ROSC was achieved (in order to rule out CNS pathologies that may cause arrest, noncontrast brain tomography was performed. In addition, contrast-enhanced pulmonary angiography was performed to rule out pulmonary embolism Patients with imaging findings indicating pathologies that could affect the CNS were excluded from the study. Routine imaging was not performed in the exitus group during resuscitation. However, patients who were found to have CNS pathology because of the information obtained from the caregivers of the patients in the exitus group and the examination of their past health records were excluded from the study.

The Resuscitation Process and $ETCO_2$ Measurements

When the patient arrived at the emergency department, chest compression were performed with a mechanical chest compression device (LUCAS™2; Physio-Control/Jolife AB, Lund, Sweden) to provide standardization among patients undergoing resuscitation. The advanced cardiac life support guideline

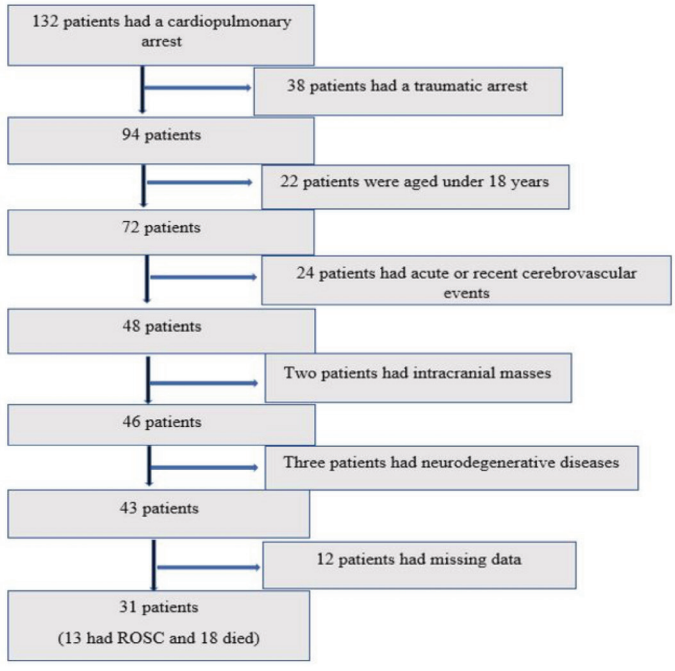

Figure 1. Flowchart showing the patients included in the study
ROSC: Return of spontaneous circulation

published in 2020 was taken as a reference for methods to be applied during resuscitation (15). The cardiac rhythm, blood pressure, saturation, and $ETCO_2$ levels of all patients admitted to the resuscitation area were continuously monitored with bedside monitors (Nihon Kohden Corp®., Vismo PVM-2703, Tokyo, Japan) throughout the resuscitation period. The first recorded $ETCO_2$ levels in both groups (G1 and G2) were considered the $ETCO_2$ levels at the beginning of resuscitation ($ETCO_2$ 1). For the patients who achieved ROSC within the first 20 min, the second $ETCO_2$ ($ETCO_2$ 2) level was recorded at the moment ROSC was achieved and the third $ETCO_2$ ($ETCO_2$ 3) level at the 20th min of resuscitation. For the patients who could not achieve ROSC within the first 20 min, the second $ETCO_2$ ($ETCO_2$ 2) level was recorded at 20 min and the third $ETCO_2$ ($ETCO_2$ 3) level was recorded when ROSC was achieved. For the patients who died, the $ETCO_2$ levels were recorded at the beginning of resuscitation ($ETCO_2$ 1), at the 20th minute of resuscitation ($ETCO_2$ 2), and when it was decided to terminate resuscitation ($ETCO_2$ 3). The decision to terminate resuscitation was made by considering the duration of the patient's arrest until the emergency ambulance team arrived, duration of resuscitation in the emergency department, patient age, changes in cardiac rhythm observed during the resuscitation period, and measured $ETCO_2$ levels.

Blood Sample Collection

Experienced nurses (nurses with at least 5 years of experience in the emergency department) collected blood samples from the antecubital region of the resuscitated patients using Ayset 10 mL hypodermic needle syringes (Ayset® Tıbbi Ürünler San. A. S., Adana, Turkey) and placed them into BD Vacutainer® Barricor™ biochemistry tubes (Becton, Dickinson and Company).

In G1, blood samples were taken at the beginning of resuscitation (GFAP 1-copeptin 1), at the 20th minute of resuscitation (GFAP 2-copeptin 3), and when it was decided to terminate resuscitation (GFAP 3-copeptin 3). In G2, the first blood sample was collected at the start of resuscitation (GFAP 1-copeptin 1). In patients who received ROSC before 20 min, a second blood sample (GFAP 2-copeptin 2) was taken as soon as ROSC was achieved. For the patients who received ROSC after 20 min, the second blood sample (GFAP 2-copeptin 2) was taken at the 20th minute of the resuscitation process. The third sample (GFAP 3-copeptin 3) was taken at the 20th minute in the patients that achieved ROSC before 20 min and at the time of ROSC in those that achieved ROSC later.

After the blood samples were allowed to coagulate for 5 min at room temperature, they were centrifuged and serum samples were separated. The samples were frozen at -80 °C and stored until analysis. After the serum samples were dissolved under suitable conditions, all analyses were performed in a single session at the medical biochemistry laboratory of our hospital.

Biochemical Analyses

In the serum samples, GFAP levels were analyzed with the enzyme-linked immunosorbent assay (ELISA) kits of BTLAB (Cat No: E2094Hu and E1129Hu, respectively; Bioassay Technology Laboratory, Zhejiang, China) using the Dynex ELISA reader (Dynex Technologies Headquarters, Chantilly, USA) according to the manufacturer's standard protocol. All samples were run in duplicate and statistical analyses were performed by taking the averages of the measurements. For the study, the intra-assay coefficient of variance (CV) was determined as <8% and the inter-assay CV as <10%.

Statistical Analysis

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences v. 20 software package. Data were presented as mean, standard deviation, median, minimum, and maximum values, percentages, and numbers. The normality of the distribution of continuous variables was evaluated using the Shapiro-Wilk W and Kolmogorov-Smirnov tests. In the comparisons between two independent groups, the independent-sample t-test was used when the normal distribution condition was met, and the Mann-Whitney U test was used otherwise. The relationship between quantitative variables was examined with the Pearson and Spearman correlation tests in data with and without a normal distribution, respectively. ROC analysis was used to investigate the use of quantitative variables in diagnosis.

In the multivariate analysis, risk factors were analyzed between the groups using logistic regression analysis of the identified possible risk factors. The results of the logistic regression model are presented in the odds ratio (OR) and 95% CI values of OR. The statistical significance level was taken as $p<0.05$.

Results

When the demographic characteristics of the patients were examined (Table 1), the median age of the patients was 60.10 years, and 24 (77.4%) patients were male. The resuscitation outcome was ROSC in 13 (41.9%) of the 31 patients.

When the $ETCO_2$, GFAP and copeptin levels of the groups were compared (Table 2), the initial median $ETCO_2$ level of G1 was determined as 12 (4-23) mm/Hg in G1 and that of G2 was found to be 14 (7-29) mm/Hg in G2, indicating no statistically significant difference ($p=0.190$). The initial median GFAP level was 1.53 (0.36-4.89) ng/mL for G1 and 3.78 (1.20-7.76) ng/mL for G2, and there was a statistically significant difference between the two groups ($p=0.004$). The initial median copeptin levels of G1 and G2 were

5.33 (1.71-11.01) ng/mL and 6.34 (0.81-3.61) ng/mL, respectively, revealing a statistically significant difference (p=0.031). Figure 1 presents the $ETCO_2$, GFAP, and copeptin levels of the patients according to the groups.

Table 1. Patient demographic data

Variable	Median (min/max)	
Age (median-min/max)	60.10 (20/82) years	
Resuscitation duration (min)	30.0 (15.0/60.0) min	
Variable	**n**	**%**
Gender		
Male	24	77.4
Female	7	22.6
Place of arrest		
OHCA	20	64.5
IHCA	11	35.5
Resuscitation outcome		
Group 1	18	58.1
Group 2	13	41.9

OHCA: Out-of-hospitals cardiac arrest, IHCA: In-hospital cardiac arrest, Group 1: Patients that died, Group 2: Patients with the return of spontaneous circulation, min-max: Minimum-maximum

Table 3 shows the results of the comparison of the differences in $ETCO_2$, GFAP and copeptin levels measured at different times according to the groups. Differences between the group medians are given in percent units (%). Accordingly, when the changes in the $ETCO_2$ values from minute 0 to 20 were examined, the median value was determined as 4.39% in G1 and 11.15% in G2, and there was a significant difference between the two groups (p=0.001). The median value for the changes in the GFAP level from minute 0 to 20 was found to be -2.60% in G1 and 221.90% in G2, indicating another statistically significant difference (p=0.007). The median values for the changes in the copeptin level from minute 0 to 20 were 10.84% and 18.55% for G1 and G2, respectively, and the difference between the groups was not statistically significant (p=0.246).

The correlation between the $ETCO_2$ differences and the GFAP and copeptin differences according to the groups is given in Table 4. Accordingly, there was a negative correlation between $ETCO_2$ 1-2 and copeptin 2-3 differences, and this was statistically significant (r=-0.777; p=0.002).

Table 5 presents the cut-off values for the percent changes in $ETCO_2$, GFAP, and copeptin levels in the prediction of resuscitation

Table 2. $ETCO_2$, GFAP and copeptin levels of the study groups

Variable	Group 1		Group 2		p value
	Median	Min-max	Median	Min-max	
$ETCO_2$-1 (mm/Hg)	12	4-23	14	7-29	0.190
$ETCO_2$-2 (mm/Hg)	17	6-25	25	18-38	**0.000**
$ETCO_2$-3 (mm/Hg)	13	3-25	28	12-37	**0.000**
GFAP-1 (ng/mL)	1.53	0.36-4.89	3.78	1.20-7.76	**0.004**
GFAP-2 (ng/mL)	1.33	0.47-6.15	1.20	0.30-2.29	0.327
GFAP-3 (ng/mL)	2.52	0.24-11.47	1.56	0.81-3.61	0.128
Copeptin-1 (ng/mL)	5.33	1.71-11.01	6.34	4.03-25.41	**0.031**
Copeptin-2 (ng/mL)	4.83	1.99-11.17	5.17	4.19-7.35	0.689
Copeptin-3 (ng/mL)	6.78	1.86-27.99	4.57	1.43-5.48	**0.004**

$ETCO_2$: End-tidal carbon dioxide, GFAP: Glial fibrillary acidic protein, Group 1: Patients that died, Group 2: Patients with the return of spontaneous circulation, min-max: Minimum-maximum

Table 3. Comparison of the percentage changes in $ETCO_2$, GFAP and copeptin levels between the groups

Variable	Group 1		Group 2		p value
	Median	Min/max	Median	Min-max	
$ETCO_2$ 1-2 difference (%)	4.39	-6.00/15.00	11.15	5.00/16.00	**0.001**
$ETCO_2$ difference (%)	-2.61	-13.00/5.00	1.61	-16.00/9.00	**0.033**
GFAP 1-2 difference (%)	-2.60	-407.00/315.60	221.90	-76.66/660.50	**0.007**
GFAP 2-3 difference (%)	103.25	-466.20/1043.80	22.10	-84.60/189.40	0.215
Copeptin 1-2 difference (%)	-10.84	-63.19/552.28	-18.55	-83.48/34.04	0.246
Copeptin 2-3 difference (%)	56.44	-83.33/415.16	-16.56	-71.68/1.79	**0.001**

$ETCO_2$: End-tidal carbon dioxide, GFAP: Glial fibrillary acidic protein, Group 1: Patients that died, Group 2: Patients with the return of spontaneous circulation, min-max: Minimum-maximum

outcome, and the ROC analysis of these values are given in Figures 2, 3, 4. Accordingly, the $ETCO_2$ 1-2 difference, $ETCO_2$ 2-3 difference, GFAP 1-2 difference, and copeptin 2-3 difference were statistically significant in G1 and G2 ($p<0.05$). When the cut-off value of the $ETCO_2$ 1-2 difference was taken as 8.50% in G1, the sensitivity was 84.6% and the specificity was 77.8% (AUC=0.182, p=0.003). At a cut-off value of 0.50%, the $ETCO_2$ 2-3 difference had a sensitivity of 76.9% and specificity of 66.7% in G1 (AUC=0.274, p=0.034). At the 184.3% cut-off value, the GFAP 1-2 difference had 5.6% and sensitivity and 46.2% specificity in G1 (AUC=0.214, p=0.007). Lastly, the copeptin 2-3 difference taken as 4.543% in G1, the sensitivity and specificity values were determined as was 72.2% and 64.5%, respectively (AUC=0.850, p=0.001) (Figure 5).

Discussion

It is difficult to predict the outcome of resuscitation in the early period of the resuscitation process. The optimal resuscitation termination time and methods used for this decision remain controversial. In this study, we evaluated the value of GFAP and copeptin levels in predicting the outcome of resuscitation. On completion of the study, we determined that the GFAP and copeptin levels were not sufficient to guide the decision to terminate resuscitation when measured at the beginning of resuscitation, but changes in these levels measured in series could predict mortality.

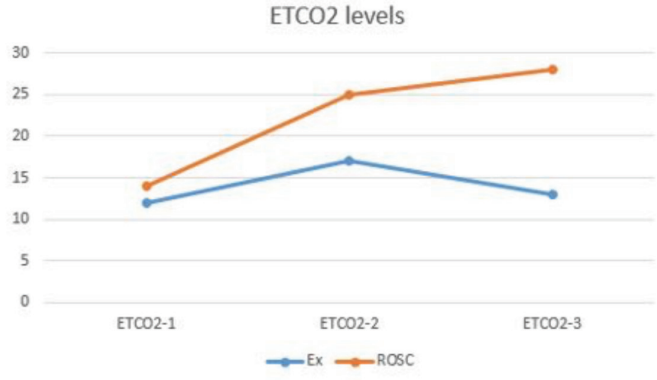

Figure 2. $ETCO_2$ levels of the groups

$ETCO_2$: End-tidal carbon dioxide, ROSC: Return of spontaneous circulation

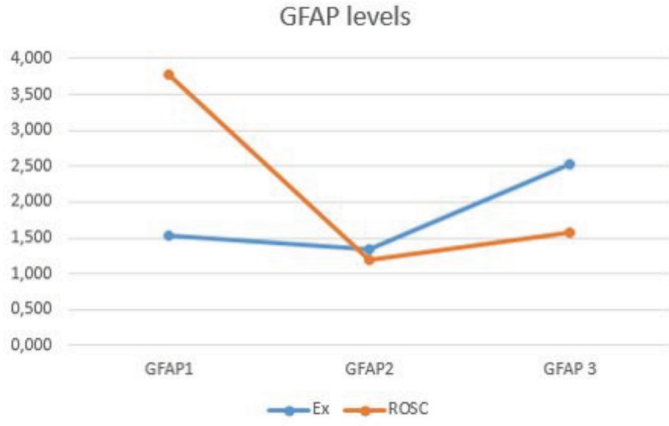

Figure 3. GFAP levels of the groups

ROSC: Return of spontaneous circulation, GFAP: Glial fibrillary acidic protein

Table 4. Correlation of percent changes in $ETCO_2$ with those in GFAP and copeptin

Variable		Group 1				Group 2			
		GFAP 1-2	GFAP 2-3	Copeptin 1-2	Copeptin 2-3	GFAP 1-2	GFAP 2-3	Copeptin 1-2	Copeptin 2-3
$ETCO_2$ 1-2	r	-0.216	-0.039	-0.093	-0.361	0.244	0.227	0.233	-0.777
	p	0.389	0.879	0.714	0.141	0.422	0.455	0.444	**0.002**
$ETCO_2$ 2-3	r	0.296	0.081	-0.366	-0.047	0.088	0.157	-0.097	0.055
	p	0.232	0.749	0.135	0.854	0.774	0.607	0.753	0.858

*Spearman correlation analysis.
$ETCO_2$: End-tidal carbon dioxide, GFAP: Glial fibrillary acidic protein, Group 1: Patients that died, Group 2: Patients with the return of spontaneous circulation

Table 5. Cut-off variations in $ETCO_2$, GFAP, and copeptin percent changes in resuscitation

Variable	Cut-off	Odds ratio	Sensitivity (%)	Specificity (%)	p value
$ETCO_2$ 1-2 difference	8.50	0.182 (0.031-0.332)	0.846	0.778	**0.003**
$ETCO_2$ 2-3 difference	0.50	0.274 (0.080-0.467)	0.769	0.667	**0.034**
GFAP 1-2 difference	184.30	0.214 (0.046-0.381)	0.056	0.462	**0.007**
GFAP 2-3 difference	34.60	0.632 (0.434-0.831)	0.556	0.538	0.215
Copeptin 1-2 difference	-23.175	0.624 (0.421-0.827)	0.611	0.385	0.246
Copeptin 2-3 difference	4.543	0.850 (0.702-0.998)	0.722	0.645	**0.001**

$ETCO_2$: End-tidal carbon dioxide, GFAP: Glial fibrillary acidic protein

In the literature, there is no study on the usability of GFAP values measured at the time of resuscitation to predict the outcome of this intervention However, in the evaluation of post-resuscitative patients in the intensive care unit, studies have investigated the predictive ability of GFAP for mortality in patients that achieved ROSC. In these studies, it was observed that patients with increased GFAP values after resuscitation had poor outcomes (5,8). In one of the studies, it was emphasized that patients whose GFAP levels increased because of the impaired blood-brain barrier due to global hypoxia during resuscitation had poor post-resuscitative outcomes (16). In addition, Helwig et al. (8) showed that high GFAP values were associated with dysfunctional survival in post-resuscitative patients. In the current study, the GFAP values of all the patients were found to be well above the reference values at the beginning of resuscitation, but there was a significant decrease in the consecutively measured GFAP levels in G2 (AUC=0.214). The GFAP values decreased in G1 but no significant difference was observed in comparison with G2. Although the increase in the final GFAP levels in G2 continued, possibly due to global brain injury, this increase was still significantly higher in G1. Only three of the 13 patients in G2 survived and were discharged from the hospital. In our patients with ROSC, the GFAP values continued to increase, albeit slightly, possibly due to global brain damage; therefore, the outcome of these patients was poor. According to this information, the GFAP levels evaluated at the beginning of resuscitation in non-traumatic cardiac arrest patients have no clinical applicability in predicting the outcome of resuscitation, but we consider that the examination of this parameter at various times during resuscitation can predict the related outcome, as in $ETCO_2$ levels.

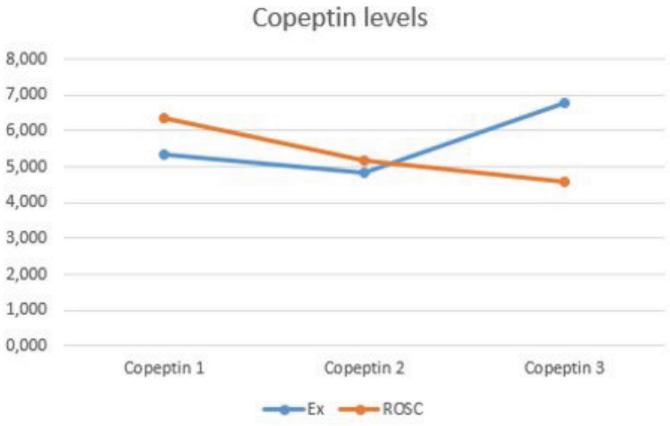

Figure 4. Copeptin levels of the groups

ROSC: Return of spontaneous circulation

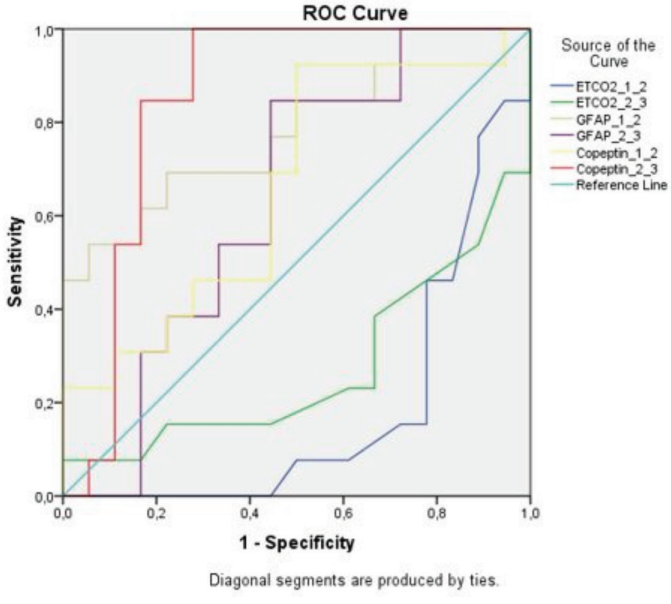

Figure 5. Receiver operating characteristic plot of the percent changes in $ETCO_2$, GFAP and copeptin levels according to the patients who died

$ETCO_2$: End-tidal carbon dioxide, GFAP: Glial fibrillary acidic protein

Copeptin, which plays a role in hemodynamic and osmotic regulation, has been associated with increased mortality and morbidity in critical diseases (17). In a study investigating copeptin levels in patients who had had a cardiac arrest, the copeptin levels at the time of admission to the hospital were found to be higher in the cardiac arrest group compared with healthy volunteers (13). In the same study, copeptin levels were found to be lower in cardiac arrest cases in which ROSC was achieved than in the mortality group. Similarly, in a study conducted by Ostadal et al. (18) with cardiac arrest patients, the copeptin values measured at the time of admission were found to be lower in the ROSC group than in the mortality group. However, that study was different from ours in that the authors started therapeutic hypothermia in patients with OHCA as soon as they arrived at the hospital. In contrast, we determined that the initial copeptin values were higher in G2 than in G1. This may be due to metabolic slowdown caused by therapeutic hypothermia created by Ostadal et al. (18). However, in Ostadal et al. (18) and Cakmak et al.'s (13) studies, the copeptin levels were only measured at the beginning of resuscitation, whereas in our study, these levels were sequentially measured and evaluated three times. In the evaluation of the patients, the copeptin levels measured at the 20th minute decreased compared with the initial copeptin values. However, the copeptin levels decreased to a greater extent in patients with ROSC (AUC=0.624), albeit not at a statistically significant level. The copeptin values measured at the time of the termination of resuscitation differed between the groups compared with the copeptin values measured at the 20th minute. The copeptin levels continued to increase in G1 after the 20th minute, while it continued to decrease in G2. When the cut-off value was taken as 4.543% in G1, the difference between the copeptin levels measured at the 20th minute of resuscitation

and those measured at the time of termination of resuscitation, the sensitivity and specificity values were determined as 72.2% and 64.5%, respectively (AUC=0.850). Therefore, we consider that copeptin values measured once during resuscitation are not sufficient to predict the outcome of resuscitation; rather, the continued decrease in copeptin levels in serial measurements would be useful in this prediction.

According to the results of previous studies, the value of $ETCO_2$ measured at the beginning of resuscitation in the decision to terminate resuscitation is unclear. However, it has been suggested that $ETCO_2$ values measured as <10 mmHg within the first 20 min predicts that ROSC cannon be achieved (19). In a study by Eckstein et al. (20), initial $ETCO_2$ levels of more than 10 mmHg and no more than 25% decrease from the initial value were reported to be valuable in terms of indicating success in ROSC. In our study, $ETCO_2$ levels measured at the 20th minute of resuscitation were found to be higher than those measured at the beginning of resuscitation in both groups. It was observed that the $ETCO_2$ values measured at the 20th minute increased to a lower extent in G1 than in G2 compared to the initial values. It was also determined that the $ETCO_2$ values measured at the termination of resuscitation were lower than those measured at the 20th minute in G1, while the $ETCO_2$ values measured at the time of ROSC increased compared to those measured at the 20th minute in G2. The $ETCO_2$ values may have increased because of cerebral and coronary perfusion provided by effective chest compression in the first 20 min of resuscitation in all patients. In patients who died, impaired perfusion in the later stages of resuscitation (decreased tissue perfusion due to adverse effects on microcirculation mediated by the α-1 agonist effect of adrenaline) and decreased venous return may have led to a decrease in the $ETCO_2$ values (4).

Study Limitations

The major limitation of our study is that it was conducted with a few patients. In addition, because GFAP and copeptin were examined using the ELISA method, the analysis took a long time. Thus, GFAP and copeptin levels could not be measured at the time of resuscitation, and the blood samples were frozen after centrifugation for later analysis. Although there are point of care GFAP devices approved by the United States Food and Drug Administration (21), we were not able to use them in our study due to their unavailability in Turkey. In addition, hemolysis may have occurred during blood collection, transfer of samples to the laboratory, and centrifugation, which may have affected our results. Therefore, it would be more appropriate to use methods and, if possible, point of care devices for biochemical parameters to obtain results at the time of resuscitation and reduce the risk of hemolysis.

Conclusion

The optimal resuscitation termination time and methods used to determine this time remain controversial. In our study, we determined that the GFAP and copeptin levels measured at the beginning of resuscitation were not sufficient to guide the decision to terminate resuscitation, but the GFAP level measured at the 20th minute being significantly lower than the initial level was a predictor of ROSC. Therefore, we consider that the duration of resuscitation can be prolonged in these patients regardless of their $ETCO_2$ values. However, we observed that the gradual increase in copeptin levels after the 20th minute was associated with mortality, and thus we recommend extending the duration of resuscitation in these patients.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Atatürk University Local Clinical Research Ethics Committee (number: 41/09, date: 30/12/2021).

Informed Consent: Informed consent for participation was obtained from their legal representatives.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.T., A.G., Design: F.T., E.T., A.G., K.K., Data Collection or Processing: F.T., A.G., N.Ö., Analysis or Interpretation: F.T., E.T., N.Ö., K.K., Literature Search: F.T., E.T., N.Ö., K.K., Writing: F.T., E.T., A.G., N.Ö., K.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Comparison of Hair Knotting with Primary Suture and Stapler Techniques in Scalp Lacerations: A Prospective, Observational Study

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Abstract

Aim: We aimed to compare the primary suture and stapler techniques with the hair knotting technique in patients presenting to the emergency department with scalp lacerations and investigate their efficacy in emergency service practice.

Materials and Methods: This was a single-center prospective observational study in which patients were divided into three groups according to the treatment technique of hair knotting, stapler, and primary suture. Patients with a hair length greater than 3 cm and a linear incision less than 10 cm were included in the study. The duration of the procedures and the patients' post-treatment complications, cosmetic problems, pain scores, and satisfaction status were evaluated.

Results: A total of 120 patients were included in the study. The median length of stay in the emergency department in the hair knotting group was 23 min, which was shorter compared to the remaining stapler and primary suture (p=0.003 and p=0.001). The complication rates evaluated on days 7 and 14 were lower in the hair knotting group than in the primary suture group (p=0.002 and p=0.012, respectively). The hair knotting group also had a lower rate of cosmetic problems on days 0, 7, and 14 compared with the primary suture group (p=0.014, p=0.003, and p=0.027, respectively).

Conclusion: Hair knotting can be used as an alternative technique to the stapler and suture techniques in the emergency department due to its lower cost, less painful nature of the procedure, shorter stay of patients in the emergency department, and requirement of no sedation or local anesthesia.

Keywords: Scalp laceration, stapler, hair knotting, primary suture, emergency service

Introduction

Many trauma patients present to emergency services every year (1). Scalp lacerations are seen in 5% of these patients (2). The treatment of existing lacerations is traditionally performed with primary sutures, staplers, and tissue adhesives (3). Among these methods, suturing is the most commonly used laceration repair method (4), but due to its invasive nature, the procedure both takes a long time and results in pain in the patient (5). Another method used for treating scalp lacerations is the use of staplers, which is preferred in the emergency department due to its fast application. However, this procedure has certain disadvantages, such as the possibility of injury to the person applying it, and scalp punctures (6).

The ideal treatment management of a scalp laceration would be a procedure that can be applied in a short time without incurring pain and has good cosmetic outcomes and minimum complications (2). Hair knotting, first described by Applebaum et al. (7), is a technique that provides closure of the wound by knotting hair, as the name implies. With this technique, a less invasive procedure is performed on the patient in the emergency department. In addition, the hair knotting technique has lower cost. Furthermore, in the pediatric population, sedation and related side effects can be avoided and patients can leave the emergency department in a shorter time.

In this study, we aimed to compare the primary suture and stapler techniques with the hair knot technique in patients admitted

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to the emergency department with scalp lacerations and to investigate their efficacy in emergency service practice.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted between March 1, 2021 and November 31, 2021 in the emergency department of a tertiary hospital. The study was initiated after receiving approval from the Atatürk University Faculty of Medicine Local Ethics Committee (number: B.30.2.ATA.0.01.00/417, date: 01.10.2020). Written informed consent was obtained from all volunteer patients participating in the study or their relatives. The study was conducted in accordance with the principles of Good Clinical Practices of the Declaration of Helsinki and the CONSORT directive.

Sample Size and Patients

The G-Power 3.1 software was used to calculate the sample size required for the study. To calculate the sample size, the medium effect size was taken as 0.5, type 1 error as 0.05, and power as 0.80. The required sample size was calculated as 40 patients for each group (120 patients with an allocation ratio of 1:1:1) at 10% loss.

Patients from all age groups with scalp lacerations were included in the study. Other inclusion criteria were having a hair length of 3 cm and above, having linear lacerations but no stellar lacerations, and having an incision length of less than 10 cm. Patients with a hair length shorter than 3 cm, those with an incision longer than 10 cm, those with active bleeding, cases in which bleeding did not stop after applying pressure for 5 min, patients with severely contaminated wounds, unconscious patients, those with unstable vital signs, and pregnant women were excluded from the study.

Randomization and Outcomes

The patients were divided into three treatment groups: hair knotting, stapler, and primary suture. The technique to be applied to the patients was randomly decided by the physician. All patients were treated by emergency medicine specialists. The primary outcomes were complications (pain, redness, hair loss, wound dehiscence, and wound drainage) and cosmetic problems that occurred after treatment. The secondary outcomes were the pain score of the patients according to the visual analog scale (VAS) administered during the procedure (10-point scale with 0 indicating no pain and 10 representing worst pain ever experienced) and the duration of the procedure.

Study Variables and Intervention

The patients' age, gender, hair color, hair length, incision length, and the type of trauma was recorded on the previously prepared forms. The treatment to be applied was decided by the physician randomly. The decided method was applied to each patient. Then, whether the patient received sedation or local anesthesia and the duration of the procedure were recorded on the same form. After the procedure, the patients' satisfaction with the procedure, whether the wound caused any cosmetic problem visually, and the pain levels during the procedure were recorded by asking the patient or his/her relatives. The patients were evaluated by the physician on days 7 and 14 after treatment in terms of wound-related complications. Satisfaction with the procedure and presence of cosmetic problems were determined by asking the patient or his/her relatives and recorded in the form. The satisfaction status and cosmetic problems were evaluated as present or absent. Cognitive sedation was given to some patients in the pediatric age group for patient comfort. The VAS scores of these patients were evaluated as 0, and their parents were asked about their satisfaction.

In the primary suture group, the wound was cleaned according to standard procedures. Local anesthesia was applied around the wound. The wound was sutured using Prolene material. After one week, the stitches were removed.

In the stapler group, the wound was cleaned. Local anesthesia or sedation was applied around the wound to only some patients who were agitated. Using a stapler, the wound lips were brought together and stapled. The stapler materials were removed after one week.

In the hair knotting group, the wound area was cleaned according to the procedures. Local anesthesia or sedation was not given to any patient. At least 10-15 strands of hair on both sides of the wound were brought together and knotted over the wound. At least three knots were tied. No tissue glue was used to prevent the knot from opening. The stitches were not removed. The patients were checked every two days to evaluate hair growth. The hair knot was not untied at each dressing. The knot was untied after wound healing.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences software version 25.0 (IBM Corp., Armonk, New York, USA). The distribution of variables was evaluated for normality using the Kolmogorov-Smirnov test. Descriptive statistics were given as frequency (n) and percentages (%) for categorical variables. In the comparison of continuous variables with more than two independent groups, analysis of variance

(ANOVA) was used when the normal distribution condition was met and the Kruskal-Wallis test otherwise. Following the Kruskal-Wallis test, the Kruskal-Wallis one-way ANOVA (k samples) was used as a post-hoc test. In 2x2 comparisons between categorical variables, the Pearson chi-square test was used if the expected value was calculated as >5, the chi-square Yates test if 3-5, and Fisher's Exact test if <3. The statistical significance level was taken as $p<0.05$.

Results

Patient Population and Characteristics

A total of 120 patients (40 patients in each group) were included in the study. The median age of the patients was 24 [minimum 1-maximum (min-max) 70] years. The number of female patients was 27 (67.5%) in the hair knotting group, 14 (35.0%) in the stapler group, and nine (22.5%) in the primary suture group. Five (12.5%) of the patients in the stapler group were sedated. The detailed demographic and characteristic features of the patients are given in Table 1.

Comparison of Groups

When the length of laceration was evaluated according to the groups, the median length of laceration was 3 cm (min-max: 2-7 cm) in the hair knotting group, 4 cm (min-max: 2-9 cm) in the stapler group, and 3.5 cm (min-max: 2-8 cm) in the primary suture group, indicating no statistically significant difference between the groups (p=0.102 for hair knotting vs. stapler, p=0.872 for hair knotting vs. primary suture, and p=0.264 for stapler vs. primary suture) (Table 2).

Table 1. Demographic characteristics of the patients

		The hair knotting group (n=40, 100%)	Stapler group (n=40, 100%)	The primary suture group (n=40, 100%)	Total (n=120, 100%)
Age	Median (min-max)	13 (3-36) years	28 (1-62) years	27 (2-70) years	24 (1-70) years
Gender	Female	27 (67.5%)	14 (35.0%)	9 (22.5%)	50 (41.7%)
	Male	13 (32.5%)	26 (65.0%)	31 (77.5%)	70 (58.3%)
Hair color	White	3 (7.5%)	7 (17.5%)	5 (12.5%)	15 (12.5%)
	Brown	14 (35.0%)	7 (17.5%)	6 (15.0%)	27 (22.5%)
	Blonde	4 (10.0%)	5 (12.5%)	3 (7.5%)	12 (10%)
	Black	19 (47.5%)	21 (52.5%)	26 (65.0%)	66 (55%)
Hair length	<3 cm	0 (0%)	3 (7.5%)	0 (0%)	3 (2.5%)
	3-6 cm	7 (17.5%)	12 (30%)	21 (52.5%)	40 (33.3%)
	>6 cm	33 (82.5%)	25 (62.5%)	19 (47.5%)	77 (64.2%)
The type of trauma	Beaten	3 (7.5%)	7 (17.5%)	2 (5.0%)	12 (10%)
	Fall from height	19 (47.5%)	13 (32.5%)	17 (42.5%)	49 (40.8%)
	Isolated head trauma	12 (30.0%)	15 (37.5%)	17 (42.5%)	44 (36.7%)
	Car accident	6 (15.0%)	5 (12.5%)	4 (10%)	12 (12.5%)
Sedation	Applied	0 (0%)	2 (5.0%)	5 (12.5%)	5 (4.2%)
	Not applied	40 (100%)	38 (95.0%)	35 (87.5%)	115 (95.8%)
Local anesthesia	Applied	0 (0%)	5 (12.5%)	35 (87.5%)	40 (33.3%)
	Not applied	40 (100%)	35 (87.5%)	5 (12.5%)	80 (66.7%)

min-max: Minimum-maximum

Table 2. The duration of procedures and VAS scores of the groups

	The hair knotting group Median (min-max)	The stapler group Median (min-max)	Primary suture group Median (min-max)	p*	p1	p2	p3
Laceration length (cm)	3 (2-7)	4 (2-9)	3.5 (2-8)	0.223	0.102	0.872	0.264
The length of the stay in the emergency department (min)	23 (8-12)	35.5 (12-72)	42 (20-80)	0.001	0.003	0.001	0.129
The duration of procedure (min)	3 (2-6)	3 (1-6)	8.5 (5-16)	0.001	0.586	0.001	0.001
VAS scores	2 (1-3)	4 (0-5)	2 (0-4)	0.001	0.001	0.349	0.001

p*: Kruskal-Wallis test, p1: Hair knotting vs. stapler, p2: Hair knotting vs. primary suture, p3: Stapler vs. primary suture, min-max: Minimum-maximum, VAS: Visual analog scale

The median length of stay in the emergency department was 23 minutes (min-max: 8-12 minutes) for the hair knotting group, 35.5 minutes (min-max: 12-72 minutes) for the stapler group, and 42 minutes (min-max: 20-80 min) for the primary suture group. Accordingly, the length of stay in the emergency department was statistically significantly shorter in the hair knotting group than in both the stapler and primary suture groups (p=0.003 and p=0.001, respectively) (Table 2).

The median duration of the procedure was determined as 3 minutes (min-max: 2-6 minutes) for hair knotting, 3 min (min-max: 1-6 minutes) for the stapler application, and 8.5 min (min-max: 5-16 min) for primary suturing. While there was no statistically significant difference between the stapler and hair knotting groups in terms of the duration of procedure (p=0.586), a statistically significant difference was observed when these two groups were compared with the sutured group (p=0.001 for both) (Table 2).

The median VAS score was 2 (min-max: 1-3) in the hair knotting group, 4 (min-max: 0-5) in the stapler group, and 2 (min-max: 0-4) in the primary suture group. The VAS scores of the hair knotting and primary suture groups were lower compared with the stapler group (p=0.001 for both). However, the VAS score did not differ statistically between the hair knotting and primary suture groups (p=0.349) (Table 2).

When the groups were compared according to the complications on days 7 and 14 after treatment, the complication rate was found to be significantly lower in the hair knotting group than in the primary suture group (p=0.002 and p=0.012, respectively) (Figure 1) (Table 3).

Concerning patient satisfaction with the procedure applied, no statistically significant difference was found between the groups in terms of satisfaction evaluated on days 0, 7, or 14 (p>0.05) (Figure 2) (Table 3).

Table 3. Comparison of complications, patient satisfaction, and cosmetic problems between the groups

		The hair knotting group (n=40, 100%)	The stapler group (n=40, 100%)	The primary suture group (n=40, 100%)	p1*	p2*	p3*
Complications of 7 day	Pain	6 (15%)	7 (17.5%)	11 (27.5%)	0.201	0.002	0.164
	Redness	6 (15%)	11 (27.5%)	14 (35.0%)			
	Hair loss	0 (0%)	1 (2.5%)	2 (5.0%)			
	Wound dehiscence	1 (2.5%)	3 (7.5%)	2 (5.0%)			
	Serous wound drainage	0 (0%)	0 (0%)	1 (2.5%)			
	None	27 (67.5%)	18 (45.0%)	10 (25.0%)			
Complications of 14 day	Pain	1 (2.5%)	3 (7.5%)	5 (12.5%)	0.335	0.012	0.303
	Redness	2 (5.0%)	5 (12.5%)	8 (20.0%)			
	Hair loss	0 (0%)	0 (0%)	1 (2.5%)			
	Wound dehiscence	1 (2.5%)	1 (2.5%)	0 (0%)			
	Serous wound drainage	0 (0%)	0 (0%)	0 (0%)			
	None	36 (90.0%)	31 (77.5%)	26 (65.0%)			
Satisfaction status, day 0	Satisfied	35 (87.5%)	32 (80.0%)	30 (75.0%)	0.674	0.337	0.839
	Dissatisfied	5 (12.5%)	8 (20.0%)	10 (25.0%)			
Satisfaction status, day 7	Satisfied	36 (90.0%)	34 (85.0%)	33 (82.5%)	0.801	0.608	0.946
	Dissatisfied	4 (10.0%)	6 (15.0%)	7 (17.5%)			
Satisfaction status, day 14	Satisfied	38 (95.0%)	36 (90.0%)	34 (85.0%)	0.739	0.301	0.739
	Dissatisfied	2 (5.0%)	4 (10.0%)	6 (15.0%)			
Cosmetic problem, day 0	Satisfied	8 (20.0%)	15 (37.5%)	20 (50.0%)	0.222	0.014	0.461
	Dissatisfied	32 (80.0%)	25 (62.5%)	20 (50.0%)			
Cosmetic problem, day 7	Satisfied	2 (5.0%)	10 (25.0%)	14 (35.0%)	0.067	0.003	0.501
	Dissatisfied	38 (95.0%)	30 (75.0%)	26 (65.0%)			
Cosmetic problem, day 14	Satisfied	1 (2.5%)	7 (17.5%)	9 (22.5%)	0.127	0.027	0.791
	Dissatisfied	39 (97.5%)	33 (82.5%)	31 (77.5%)			

*Chi-square test.
p1: Hair knotting vs. stapler, p2: Hair knotting vs. primary suture, p3: Stapler vs. primary suture

Cosmetic problems were present in 20%, 5.0% and 2.5% of patients in the hair knotting group on days 7 and 14, respectively, whereas these rates were determined as 50%, 35% and 22.5%, respectively for the primary suture group, indicating that the hair knotting group had statistically significantly lower values in all evaluation times (p=0.014, p=0.003 and p=0.027, respectively) (Table 3) (Figure 3).

Discussion

In this study, we found that the hair knotting technique could be an effective alternative to the stapler and primary suture methods for treating patients with scalp lacerations who have an appropriate hair length. Hair knotting causes fewer complications and cosmetic problems than primary suturing. In the hair knotting technique, patients also feel less pain because no invasive procedure is performed. Hair knotting can be performed in a shorter time than primary suturing; therefore, the length of stay in the emergency department is shorter for patients who have undergone hair knotting compared to the other techniques.

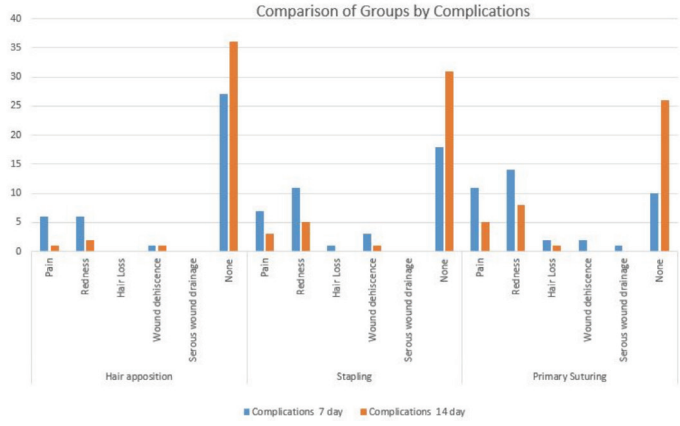

Figure 1. Comparison of the groups according to the presence of complications on days 7 and 14

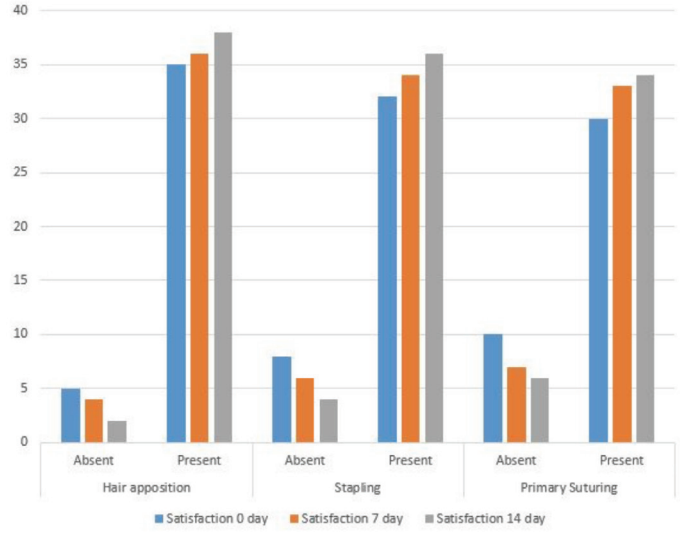

Figure 2. Comparison of the groups according to patient satisfaction on days 0, 7 and 14

Hock et al. (8) evaluated the complications of hair knotting and stapler techniques in patients with scalp lacerations on the seventh day after treatment. The rate of bleeding and infection was found to be similar in both groups. Similarly, Karaduman et al. (9) stated that there was no difference between the hair knotting, stapler, and primary suture techniques in terms of complications evaluated on day 7. Ong et al. (10), on the other hand, reported fewer complications with the hair knotting group on the seventh day after treatment compared with the primary suture technique in scalp lacerations. In our study, we observed fewer complications on days 7 and 14 among the patients who underwent hair knotting compared with those who underwent primary suturing. The most common complications seen on day 7 in all groups were pain and redness. On day 14, the most common complication was redness in all groups. Serous wound drainage was in only one patient in the primary suture group.

Hock et al. (8) determined that patient satisfaction with hair knotting was higher than that with suture for treating scalp lacerations. The authors attributed this higher satisfaction rate of hair knotting to the rapid implementation of the technique, no anesthesia requirement, and stitches not being removed. Karaduman et al. (9) evaluated patient satisfaction with the hair knotting, stapler, and suture techniques used in scalp lacerations on the 30th day after treatment and reported that 97% of the patients stated that they would prefer hair knotting. In the current study, the satisfaction rate of patients who were treated with hair knotting was higher than those treated with stapler and suture techniques. The 14th-day satisfaction the patients who

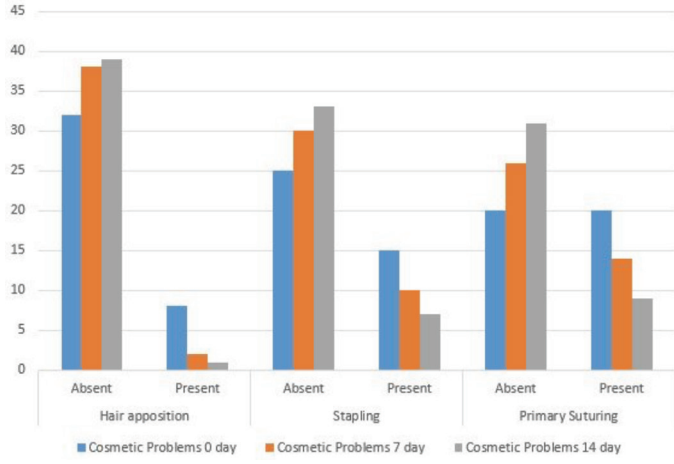

Figure 3. Comparison of the groups according to the presence of cosmetic problems on days 0, 7 and 14

underwent hair knotting treatment was 95%. However, when the groups were compared statistically, there was no significant difference. This may be due to the patients' similar response to treatment in all three groups.

Kanegaye et al. (11) evaluated the cosmetic outcomes of suture and stapler methods applied to the pediatric population with scalp lacerations on the seventh day after treatment and reported no statistically significant difference between the groups. In our study, the hair knotting group did not statistically significantly differ from the stapler group in terms of cosmetic problems evaluated on days 0, 7 and 14 of treatment; however, a significant difference was detected between the hair knotting and primary suture groups. We consider that this difference in cosmetic problems may be due to the absence of suture removal in the hair knotting technique and excessive hair loss in patients receiving primary suture treatment.

There are publications reporting that hair knotting takes a shorter time to perform than suturing and stapleing (8,9,11). There are also studies suggesting that stapler treatment in scalp lacerations is performed in a shorter time than primary suture treatment (12-15). In our study, it was determined that the hair knotting treatment had a similar duration of procedure compared to the stapler technique and took a shorter time than primary suturing. We also observed that the duration of the procedure was shorter in the stapler group than in the primary suture group. The reason why stapler treatment had a similar duration to hair knotting was that two patients in the stapler group received sedation and five patients received local anesthesia.

Because hair knotting is performed in a short time for treating scalp lacerations and requires no sedation or local anesthesia, patients' length of stay in the emergency department is shorter compared to those that have undergone suturing. This contributes to the rapid circulation of patients in emergency services.

In a previous study, comparing the pain levels of patients who underwent hair knotting and primary suturing treatments for scalp lacerations, it was determined that the VAS score of the patients in the hair knotting group was 2, indicating less pain compared to the primary suture technique (8). In the current study, the VAS score of the patients who underwent hair knotting was similar to those who underwent primary suture treatment but lower than those who received stapler treatment. In the primary suture group, sedation or local anesthesia was applied to the patients before the procedure. In our study, the VAS score of the sedated patients was evaluated as "0" (no pain). This explains why there was no significant difference in the pain levels of the patients in the primary suture and hair knotting groups.

Study Limitations

Patients with short hair or no hair not being included in the appropriate patient profile for hair knotting is among the limitations of this study. In addition, the treatment methods to be applied to the patients were randomly selected by the physicians. Finally, the sedation procedure was performed in some patients, and the VAS pain scores of these patients were accepted as 0. The reason for not excluding patients who underwent sedation from the study was to more clearly determine the length of stay in the emergency department and the duration of procedures.

Conclusion

Hair knotting is a technique that can be used as an alternative to primary suture and stapler treatments in emergency services. The advantages of the hair knotting technique over the other two techniques include the less painful nature of the procedure, shorter length of stay in the emergency department, requirement of no sedation or interventional procedure, and lower costs.

Ethics

Ethics Committee Approval: The study was initiated after receiving approval from the Atatürk University Faculty of Medicine Local Ethics Committee (number: B.30.2.ATA.0.01.00/417, date: 01.10.2020).

Informed Consent: Written informed consent was obtained from all volunteer patients participating in the study or their relatives.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.G., E.T., İ.Ö., E.Y.Ç., Concept: A.G., İ.Ö., E.Y.Ç., Design: A.G., İ.Ö., Data Collection or Processing: A.G., E.T., F.T., Analysis or Interpretation: A.G., F.T., Literature Search: A.G., E.T., E.Y.Ç., Writing: A.G., F.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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Comparison of Myocardial Infarction Frequency in Normal and Late Period Populations After Carbon Monoxide Poisoning

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Abstract

Aim: Carbon monoxide (CO) poisoning is still an important factor in the rate of emergency visits. For this reason, we aimed to compare the incidence of myocardial infarction (MI) late after discharge of CO poisoning and its types as compared with the normal population.

Materials and Methods: A total of 1369 patients with a diagnosis of CO intoxication and 1617 patients without a history of cardiac disease who were admitted to the emergency department between January 2005 and December 2010 were included in the study. Patients with a COHb level above 10% and the control group was followed up for 60 months for MI. The patients were divided into three groups: inferior, anterior, and non-ST elevation MI.

Results: At the end of sixty months of follow-up, MI was determined in 103 (7.52%) of the CO group and 61 (3.77%) of the control group. When both groups were considered together, a significant relationship was found with gender, mortality, diabetes, hypertension, and use of tobacco products. However, when the CO group was evaluated sequentially, it was seen that it was only associated with gender, mortality, and MI types. MI groups were statistically significant with other variables except gender. In univariate and multivariate linear regression analyses, age, COHb, Tn level, and CO exposure time was found to cause increased mortality and risk of MI. After follow-up, inferior MI and mortality were higher in the patient group, and anterior MI and mortality were higher in the control group.

Conclusion: Acute COHb and Tn levels may be important values in defining the risk of late MI development in patients discharged after CO poisoning.

Keywords: Carbon monoxide poisoning, emergency department, late-period myocardial infarction

Introduction

Carbon monoxide (CO) poisoning, which is the leading cause of toxic deaths, constitutes an importImportantof emergency department (ED) admissions (1,2). Carboxyhemoglobin (COHb), which is formed by binding to hemoglobin with an affinity 240 times higher than oxygen, disrupts the distribution of oxygen to textures and carrying of oxygen Allosteric change occurs when uni of the CO binds to the heme part of the hemoglobin. The binding of the residual three oxygens to Heme increases and the emancipation of oxygen to tissues decreases (3,4). CO has more affinity for cardiac myoglobin than hemoglobin. Therefore, myocardial depression and hypotension may occur due to tissue hypoxia. CO combines with myoglobin and causes a decrease in partial oxygen in muscle tissue and ultimately causes rhabdomyolysis (4-6). Myocardial infarction (MI) can often be associated with CO exposure.

Even 5-10% increases in COHb level in people with coronary disease before can trigger Angina that occurs during exercise. High levels of COHb can lead to myocardial depression even in young and healthy individuals (6). Electrocardiogram (ECG) and cardiac troponin (Tn) should be studied in order not to overlook silent ischemia. Tns are sensitive and specific markers of heart muscle damage. In 2000, they were accepted as standard markers in the diagnosis of acute MI (7-10).

In the study, it was aimed to evaluate the relationship between Tn and COHb levels with the types of MI who presented with ED because of CO poisoning and that could develop in the late period after the patient was discharged.

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Materials and Methods

In this cross-sectional cohort study, two groups above 18 years old who were referred to the ED between January 2005 and December 2010 were included. While the patients diagnosed with CO poisoning formed the patient group, and those who had recently been admitted to the emergency service with CO poisoning and had no history of cardiac disease formed the control group. While determining the control group, attention was paid to the age of the patients and to be close to the age of the cases diagnosed with CO poisoning.

Patients diagnosed with CO poisoning were divided into two groups at late-period (1-60 months) as acute coronary syndrome (ACS) development and non-development after discharge. Patients with ACS were divided into three groups inferior MI group (inferior, right ventricular, inferolateral, inferoposterior and posterior MI), anterior MI group (septal, anterior, lateral, high lateral and diffuse anterior MI), and non-ST elevated MI group.

Patients with previous diagnosis of infectious or inflammatory disease or malignancy, previous treatment for severe anemia or other hematological diseases or anemia, and those given erythrocyte suspension in the last six months were excluded from the search. After the patients were discharged from CO poisoning, they were followed up retrospectively for 60 months with an annual automation system.

Statistical Analysis

Data obtained in the study were analyzed using IBM Statistical Package for the Social Sciences Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to analyze the normal distribution of the variables. The Student's t-test was used for the variables with normal distribution, and the Mann-Whitney U test was used when examining the differences between the groups for those with non-normal distribution. Chi-square analysis was performed to examine the relationships between the nominal variable groups. Correlation analysis was performed using CO poisoning patient and control groups variables. In addition, univariate linear regression analysis was performed with all the variables in the CO poisoning patient and control groups variables. Predictive values were determined by multivariate linear regression analysis for the significant parameters in the univariate analysis. When interpreting the results, $p<0.05$ was considered statistically significant.

Results

The mean age of the patients was 51.71±17.62 years (52% male, 45.8% patients), and the mean follow-up period was 60 months (range 19 to 88). After sixty months of follow-up, MI was observed in 103 (7.52%) of 1369 patients in the CO group and in 61 (3.7%) of 1617 patients in the control group. The clinical and demographic characteristics of the patients are noted in Table 1.

After sixty months of follow-up, CO poisoning and control groups were found to be statistically significant with developing ACS and diabetes mellitus, hypertension, tobacco use, gender, mortality, and MI types (p=0.001, Table 2).

In the chi-square analysis between ACS and variables that developed after CO poisoning, diabetes mellitus (p=0.091), hypertension (p=0.954), and tobacco use (p=0.621). Were found to be statistically significant with gender, mortality, and MI types (p=0.001, Table 3).

As a result of sixty months of follow-up, in the chi-square analysis of MI types with variables, it was found to be statistically significant with gender (p=0.061), mortality, control and patient groups, hypertension, diabetes mellitus, and use of tobacco products (p=0.001, Table 4).

In univariate analysis, age, emergency admission time, mortality, aspartate amino transferase, alanine aminotransferase (ALT), alkaline phosphatase, C-reactive protein (CRP), Tn, and COHb levels were found to be prognostic indicators. However, in multivariate linear regression analysis, factors including age, the duration of emergency admission, mortality, ALT, CRP, Tn, and COHb were associated with increased MI risk (Table 5).

The correlation between Tn, COHb, mortality, exposure time to CO, and MI types with 60-month cardiac follow-up after CO poisoning was statistically significant (p=0.001, Table 6).

Discussion

In this study, we tried to determine MI types and prognosis after CO poisoning. CO poisoning can be acute or chronic. Since CO has a higher affinity to hemoglobin than oxygen, oxygen is delivered to tissues in fewer amounts. Thus cardiac toxicity may cause myocardial hypoxia. However, the direct toxic effect on myocardial mitochondria plays a more important role (11-14).

In the case of CO poisoning, the cause of cardiac damage is based on 2 mechanisms. The first is ischemic devastation provoked by COHb binding to heme proteins in lieu of oxygen, and the second is toxic damage directly induced by CO (2,15-19). While the cell undergoes direct toxic damage at the mitochondrial level with CO, cytochrome c oxidase inhibition and decreased glutathione levels occur (20,21). This results in anaerobic metabolism in cardiac myocytes, resulting in hypoxia, lactic acidosis, and apoptosis. The cause of endothelial damage is the induction

of the enzyme that occurs during apoptosis formation (22). In contrast, CO stimulates the oxidation of low-density lipoproteins and this increases the free radical formation by inducing peroxynitrite nascency in plasma (23,24). It has been shown that CO exposure triggers venous, arterial, and even stent thrombosis and has a prothrombotic effect (25-30).

In many studies conducted so far, gender and age vary. There were 1441 (48.2%) men in our study and the average age were 51.72 years. In the control group, there were 630 (38.9%) males and their mean age was 63.33 years, and in the patient group, 810 (59%) males and their mean age was 36.2 years. Türkmen and Akgöz (31) found 61.62% males and an average age of 37.73 years in their study; in the Durak (32) study, 71.83% males and 33.39 years of average age were determined. However, Hosseininejad et al. (33) in the meta-analysis study found that of the 4620 people included in the study, 40.12% were male and the average age was 31.68 years. The average age in our study was slightly higher. This may be due to the family and social structure and the other to the general increase in the age average of society. Cardiac involvement can occur immediately after exposure to CO or a few days later. Arrhythmias such as palpitations, sinus tachycardia, atrial fibrillation, and ventricular extrasystole may be observed. In severe cases, bradycardia and complete atrioventricular block may be seen (34). In those with ischemic heart disease, angina pectoris and MI can be triggered. ECG ST segment and T wave changes are common. Transient right and/or left ventricular wall motion disorders may be present (35). In the study published by Lippi et al. (36), the damage caused by CO to the cell; it has been reported that it may cause various cardiac clinical pictures such as cardiomyopathy, angina, MI, arrhythmia, heart failure, pulmonary edema, cardiogenic shock and sudden death. Cases of silent MI caused by acute CO poisoning without chest pain have been reported in the literature. CO cardiotoxicity may be clinically latent and often remain undiagnosed due to specific ischemic changes in ECG and inadequate symptoms (37,38).

There are many studies on ACSs. However, there is no clear information about MI frequency in studies. Sanchis-Gomar et al. (39) found the frequency of MI to be 1.1% in women and 1.7% in men. However, Turkey Cardiovascular Diseases

Table 1. Baseline characteristics of study patients

		Five-year follow-up patients with			Troponin level after carbon monoxide patients with		
	All patients n=2986 Mean±SD	**Control group n=1617 Mean±SD**	**CO patients group n=1369 Mean±SD**	**p value**	**(+) Troponin n=103 Mean±SD**	**(-) Troponin n=1266 Mean±SD**	**p value**
Age (y)	51.72±17.62	63.22±10.51	36.24±15.62	**0.001**	65.44±13.25	33.51±13.20	**0.001**
Female	1545 (51.8%)	987 (61.04%)	559 (40.83%)	**0.001**	64 (62.13%)	752 (59.39%)	**0.024**
Male	1441 (48.2%)	630 (38.96%)	810 (59.17%)		39 (37.87%)	521 (40.61%)	
CRP (mg/L)	4.15±6.23	4.13±6.17	4.19±6.29	0.876	6.26±5.04	3.86±5.99	**0.001**
CO ET (h)	-	-	3.12±2.06	**0.014**	7.10±2.97	2.76±1.61	**0.001**
WBC (10^3/uL)	10.23±3.82	10.22±3.80	10.23±3.83	0.954	11.41±3.29	10.14±3.90	**0.001**
RDW (%)	14.67±1.83	14.67±1.83	14.66±1.81	0.895	14.82±2.00	14.68±1.79	0.327
MPV (fL)	8.43±1.01	8.43±1.03	8.42±0.99	0.797	8.44±0.97	8.42±0.98	0.989
MCHC (g/dL)	33.35±3.59	33.33±3.50	33.38±3.69	0.899	33.34±4.19	33.34±3.38	0.295
MCV (fL)	87.45±7.64	87.31±7.60	87.68±7.71	0.129	87.42±7.60	87.50±7.67	0.829
MCH (pg)	29.28±2.25	29.29±2.24	29.46±2.24	**0.015**	29.38±2.77	29.45±2.19	0.492
BS (mg/dL)	120.82±45.78	120.86±45.82	120.71±45.84	0.521	133.32±44.28	119.89±45.97	**0.004**
AST (U/L)	31.31±23.61	31.21±23.94	31.35±23.21	0.376	45.34±17.32	30.27±22.41	**0.001**
ALT (U/L)	29.40±24.08	29.32±24.31	29.40±23.81	0.587	45.64±20.14	27.91±22.58	**0.001**
ALP (U/L)	107.21±55.25	106.69±55.86	107.59±54.36	0.377	154.85±52.94	102.94±51.41	**0.001**
COHb (%)	-	-	31.63±10.11	**0.001**	55.08±6.23	28.83±6.86	**0.001**
Tn (ng/dL)	-	-	0.92±1.24	**0.001**	1.52±1.39	0.24±0.08	**0.001**

$p<0.05$.
Statistical data were obtained with the Mann-Whitney U test. $p<0.05$ value was considered statistically significant.
(+): Positive, (-): Negative, CRP: C-reactive protein, CO ET: Carbon monoxide exposure time, WBC: White blood cell, RDW: Red cell distribution width, MPV: Mean platelet volume, MCHC: Mean corpuscular hemoglobin concentration, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, BS: Blood sugar, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, CK: Creatine kinase, CK-MB: Creatine kinase-muscle brain, COHb: Carboxyhemoglobin, Tn: Troponin, SD: Standard deviation

Prevention and Control Program Action Plan (40) women in the study 1.33%, 3.03% in men was found to be acute MI. In our study, patients discharged after CO poisoning was followed for 60 months. These data were retrospectively recorded annually. After CO poisoning, MI types that were not previously detected in the literature were examined. At the end of this 60-month follow-up, it was observed that MI developed in 103 (7.52%) patients in the CO group. In spite of the higher mean age of the control group 61 (3.7%) cases had MI. The 2-fold higher MI frequency may be a predictive indicator of MI that may develop CO intoxication. Tn and COHb values in all patients of the Co patient group were significantly higher than those without MI at the 60-month follow-up. Inferior MI in the CO patient group and anterior MI in the control group was more common. While most MI cases in the control group were diagnosed with hypertension, most cases developing MI after intoxication was normotensive patients. This could be due to two reasons. First, the inferior group MI is generally hypotensive and bradycardic. Second, the sinus node is close to the right coronary artery. It was most common in mortality in MI with ST elevation, especially in the inferior MI group.

Henry et al. (41) found that acute myocardial damage in patients with CO poisoning, followed for an average of 7.6 years, is a long-term risk of death. In another study with 10.6 years follow-up after CO poisoning, it was found to be a neutral predictor of all long-term mortal situations. Huang et al. (42) found that CO intoxication increases the risk of death in the long term. Lee et al. (43) showed that CO intoxication increases the risk of CAD and heart failure in the long term.

In our study, during the 60-month follow-up, mortality was detected as 31 (2.2%) in the CO patient group and 19 (1.1%) in the control group. In all cases with mortality in the CO patient group, it was determined that the COHb level was above 40 and the accompanying Tn elevation. Mortality in the CO patient group was common in the inferior MI group, and in the control

Table 2. Analysis of patient and control groups according to variables after five years of follow-up

	Five-year follow-up		χ^2	p value
	The CO patient group n (%)	Control group n (%)		
Gender				
Male	559 (18.7)	987 (51.8)	**121.228**	**<0.001**
Female	810 (27.1)	630 (21.1)		
Mortality				
No	1338 (44.8)	1598 (53.5)	**5.344**	**<0.021**
Yes	31 (1.0)	19 (0.6)		
HT				
No	1152 (38.6)	842 (28.2)	**343.844**	**<0.001**
Yes	217 (7.3)	775 (26.0)		
DM				
No	1026 (34.4)	1009 (33.8)	**53.759**	**<0.001**
Yes	343 (11.5)	608 (20.4)		
Tobacco				
No	379 (12.7)	1137 (38.1)	**539.060**	**<0.001**
Yes	990 (33.2)	480 (16.1)		
MI				
No	1266 (42.4)	1556 (52.1)	**40.054**	**<0.001**
Inferior	64 (2.1)	16 (0.5)		
Anterior	30 (1.0)	39 (1.3)		
NSTEMI	9 (0.3)	6 (0.2)		

Statistical data were obtained with the chi-square test. p<0.05 value was considered statistically significant.
DM: Diabetes mellitus, HT: Hypertension, MI: Myocardial infarction, NSTEMI: Non-ST elevation MI, CO: Carbon monoxide

Table 3. Analysis of variables with AMI according to 5-year follow-up in the CO patient group

	Troponin		χ^2	p value
	Negative n (%)	Positive n (%)		
Gender				
Male	514 (40.6)	38 (38.8)	**8.893**	**<0.002**
Female	756 (59.4)	60 (61.2)		
Mortality				
No	1338 (97.7)	31 (2.3)	**140.923**	**<0.001**
Yes	80 (81.6)	18 (18.4)		
DM				
No	850 (93.6)	58 (6.4)	4.799	>0.091
Yes	421 (91.3)	40 (8.7)		
HT				
No	849 (92.9)	64 (7.1)	0.095	>0.954
Yes	422 (92.5)	34 (7.5)		
Tobacco				
No	763 (92.5)	61 (7.5)	0.953	>0.621
Yes	508 (93.2)	37 (6.8)		
MI				
No	1266 (99.7)	3 (0.3)	**1315.788**	**<0.001**
Inferior	1 (1.7)	61 (98.3)		
Anterior	0 (0)	29 (100)		
NSTEMI	2 (22.2)	7 (77.8)		

Statistical data were obtained with the chi-square test. p<0.05 value was considered statistically significant.
DM: Diabetes mellitus, HT: Hypertension, MI: Myocardial infarction, NSTEMI: Non-ST elevation MI, CO: Carbon monoxide

Table 4. Analysis of patients who developed AMI after five years of follow-up with variables						
Acute myocardial infarction						
	No n (%)	**Inferior n (%)**	**Anterior n (%)**	**NSTEMI n (%)**	**χ^2**	**p value**
Gender						
Male	1476 (49.4)	38 (1.3)	27 (0.9)	5 (0.2)	7.363	0.061
Female	1346 (45.1)	42 (1.4)	42 (1.4)	10 (0.3)		
Mortality						
No	2796 (93.6)	69 (2.3)	58 (1.9)	13 (0.4)	**178.269**	**0.001**
Yes	26 (0.9)	11 (0.4)	11 (0.4)	2 (0.1)		
Five-year CO						
Follow-up	1266 (42.4)	64 (2.1)	30 (1.0)	9 (0.3)	**40.054**	**0.001**
Cont	1556 (52.1)	16 (0.5)	39 (1.3)	6 (0.2)		
HT						
No	1928 (64.6)	27 (0.9)	31 (1.0)	8 (0.3)	**58.434**	**0.001**
Yes	894 (29.9)	53 (1.8)	38 (1.3)	7 (0.2)		
DM						
No	1960 (65.6)	39 (1.3)	30 (1.0)	6 (0.2)	**40.910**	**0.001**
Yes	862 (28.9)	41 (1.4)	39 (1.3)	9 (0.3)		
Tobacco						
No	1390 (46.6)	57 (1.9)	54 (1.8)	15 (0.5)	**51.422**	**0.001**
Yes	1432 (48.0)	23 (0.8)	15 (0.5)	0 (0.0)		

Statistical data were obtained with the chi-square test. P<0.05 value was considered statistically significant.
NSTEMI: Non-ST elevation myocardial infarction, CO: Carbon monoxide, AMI: Acute myocardial infarction

Table 5. Univariate and multivariate linear regression analysis for predicting the development of acute myocardial infarction in the CO patient group										
Acute myocardial infarction										
	Univariate					**Multivariate**				
	R square	**F**	**β**	**t**	**p value**	**R square**	**F**	**β**	**t**	**p value**
Age	**0.112**	**172.753**	**-0.214**	**-6.510**	**<0.001**			**0.002**	**59.675**	**<0.001**
CO ET (h)	**0.105**	**159.865**	**-0.067**	**-2.836**	**<0.005**			**0.011**	**3.697**	**<0.001**
Mortality	**0.303**	**6.081**	**0.249**	**4.881**	**<0.001**			**-0.678**	**9.925**	**<0.001**
ALT	**0.014**	**19.179**	**0.109**	**4.983**	**<0.001**			**0.000**	**0.798**	**<0.029**
CRP	**0.016**	**12.169**	**0.140**	**8.496**	**<0.001**	**0.883**	**359.259**	**0.004**	**4.986**	**<0.001**
Tn	**0.223**	**391.213**	**0.114**	**9.005**	**<0.001**			**0.051**	**5.529**	**<0.001**
COHb	**0.386**	**859.500**	**-0.810**	**-22.78**	**<0.001**			**0.007**	**10.259**	**<0.001**
BS	0.001	0.685	0.153	3.925	>0.408					
AST	**0.006**	**7.840**	**0.131**	**5.643**	**<0.005**					
ALP	**0.029**	**40.904**	**0.010**	**0.347**	**<0.001**					

Statistical data were obtained with uni/multivariate regression analysis. P<0.05 value was considered statistically significant.
CO ET: Carbon monoxide exposure time, COHb: Carboxyhemoglobin

Table 6. Correlation coefficients for 5-year cardiac follow-up		
Acute myocardial infarction		
	R	**p value**
Mortality	**0.234**	**<0.001**
COHb	**0.621**	**<0.001**
Tn	**0.472**	**<0.001**
CO ET(h)	**0.234**	**<0.001**
AMI	**0.384**	**<0.001**

Statistical data were obtained by correlation analysis. p<0.05 value was considered statistically significant.
CO ET: Carbon monoxide exposure time, COHb: Carboxyhemoglobin, AMI: Acute myocardial infarction

group, anterior MI was common. The correlation between MI and mortality was positively correlated.

This is the first study to establish whether high co levels are a long-term detached risk factor for MI types. Kalay et al. (44) emphasized that increased CO levels in blood and extended duration of exposure to CO poisoning are risk factors for MI development. In our study, the exposure time and rate of cardiac damage were similar.

As a result, the high COHb and Tn values in the acute period of the patients who applied to the ED with CO poisoning and the MI frequency in the late period after discharge were more than two times higher than the normal population. In addition, while anterior MI and mortality were common in the normal population, inferior MI and mortality were found to be higher in the CO patient group. These data show that patients are in a higher risk group after CO discharge.

Study Limitations

The major limitation of the study is that it is not multi-centered and retrospective. Therefore, it was difficult to reach some data.

Conclusion

Cardiac disorders that may develop in the future can be easily overlooked in CO poisoning, especially if the patients are asymptomatic. Considering the COHb and Tn levels evaluated in our study by physicians may guide the prevention of future cardiac problems and early diagnosis.

Ethics

Ethics Committee Approval: The study was approved by the Cumhuriyet University Faculty of Medicine of Local Ethics Committee (decision no: 2012/12-09, date: 04.12.2012).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

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Factors Affect the Quality of Sleep in Elderly People with Metabolic Syndrome

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Abstract

Aim: As more studies are conducted on the effects of metabolic syndrome (MetS) on the elderly, it becomes clear that these individuals suffer from worse sleep. In this study, we examined the factors affecting sleep quality in the elderly diagnosed with MetS.

Materials and Methods: The study was conducted in the Internal Medicine Clinic of Malatya Training and Research Hospital. Elderly people over the age of 65 years, willing to cooperate, able to communicate, and scored 23 and above on the Standard Mini Mental Test were recruited. The individuals included in the study were individuals who met the criteria for MetS. A comprehensive geriatric evaluation form was applied to elderly individuals.

Results: The study's 378 participants had mean age of 72.05±6.56 years. People over the age of 60 who had high values for both their body mass index (BMI) and their waist-hip ratio also had high Pittsburgh Sleep Quality Index scores ($p<0.05$). The factors affecting sleep quality were examined by regression analysis. As a result of, having a BMI of 30 or higher [odds ratio (OR): 2.831, confidence interval (CI): 0.081-2.525], being 75 or older (OR: 2.021, CI: 0.081-2.525), being totally or partially dependent on others for the performance of daily activities (OR: 5.024, CI: 2.408-5.165), and using multiple drugs (OR: 2.831, 0.734-2.901), an increased likelihood of falling (OR: 4.871, CI: 1.056-6.146), an increased likelihood of depression (OR: 3.850, CI: 1.355-3.973) increases sleep quality index scores.

Conclusion: The elderly individuals who already have MetS are more likely to have poor sleep quality due to the accumulation of many detrimental factors that arise as a direct result of MetS.

Keywords: Elderly, metabolc syndrome, sleep quality index

Introduction

Sleep is one of the most crucial elements in maintaining good health. Similar to how there is a reversible state of unconsciousness, there is also an active state of regeneration that enables the body to get ready for new life while also allowing the body to rest (1). Sleep is a fundamental human need that supports not only productivity but also physical and psychological well-being as well as cognitive abilities like memory and concentration. The positive effects of sleep disorders and irregularities negatively impact people's ability to focus, memory loss, experience anxiety, depression, and psychosis, as well as their sensitivity to pain, irritability, appetite loss, and constipation (2,3). According to some studies, there is a direct correlation between a rise in HbA1c and a decline in sleep quality (4,5). In society, chronic sleep loss and the issues it causes are very prevalent. Long-term sleep loss and a decline in sleep quality have an impact on disease and death rates. Numerous studies have demonstrated that they reduce insulin sensitivity and glucose tolerance. Researchers have discovered that sleeping for fewer than six hours a night increases the risk of developing the metabolic syndrome (MetS) (6,7). Poor sleep quality is a significant contributor to the development of obesity and has been linked to studies of the MetS, sleep apnea, and obesity in men more frequently than in women (8,9). The last ten years have seen an increase in sleep-related issues and sleep disorders, and at the same time, global epidemic levels of MetS

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and obesity have been reached. According to the most recent epidemiological study, 50-70 million Americans have chronic sleep disorders such as insufficient sleep, insomnia, and sleep apnea (8). Understanding the role of risk factors in metabolic diseases, such as MetS, is crucial for halting disease onset and progression. This study sought to determine how well patients with MetS slept across three provinces.

Materials and Methods

Design, Sampling, and Ethical Issues

To identify the variables influencing sleep in patients with MetS and to ascertain how and where they affect sleep issues associated with MetS, the research was designed as a descriptive study.

Due to the G-power analysis showing that the "critical χ^2" value for this study was 22.07 with a margin of error of 0.05, 90% power, and an effect size of 0.3, it was decided that 350 participants were needed for the study. After accounting for dropouts, the final sample size was 378 participants.

The study was conducted on 378 patients with MetS being treated at the Internal Medicine Clinic of Malatya Training and Research Hospital who met the inclusion criteria and provided voluntary oral and written consent between October and November 2022.

The study was conducted according to the criteria of the Declaration of Helsinki and approved by the Malatya Turgut Özal University Local Ethics Committee. All the study participants provided their informed consent.

Data Collection

A sociodemographic form with 33 questions on sociodemographic characteristics and sleep problems was applied to the m MetS patients, along with the Pittsburgh Sleep Quality Index (PSQI), developed in 1989 by Buysse et al. (5) and tested for validity and reliability in Turkey by Ağargün et al. (6) in 1996.

PSQI

The questionnaire's objectives are to evaluate sleep quality and determine who has and does not have sleep problems. Subjective sleep quality, sleep latency (SL), sleep duration, habitual sleep efficiency (HSE), sleep disorders, use of sleeping pills, and daytime dysfunction are the seven subscales that make up this scale. Answers are graded on a scale of 0 to 3 with a maximum score of 21. If you receive a six or higher, you are not getting enough sleep.

To assess the quality of sleep in psychiatry and clinical research, Buysse et al. (5) created the PSQI in 1989. The PSQI's clinical follow-up process of 18 months, other sleep quality scales found in the literature, and clinical observations of patients with sleep disorders were all used to create the items in the questionnaire. On PSQI, a global score of more than 5 denotes poor sleep quality. Ağargün et al. (6) evaluated the validity and reliability of the scale in Turkey, and they discovered that it had a Cronbach's alpha reliability coefficient of 0.804.

Anthropometric Measurements, Body Mass Index, and Blood Pressure

Anthropometric measurements were measured by well-trained examiners while subjects wore only their underwear and no shoes. Weight and height were measured to the nearest 0.1 kg and 1 cm while the participant stood, respectively, using a strain gauge scale and a stadiometer (Seca 769, Hamburg, Germany). The following formula was used to calculate body mass index (BMI): weight in kilograms divided by height in square meters (m). The waist and hip circumferences were measured to the nearest 0.1 cm with a flexible metric measuring tape while the subject was standing upright. The circumference of the waist was measured around the abdomen at the umbilicus. Hip circumference was measured in a horizontal plane at the buttocks' maximum posterior extension. Waist/hip ratio (WHR) was determined by dividing waist circumference by hip circumference, and waist/height ratio was determined by dividing waist circumference by height (cm).

Each participant, including blood pressure, was collected. After a 5-min rest, systolic and diastolic blood pressures was measured twice with validated and calibrated electronic sphygmomanometers.

Diagnostic Criteria for Metabolic Syndrome

A modified NCEP MetS-according to ATP III, was defined as the presence of three or more of the following conditions: (1) hypertension: systolic blood pressure ≥130 mm High or diastolic blood pressure ≥85 mm High or use of antihypertensive agents; (2) hyperglycemia: fasting blood glucose level ≥100 mg/dL; (3) low serum HDL-C for men ≤40 mg/dL for women and ≤50 mg/dL; (4) hypertriglyceridemia: triglycerides levels ≥150 mg/dL; and (5) abdominal obesity: men BC ≥90 cm for women and ≥80 cm (6).

Daily Living Activities (IADL)

In 1969, Lawton and Brody (10,11) created the IADL index to assess people's instrumental daily living activities. The IADL index consists of eight questions about phone use, cooking, shopping, doing daily housework, washing clothes, driving, drug use, and money management. The IADL index assigns a score of 0 to dependent relationships, 9 to semi-dependent relationships, and 17 to independent relationships. These evaluations of

people's daily lives and instrumental activities are widely used both internationally and in our country.

Yesavage Geriatric Depression Scale

Validity and reliability research was conducted after it was created by Yesavage et al. (12). It is a self-reporting questionnaire with 30 simple questions designed for the elderly. The cutoff point for making a depression diagnosis was set at 13. Factors such as mood swings, emotional volatility, irritability, social withdrawal, intrusive thoughts, and pessimistic assessments of the past, present, and future are measured. Avoiding questions about somatic symptoms such as sleep problems, sexual dysfunction, and aches and pains in the body, which are common in the elderly due to physical diseases, and providing only "yes" or "no" answers simplifies the scale and makes it more manageable for those with limited health literacy. Each affirmative response earns one point, while each negative response earns no points. The severity of a person's depression is proportional to how high they score on this scale.

The Timed Get-up-and-Go

The functional abilities of the elderly were measured using the Timed Get-up-and-Go test. Podsiadlo and Richardson (13,14) devised test monitors the tempo of the elderly in three different motions: standing, walking, and turning. The elderly were given the order to stand up from their seats, walk three meters in a straight line, make a right or left turn, and return to their original chairs. A timer recorded how many seconds had passed between when the person got up and sat back down. During the time of examination, the use of canes, crutches, and other similar devices was forbidden. The exam is taken twice with the top score kept. The time taken to complete the walk was significantly longer than normal, indicating that the person's walking ability was impaired.

Statistical Analysis

Statistical Package for the Social Sciences 22.0 was used for data analysis. Using the collected data, a descriptive study was created in which the quantitative variables were expressed as mean±standard deviation and the qualitative variables as an absolute value with confidence intervals (CIs). To compare measurements, Student's t-test and the Mann-Whitney U test were used. The Spearman r-value was used to calculate the quantitative variable correlation, while two statistics were used to calculate the qualitative variable correlation. Multiple logistic regression analysis was used to determine which variables influenced a dichotomic dependent variable, with the dichotomic variable serving as the dependent variable and the other variables included in the model serving as covariables.

Results

The study included 378 people with a mean age of 72.05±6.56 years old. Table 1 shows the distribution of the elderly's PSQI mean scores based on their characteristics. PSQI mean scores increased as individuals' ages increased, according to the age groups of the elderly. The average PSQI score of women was higher than that of men ($p<0.05$). Individuals with a primary school education or higher, married people, and people who live with their children had lower PSQI scores than the other groups ($p<0.05$). Individuals' PSQI scores have risen when they smoke. PSQI scores of the elderly with high BMI and WHR values were also found to be high ($p<0.05$). The elderly with malnutrition and people who used 10 or more drugs per day had a higher PSQI score.

Table 2 shows the correlation analysis between elderly PSQI scores and BMI, daily drug use, daily life activity scale score, elderly depression scale score, and Timed Get-up-and-Go test. PSQI was found to have a positive correlation with BMI, number of drugs taken daily, Yesavage Geriatric Depression Scale, and Timed Get-up-and-Go, but a negative correlation with IADL.

The PSQI score was used as a dependent variable in a linear regression analysis of all independent variables showing statistically significant differences. Therefore, having a BMI of 30 or higher [odds ratio (OR): 2.831, CI: 0.081-2.525], being 75 or older (OR: 2.021, CI: 0.081-2.525), being totally or partially dependent on others for the performance of daily activities (OR: 5.024, CI: 2.408-5.165), and using multiple drugs (OR: 2.831, 0.734-2.901), an increased likelihood of falling (OR: 4.871, CI: 1.056-6.146), an increased likelihood of depression (OR: 3.850, CI: 1.355-3.973). One of the factors found to improve people's sleep quality index scores was having an albumin concentration of less than 4 mg/dL (OR: 2.107, CI: 0.235-3.538) (Table 3).

Discussion

Sleep is an essential part of our bodies and lives (15). The elderly population has a higher prevalence of sleep disorders, which can have negative effects on both their physical and mental health. Recommendations for treating sleep disorders in the elderly can't be made until the underlying causes are identified (16).

According to the research conducted by Chaput et al. (17), those who get less than six hours of sleep per night are more likely to develop MetS, while those who get nine hours or more of sleep per night do not face an increased risk of developing MetS. For example, Kobayashi et al. (18) MetS was found to be more prevalent in people who slept less than 6 hours per night, according to his study. Najafian et al. (19) While shorter sleep

Table 1. The distribution of the elderly according to their characteristics PSQI score means					
Variables	**n (378)**	**%**	**X±SD**	**Test value**	**p**
The age group (y)					
65-69	41	10.85	4,76±3.15	10.321	**0.001**
70-74	67	17.72	5.47±2.81		
75-79	78	20.63	5.74±3.11		
80-84	89	23.54	7.06±3.28		
85+	103	27.25	8.23±2.69		
Sex					
Female	221	58.47	6.21±3.18	11.650	**0.001**
Male	157	41.53	5.33±3.11		
Educational status					
Illiterate/barely literate	294	77.88	6.23±3.25	28.331	0.001
Elementary school and above	84	22.22	5.96±3.67		
Marital status					
Married	88	23.26	4.18±3.41	15.896	**0.001**
Widowed/divorced	290	76.74	6.25±3.44		
Cohabitation					
Spouse	73	19.31	5.07±2.71	13.525	**0.001**
Living alone	112	29.63	6.37±3.21		
Families of their children	105	27.78	4.21±2.13		
Nursing home	88	23.28	4.56±2.21		
Smoking status					
Not smoking or quitting/smoking	306/72	80.95/19.05	4.57±2.28-7.96±3.76	2.224	0.348
Regular physical activity status					
yes/nor or not regularly	201/177	53.17/46.82	3.21±1.08-5.06±2.56	3.981	0.023
BMI (kg/cm^2)				18.901	0.029
20-25 normal	36	9.52	4.34±2.19		
25-30 pre-obesity	112	29.63	5.26±2.89		
30-35 I. obesity	87	23.02	7.37±4.08		
35-40 II. obesity	65	17.20	7.57±2.91		
40 and upper III. obesity	41	10.85	8.67±4.18		
Waist/hip ratio			p=0.004		
Female					
0.85 and under	56	25,34	5.33±2.91		
Upper >0.85	165	74,66	7.61±3.69		
Male					
0.90 and under	44	28,03	5.91±2.63		
Upper >0.90	113	71,97	7.28±2.88		
MNA-SF					
12-14 good feeding	189	50.00	6.21±2.91	2.990	0.043
8-11 under the risk of malnutrition	145	38.36	4.21±1.72		
0-7 malnutrition	44	11.64	7.21±3.74		
Daily regular drug use					
Daily 3 drugs and under	21	5.56	5.88±2.96	16.389	0.011
Daily 4-6 drug	223	58.99	5.06±2.28		
Daily 7-9 drug	101	26.72	4.45±1.74		
Daily 10 and upper drug	33	8.73	6.21±3.65		

MNA-sf: Mini nutritional assessment-short form, SD: Standard deviation, PSQI: Pittsburgh Sleep Quality Index, BMI: Body mass index

Table 2. Correlations between PSQI score and BMI, daily drug use, daily life activity scale score, elderly depression scale score, and Timed Get-up-and-Go test score

	PSQI	BMI	The number of drugs used regularly per day	IADL	YGDS	TGUG
PSQI	1.00	0.455**	0.244*	-0.446**	0.429**	0.275*
BMI		1	0.351**	-0.267**	0.079	0.645**
The number of drugs used regularly per day			1	-0.282**	0.247*	0.424**
IADL				1	-0.249*	-0.524**
YGDS					1	0.353**
TGUG						1

Spearman correlation, *p<0.05,**p<0.005.
PSQI: Pittsburgh Sleep Quality Index, BMI: Body mass index, IADL: Instrumental activities of daily living, YGDS: Yesavage geriatric depression scale, TGUG: Timed Get-up-and-Go

Table 3. Results of linear regression analysis involving the factors affecting the PSQI

Independent variables		B	SE	Wald	Odds ratio	95% CI	p
Age (y)	Advanced old age	0.274	0.125	0.113	**2.021**	0.081-2.525	0.007
	Under 75				Reference		
IADL	Dependent or semi-dependent	1.674	0.309	0.454	**5.024**	2.408-5.165	0.001
	Independent				Reference		
The number of drugs used regularly per day	5 and under	1.283	0.533	0.306	**2.831**	0.734-2.901	0.003
	Upper >5				Reference		
YGDS	Yes	2.014	0.401	0.249	**3.850**	1.355-3.973	0.004
	No				Reference		
TGUG	20 seconds and upper	1.068	0.319	0.192	**4.871**	1.056-6.146	0.001
	<20 seconds				Reference		
Albumin (mg/dL)	4 mg/dL and under	0.784	0.365	0.081	**2.107**	0.235-3.538	0.022
	>4 mg/dL				Reference		

PSQI: Pittsburgh Sleep Quality Index, IADL: Instrumental activities of daily living, YGDS: Yesavage Geriatric Depression Scale, TGUG: Timed Get-up-and-Go, CI: Confidence interval

duration has been linked to an increased risk of developing MetS, longer sleep duration has been linked to a decreased risk. It has been shown that both insufficient and excessive sleep duration contribute to the development of MetS (19-21). MetS becomes more prevalent in older people, and so do sleep disorders.

Gender differences may also be present in a variety of other sleep-related factors, such as quality, duration, latency, and efficiency. Despite the fact that women have been shown in some studies to report more sleep-related complaints than men, despite having better sleep quality, shorter sleep duration, and longer SL (22). Some research has found no significant differences between the sexes when it comes to sleep, while other research has found that women report poorer sleep quality (23). The majority of this study's participants were women, and across all age ranges, participants scored higher on the PSQI on average the longer they had lived. The decline in sleep quality that comes with getting older is a major issue in and of itself (24). Being 75 or older was found to significantly increase the risk of developing a sleep disorder in this investigation.

People's standard of living improves along with their level of education. Health literacy improves with education, leading to greater personal accountability for health and better disease and symptom management (25). It is well established that married and cohabiting individuals report higher levels of social support and happiness (26). The majority of the study's participants could not read or write. Most patients are either single or have been divorced and are now living independently or in a care facility. It is hypothesized that this circumstance worsens patients' quality of life and raises their levels of depression and anxiety. Patients' poor quality of sleep was linked to their low quality of life and the presence of depression.

It has been shown through cohort studies that compared to non-smokers, smokers experience a greater number of insomnia-like

symptoms and poorer quality of sleep overall. Cigarette smoking has been linked to insomnia and other sleep disturbances in both sexes (27,28). Among the participants in this analysis, 80.95% had never smoked before.

It's common knowledge that the elderly have a higher drug consumption rate due to the prevalence of chronic diseases. Overall sleep quality and sleep-related components like subjective quality, sleep delay, sleep duration, external disturbances, and sleeping pill consumption significantly decline with increasing polysubstance use (13). The results of this study showed that 58.9% of patients were taking four or more medications on a daily basis. Multiple drug use was associated positively with lower PSQI scores, suggesting that it is a significant contributor to poor sleep.

The degree to which an elderly person is mobile is a significant indicator of their quality of life. Because of his limited mobility, the person becomes more reliant on others and has difficulty engaging in regular activities or retaining his sense of self (29). As we age, we walk slower and our strides become shorter (30). Insomnia in the elderly can lead to instability and an increased chance of falling (31). Results from the Timed Get-up-and-Go test, risk of falling, and sleep disorder score were positively correlated with levels of independence in ADL performance.

There is evidence that shows how being overweight makes the elderly more likely to experience a sleep disorder (32,33). Short sleep duration was associated with higher BMI and waist circumference in middle-income individuals in a study examining the association of sleep duration and quality with the risk of obesity in people over the age of 50 (34). According to Jennings et al. (35) increases in PSQI score were associated with elevations in BMI. Most of the participants in this study were classified as being of advanced age, and the results showed that there was a significant positive correlation between body mass index and PSQI score, indicating better overall sleep.

Moderate to severe insomnia has been linked to an increased risk of malnutrition (36). Sleep disorders have been linked to an increased risk of malnutrition in a number of studies that have evaluated the association between nutritional status and its correlates (37,38). However, another study found that regardless of age or gender, poor sleep quality was strongly linked to an increased risk of malnutrition (39). Similarly to other research, this one found that half of the elderly population was either malnourished or at risk for malnutrition. Having a low albumin value, an indicator of malnutrition, has also been shown to significantly raise the sleep quality index score.

Study Limitations

In this study, we look into a pressing problem in public health. In our study, we employed tried-and-true techniques and evaluation criteria that have been proven effective in numerous other studies both internationally and in Turkey. One researcher oversaw the entirety of our study to ensure consistency and reliability.

Our study is limited in its applicability to the general elderly population due to the fact that it was conducted on patients at a tertiary care hospital. Our study's limited generalizability can also be attributed to its participants' lack of formal education. Because ours is a cross-sectional, in-person survey, there is always the chance of researcher bias.

Conclusion

In order to increase the quality of sleep in the elderly and to have a quality aging process, it is necessary to take measures to improve these factors.

Ethics

Ethics Committee Approval: The study was conducted with the approval of Malatya Turgut Özal University Ethics Commission dated 17/11/2022 number 362. The study were carried out in accordance with the Helsinki Declaration 2013.

Informed Consent: Written informed consent was obtained from all individuals participating in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.Y., H.A., Concept: B.Y., H.A., Design: B.Y., N.A., H.A., Data Collection or Processing: N.A., Analysis or Interpretation: B.Y., H.A., Literature Search: H.A., Writing: B.Y., H.A.

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Japan Coma Scale as a Scale to Assessment the Severity of Multi Trauma Patients

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Abstract

Aim: The Japan Coma Scale (JCS) is a criteria standard for assessing the consciousness in prehospital and emergency care settings. Our aim was to assess the relationship between Glasgow Coma Scale (GCS) and JCS scores as well as compare them to the outcomes of trauma patientsto see if JCS can be used instead of GCS in the emergency department.

Materials and Methods: This was a case-control field study using cross-sectional data in the emergency department that evaluated 268 trauma patients, including 86 women and 182 men from September to December 2020, who were referred to the Tabriz emergency department. A checklist in the emergency department gathered patient information, which was then compiled using in-hospital charts and prehospital records. The level of consciousness of the patients was assessed using the JCS (1-3) and GCS (3-15) scales, and the outcomes were compared.

Results: Two hundred-twenty nine of the 268 patients examined were discharged, while 37 were admitted to the hospital. Unfortunately, two of the patients passed away. The relationship between GCS and JCS of patients is significant, strong, and inverse (Pv=0.001; correlation coefficient=-0.999), according to the data analysis. In the JCS, the sensitivity of the test is 64.10%, the specificity is 100%, the positive predictive value is 100%, and the negative predictive value is 94.24%. Thus, in GCS 82.05%, 100%, 100%, and 97.03%.

Conclusion: based on the findings of this study and the important correlations in patient results between GCS and JCS, using JCS instead of GCS has a major effect on improving the process of caring for trauma patients in the emergency room, and it can be recognized as a standard coma scale.

Keywords: Japan coma scale, multiple patients, emergency department

Introduction

Trauma is a leading cause of death and disability across all ages worldwide (1). Rapid transport of patients from the site of injury to the emergency department and prompt and accurate assessment of consciousness level are the most significant factors in saving lives, reducing disability and improving long-term outcomes in trauma patients (2,3). Thus, attention to the level of consciousness in patients is one of the most critical factors for triage, sorting, and patient transport to the tertiary critical care centre (2).

Importance

Immediate assessment of the consciousness of trauma patients is necessary for the emergency department (2). By and large, the Glasgow Coma Scale (GCS) is the most common measure used by emergency department paramedics and other medical professionals in a variety of settings to assess level of consciousness (4). This scale is time-consuming and complicated and therefore it may not be practical for rapid assessment (4). According to the high load of patients in the emergency department (5), work pressure and high stress level of emergency staff, present of people who lack sufficient knowledge and experience (6), moreover, The importance of time management to help emergency patients in Golden Time (7), a faster and simpler tool, which is easy to assess, easy to register, and easy to share with medical staff and medical assistants is needed.

The Japan Coma Scale (JCS), a grading system for assessing loss of consciousness, was first published in 1974 (8-10) and has since

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become a standard tool for assessing the level of consciousness on the scene by firefighters and agencies. Japan's disaster management has been confirmed. The JCS is used to classify a patient's level of consciousness into one of three categories determined by reactive eye opening: Level 1 is spontaneous eye opening; Level 2 is eye opening in response to a verbal stimulus or pain, and level 3 is no eye opening. In the emergency department, a basic evaluation scale like the JCS would be helpful and practical.

Goals of This Investigation

Although the JCS is used by paramedics in prehospital trauma care in Far Eastern countries (3), the diagnostic capacity of the JCS to assess and classify trauma patients in emergency departments is less recognized. In this study, our aim is to identify the sensitivity and specificity of JCS compared to GCS results.

Materials and Methods

Study Design and Setting

The current research design is a case-control field study that was conducted in a cross-sectional manner in the emergency department. Included data were obtained from the emergency department of Tabriz Imam Reza Hospital between September and December 2020. This department is a trauma center in northwestern Iran, East Azerbaijan province, and provides care to 11,000 patients per year. Using various approaches, this department increases the quality of trauma care and speed up the diagnosis and sorting of patients. Replacing the GCS with a simpler and easier method of assessing the level of consciousness of trauma patients is one of the most appropriate ways to improve the pace of surgery in trauma care. The study compared GCS and JCS outcomes and analyze the results to determine how sensitive and specific JCS is compared to GCS.

The Selection of Participation

Trauma patients who were transferred from the scene of the accident to the emergency department from September to December 2020 were considered eligible for inclusion.

We excluded patients who were paralyzed, deaf, had ocular trauma, or had a history of ocular disease. Also, all the patients who were transported from the scene of the accident in any way other than direct transportation by ambulance along with other rescuers.

Measurement

Data were collected with a checklist and in-hospital charts and pre-hospital records that are routinely sent to hospitals by paramedics. They included patient demographic information (age, sex), mechanism of injury, vital signs, consciousness scale ratings based on JCS and the GCS scores on arrival and in-hospital mortality were collected by check list. Patients were classified by age into the following groups: <20, 20-39, 40-59, 60-79 and ≥80 years. They were also divided into groups based on vital signs: JCS, level 1, 2, and 3 digits and GCS 3-15. Thus, patient's recovery process and the length of the hospital stay were followed.

We conducted a sensitivity analysis to solve the missing data about JCS and in-hospital mortality due to the possibility of missing patients, such as those who were in good condition, had outpatient visits, or died while being transferred to the hospital or upon arrival.

The status of "fully awake and alert" was not included in the JCS when it was first published in 1974. Strictly speaking, JCS level 1 showed spontaneous eye opening but was not fully awake and alert. However, in recent decades, fully awake and conscious patients have been labeled and classified as "stages 0". As a result, the JCS "0" in the Japan Trauma Data Bank was paired with JCS level 1 patients in our study.

Outcome

The study's primary outcome was to predict the outcome of trauma patients in the emergency department using GCS and JCS criteria at the outset, which would be useful in how patients are treated, triaged, sorted, and finally discharged, hospitalized, or died, resulting in an emergency and the secondary outcome was use of JCS to prioritize patients and its positive impact on improving the pace of triage and patient care, as well as its use instead of GCS.

Primary Data Analysis

Upon entering the hospital, we identify patients' characteristics and their GCS and JCS scores. We used JCS level as an explanatory variable and each outcome as an objective variable to see if there was a link between GCS and JCS levels and primary and secondary outcomes. We used logistic regression analysis to produce crude ORs with 95% confidence intervals for the JCS stages. We used a multivariate logistic regression analysis to measure the modified ORs of JCS levels with 95% confidence CIs for possible confounders such as age, sex, and type of injury. The JCS c-statistics for the primary and secondary outcomes were determined to assess JCS discriminatory results.

Statistical Analysis

The needed statistical population in this study was estimated at 278 based on the available records and Morgan table, which included the input of about 1000 multitrauma patients. Excell software (Microsoft®, IBM) was used to randomize patients, and those whose last digit of their case number matched the numbers

produced by the software were included in the analysis. All statistical results were calculated as point estimates with 95% Cis. All statistical analyses were performed using Statistical Package for the Social Sciences® release 20.0.0 (IBM®, Chicago Ltd).

Results

Characteristics of Study Subjects

This study included 268 trauma patients who met the inclusion criteria, including 86 women and 182 men who did not follow the normal distribution according to the Kolmogorov-Simirnov statistical method. Table 1 summarizes the characteristics of the study population. The median age of the patients was 35.47±17.89 years (CI 95%: 33.32±37.63), ranging from 21 to 45 years in the 25% to 75% range. The majority of traumas were caused by car-to-car accidents. The level of consciousness in most patients was 15 on GCS and 1 on JCS. For the distribution between JCS and GCS on arrival at the hospital, almost all JCS level 1 patients had a GCS of 14-15, JCS level 2 patients had a GCS of 10-13 and most JCS level 3 patients had a GCS ≤9 (Table 2). Two patients died from the 268 cases studied, and 229 patients were discharged; therefore, the overall in-hospital mortality was 0.74% (n=2).

Main Results

According to the study, there is a significant relationship between GCS and patient outcome, which is strong and direct (Pv<0.001; correlation coefficient=0.780). also, the JCS of patients has a significant relationship with patient outcome, but it is a strong and inverse relationship direct (Pv<0.001; correlation coefficient=-0.780). The relationship between the level of consciousness based on the JCS and patient outcome has a diagram level of 0.983 in the ROC figure (Figure 1).

According to the data analysis, the relationship between GCS and JCS of patients is significant, strong, and inverse (Pv<0.001; Correlation Coefficient=-0.999). In the JCS, the sensitivity of the test was 64.10%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 94.24%. Thus, in the GCS, test sensitivity is 82.05%, specificity is 100%, positive predictive value is 100%, and negative predictive value is 97.03% (Table 3).

Table 1. General emergency characteristics

Characteristic	No. (%)
Gender no. (%)	
Women	86 (32.08)
Men	182 (67.91)
Age y, no. (%)	
<20	61 (22.76)
20-39	113 (42.16)
40-59	70 (26.11)
60-79	19 (7.08)
≥80	5 (1.86)
The mechanism of trauma no. (%)	
Car crash with car	103 (38.43)
Car crash with motorcycle	34 (12.68)
Car crash with bike	9 (3.35)
Car to pedestrian accident	12 (4.47)
Car overturning	14 (5.22)
Bike/motorcycle overturn	17 (6.34)
Fall down	39 (14.55)
Falling from a height	40 (14.92)

Discussion

To the best of our knowledge, this is the first study to compare the outcomes of GCS and JCS in the Department of Emergency Medicine with the aim of replacing JCS with GCS. There are also a variety of standards for gathering prehospital data, clinical data during hospitalization, and trauma diagnoses, such as the abbreviated injury scale and injury severity score (ISS), among others (11). JCS is primarily concerned with eye responses. As a single test, JCS has two distinct advantages as a coma scale: flexibility and applicability, both of which should reduce interpreter errors. Communication between physicians, nurses, and paramedics must be simple, particularly in emergencies. The predictability of early outcome in trauma patients is a benefit of this study. The incredible simplicity of this criterion is one of the most significant features of JCS compared to GCS.

Table 2. Distribution between JCS and GCS

Parameters	Score	No. (%)
GCS	14-15	247 (92.16)
	13-10	15 (5.59)
	≤9	6 (2.23)
JCS	Level 1	249 (92.91)
	Level 2	15 (5.59)
	Level 3	4 (1.49)

GCS: Glasgow Coma Scale, JCS: Japan Coma Scale

Table 3. comparison between JCS and GCS

Scale	JCS	GCS (gks)
Sensitivity	64.10%	82.05%
Specificity	100%	100%
Positive predictive value	100%	100%
Negative predictive value	94.24%	97.03%

GCS: Glasgow Coma Scale, JCS: Japan Coma Scale

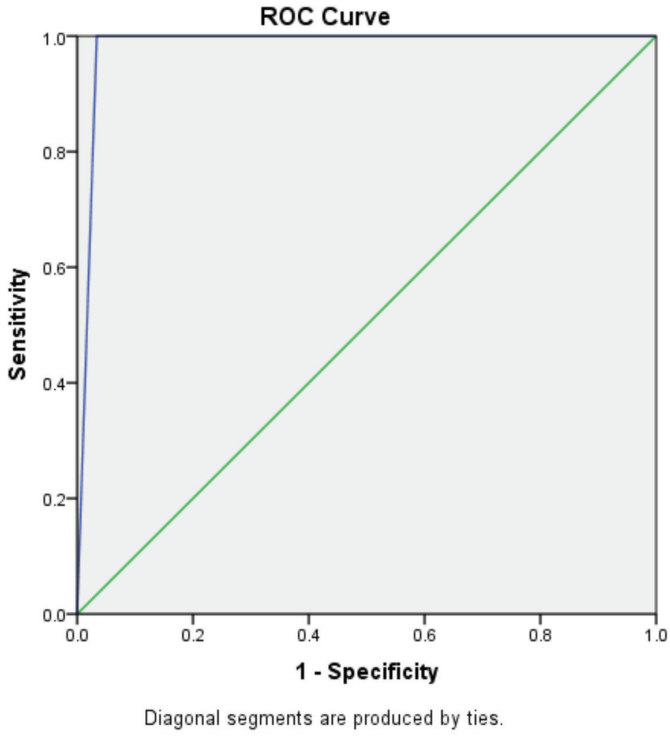

Figure 1. Relationship between JCS and patient outcome
JCS: Japan Coma Scale

The JCS is a four-point scale (ranging from 0 to 3) with only one test: eye responses. For instance, GCS is a 13-point scale (ranging from 3 to 15) that includes three tests: eye, verbal, and motor responses. JCS is similar to GCS's eye response test, but it is much easier to use. The only thing that raters need to do is check the eye responses in terms of three distinct categories: open, open only after stimuli, and closed. There is no need for specialized expertise, such as that required to determine the decerebrate or decorticate response. Moreover, the minimum time spent triaging patients, which is achieved using the JCS criterion, is another critical factor determining the outcome of trauma patients in emergencies. according to the protocol of Japanese guidelines for pre-hospital evaluation and treatment, paramedics can triage trauma patients at the scene of an accident within the first 15 seconds to evaluate the JCS level while also performing initial evaluations of the airway, respiration, and circulation (12). Although JCS has its benefits, it also has limitations. JCS, for example, does not perform well enough to determine the patient's consciousness in situations such as serious burns, ocular injuries, and facial muscle paralysis due to multiple factors such as a history of stroke and deafness.

Study Limitations

The sample size was less than the calculated amount due to the study's timing with the Coronavirus disease-2019 pandemic, which restricted hospital and research facilities, and the study was performed as a single center. Although our aim was to triage and prioritize patients, we did not evaluate the outcome or severity of patient trauma using the ISS criteria. Emergency medicine specialists and assistants measured the patients' consciousness, with the majority of them find it simple to quantify GCS. To achieve more generalizable results, it is best to use general practitioners with less experience in the study.

Conclusion

Considering the data of this study, as well as the substantial similarities in patient outcomes between GCS and JCS, and the ease and reliability with which JCS can be used in emergency situations, considering that GCS is designed for trauma patients with brain damage, but the questions related to JCS are consistent with cerebrovascular accidents, it seems appropriate to place JCS instead of GCS (gks) in trauma patients. Thus, it can be concluded that using JCS instead of GCS has a significant impact on improving the process of caring for trauma patients in the emergency department, and it can be recognized as a standard coma scale.

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Ethics

Ethics Committee Approval: The study was approved by the Islamic Azad University-Tabriz Branch of Research Ethics Committees (approval ID: IR.IAU.TABRIZ.REC.1400.041, date: 26.06.2021).

Informed Consent: Consent form was filled out by all participants.

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Authorship Contributions

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