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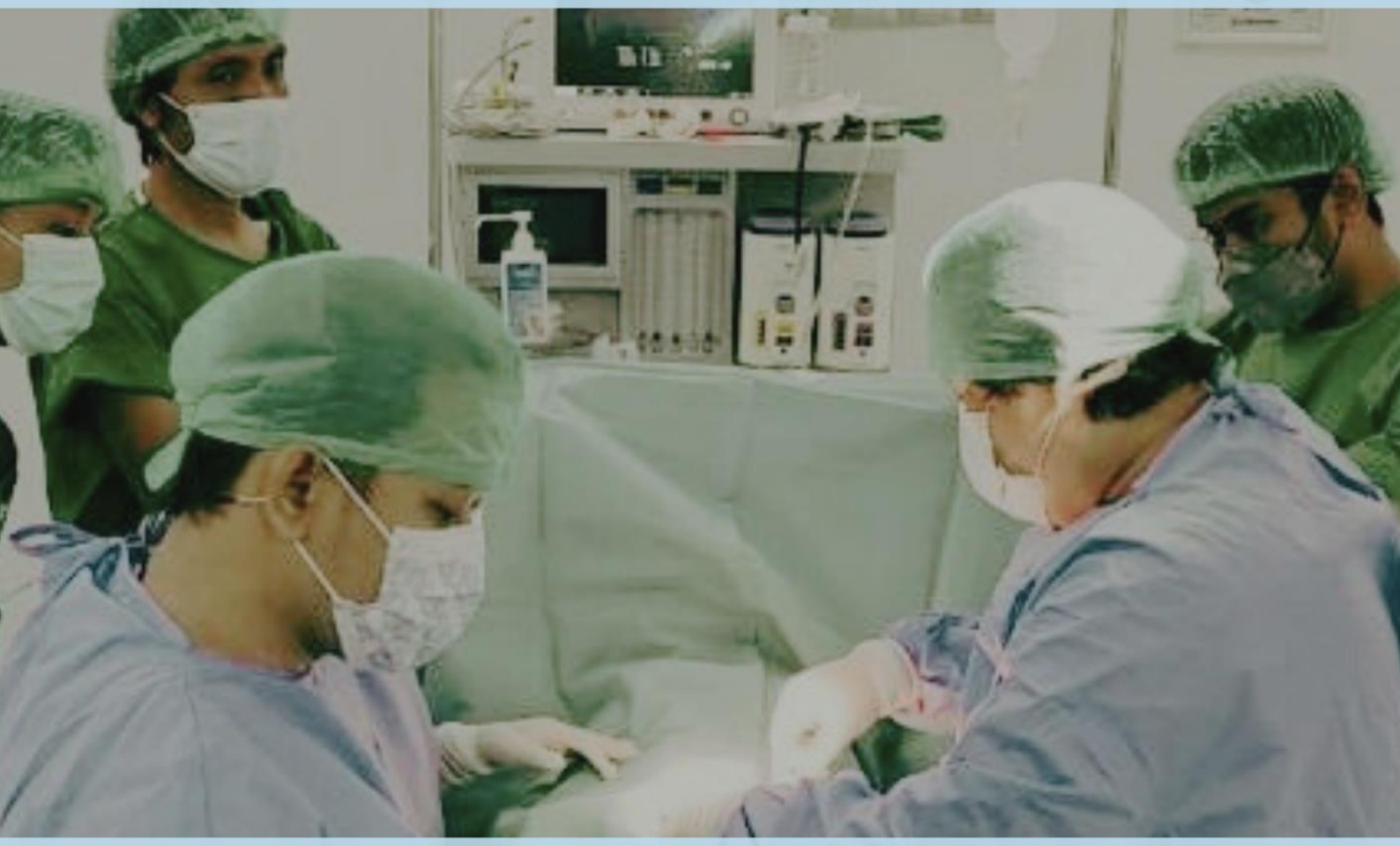

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INDONESIAN JOURNAL OF ANESTHESIOLOGY AND REANIMATION
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Original Article

# DEVELOPING AN EFFECTIVE TEAM-BASED EMERGENCY TRAINING PROGRAM FOR MEDICAL STUDENTS

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**ABSTRACT**

**Introduction:** Team-based patient management in critical care demands a knowledgeable, skillful, and responsive doctor who collaborates well on teams. Medical education is responsible for producing competent graduates who meet the above requirements. However, the current medical curriculum in Indonesia tends to focus only on individual knowledge and appraisal. There was no standardized university-based group emergency training and examination with comprehensive emergency topics beyond cardiac and trauma cases. **Objective:** This study aimed to develop and evaluate a team-based emergency training program that enhances medical students' preparedness and teamwork skills in dealing with future emergencies in the workplace. **Materials and Methods:** We developed Acute Life Threatening Events Management (ALTEM), a three-day emergency training program consisting of pre-test, lectures, guided skill practice, group (case-based) simulation exam, and post-test. Group simulation occurred in a virtual hospital with high-fidelity mannequins, actual medical equipment (i.e., beds, monitors, drugs, tools, pads), two-way mirror rooms, and simulated patient family to resemble real hospital situations. The program was then evaluated by a modified Kirkpatrick evaluation model, which measures individual perception, satisfaction, understanding, and performance related to the program. **Results:** A total of 114 participants were involved in this study. Most subjects (>80%) had a good experience with the program. ALTEM training program significantly increased communication and teamwork ($p < 0.001$) and decision-making towards critical patients ($p < 0.001$) in the univariate analysis. Communication and teamwork remained related considerably in the multivariate analysis (aOR 7.866; $p = 0.005$). **Conclusion:** The ALTEM simulation program obtained a good response from the subjects and was a prospective program to improve medical students' competence and teamwork skills in emergencies.

**Keywords:** ALTEM; Critical Care Training; Education Policy; Emergency Medical Training; Health Emergency Preparedness; Health System; Medical Education

**ABSTRAK**

**Pendahuluan:** Manajemen pasien kritis berbasis tim membutuhkan dokter yang berpengetahuan luas, terampil, dan responsif serta dapat bekerja baik dalam tim. Pendidikan kedokteran bertanggung jawab dalam menghasilkan lulusan kompeten yang memenuhi standar tersebut. Akan tetapi, kurikulum pendidikan kedokteran saat ini cenderung hanya berfokus pada pengetahuan dan penilaian secara individu. Belum ada pelatihan dan ujian kegawatdaruratan terstandar dari universitas yang berisi topik kegawatdaruratan secara komprehensif, lebih dari kasus jantung dan trauma. **Tujuan:** Penelitian ini bertujuan mengembangkan dan mengevaluasi program pelatihan kegawatdaruratan berbasis tim yang meningkatkan kesiapan dan keterampilan kerjasama tim mahasiswa kedokteran dalam menangani kasus kegawatdaruratan di tempat kerja yang akan datang. **Bahan dan Metode:** Kami mengembangkan *Acute Life Threatening Events Management* (ALTEM), program pelatihan kegawatdaruratan berdurasi tiga hari yang berisi *pre-test*, kuliah, latihan keterampilan terbimbing, ujian simulasi kelompok (berbasis kasus), dan *post-test*. Simulasi kelompok dilaksanakan di rumah sakit virtual dengan manekin berteknologi tinggi, peralatan medis (tempat tidur, monitor, obat, peralatan), ruangan dengan cermin dua arah, dan keluarga pasien simulasi agar menyerupai situasi nyata di rumah sakit. Program tersebut kemudian dievaluasi dengan modifikasi model evaluasi Kirkpatrick, yang mengukur persepsi, kepuasan, pemahaman, dan performa subjek terhadap program. **Hasil:** Sebanyak total 114 subjek berpartisipasi dalam penelitian ini. Sebagian besar subjek (>80%) memiliki pengalaman yang baik terhadap program. Program ALTEM secara signifikan meningkatkan keterampilan komunikasi dan kerjasama tim ($p<0,001$) serta kemampuan pengambilan keputusan ($p<0,001$) dalam analisis univariat. Keterampilan komunikasi dan kerjasama tim tetap memiliki hubungan signifikan dalam analisis multivariat (aOR 7,866; p



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= 0,005). **Kesimpulan:** ALTEM memperoleh respon yang baik dari subjek dan merupakan program dengan prospek baik yang dapat menunjuang kompetensi lulusan kedokteran di bidang kegawatdaruratan.

**Kata kunci:** ALTEM; Pelatihan Manajemen Pasien Kritis; Kebijakan Pendidikan; Pelatihan Kegawatdaruaratan Medis; Sistem Kesehatan; Pendidikan Kedokteran

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## INTRODUCTION

Critical care is a complex management requiring multidisciplinary collaboration, various life-saving procedures, and rapid team response. Emergency care should be done cautiously and swiftly because any delay or incorrect action could compromise patient safety. Hard skills (i.e., knowledge, practical skills) and soft skills (i.e., leadership, communication, teamwork, and decision-making) are essential to good patient care (1–3).

Patient safety is a crucial indicator of healthcare quality and is the responsibility of all stakeholders, including medical education. Medical education is vital in introducing and cultivating hard and soft skills as early as possible. Medical faculties are also responsible for producing competent doctors and the capacity to work in teams because teams manage patients in hospitals. However, medical education, including in our university, tends only to appraise knowledge and individual performance. Furthermore, medical students are not specifically trained to be leaders or collaborators, whereas doctors are leaders and collaborators in patient care. These phenomena could lead to medical students' unpreparedness in real emergencies (1–3).

Simulation is one of the strategies in medical education to increase patient safety. The simulation-based education system is proven to be better than the conventional education system, especially education for critically ill patients due to advanced medical conditions and requires rapid resuscitative effort (1–3). There were several training courses, such as Advanced Cardiac Life Support (ACLS) and Advanced Trauma Life Support (ATLS). However, in Indonesia, those programs were completed by individuals separately after they finished the government medical internship program, which was a year after graduating from the university, making medical faculties unable to assess the group performance of the medical students, including their responsiveness in emergencies.

In emergency medical care, the importance of a standardized protocol and comprehensive training cannot be overstated (4,5). WHO Global Health Estimates for 2019 stated that stroke was the leading cause of mortality, followed closely by ischemic heart disease, tuberculosis, neonatal conditions, diabetes mellitus, cirrhosis of the liver, diarrheal disease, Chronic Obstructive Pulmonary Disease (COPD), lower respiratory infections, and HIV/AIDS (6). Remarkably, the existing training programs, such as Advanced Trauma Life Support (ATLS) and Advanced Cardiac Life Support (ACLS), inadequately address this spectrum of life-threatening conditions because they focus on cardiac and trauma management, respectively. The need for a comprehensive, all-encompassing emergency standardized protocol and training becomes evident, aiming to bridge the gap in addressing critical conditions associated with those top leading causes of mortality.

Recognizing the imperative to address the deficiencies in existing emergency training, we



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have developed a new initiative, the Acute Life Threatening Events Management, at our institution, Universitas Gadjah Mada. This pilot training and study have been meticulously designed to fill the void in management protocols for critical or life-threatening conditions associated with the leading causes of mortality identified in Indonesia and other diverse medical emergencies.

This program is a practical response to our institution's urgent healthcare needs and is a blueprint for a nationwide solution. Understanding that these critical conditions transcend regional boundaries, we aspire to catalyze a broader impact by envisioning the integration of this training and study at a national level. The ultimate goal is to empower healthcare providers across the country with the knowledge and skills necessary to effectively manage acute life-threatening events associated with the prevalent causes of mortality. By fostering a culture of preparedness and responsiveness, we hope to contribute significantly to reducing the alarming mortality rates attributed to these conditions nationwide. The Acute Life Threatening Events Management initiative at Universitas Gadjah Mada signifies a localized effort and a visionary step towards enhancing emergency medical care across Indonesia.

## MATERIAL AND METHOD

### Program Development

Acute Life Threatening Events Management (ALTEM) is a simulation-based training program designed by the Department of Anesthesiology and Intensive Therapy, Gadjah Mada University / Dr. Sardjito General Hospital, Indonesia. This 3-day course (total: 30 hours) was incorporated into the medical curriculum, and the participants were trained directly by anesthesiologists from Dr. Sardjito General Hospital. The program was done periodically 4-5 times a year. Each class consisted of 30-50 participants.

A few days before the program, each participant was handed a t-shirt and manual book comprising more comprehensive topics, ranging from cardiorespiratory emergency management to emergency in neurology and internal medicine, such as acute liver failure and seizures. The manual book was written by the Department of Anesthesiology and Intensive Therapy of Gadjah Mada University.

ALTEM combines theory, practice, and exams, consisting of a pre-test, lectures, guided skill practice, group (case-based) simulation, and post-test (7).

***1. Individual pre-test***

The individual pre-test consisted of 20 multiple-choice choices about emergency management. This study did not collect the pre-test results of the participants.

***2. Refreshment lectures***

The anesthesiologists and lecturers of Dr. Sardjito General Hospital / Faculty of Medicine, Gadjah Mada University, presented lectures. Fifteen topics were presented in 3 days. The topics were (7):

a. Emergency Airway-Breathing Management
b. Management of Patients with Respiratory Distress
c. Early Detection and Principle of Management of Critical Patients
d. Rapid Sequence Intubation and Intubation Technique in Critical Patients
e. Oxygen Therapy and Ventilation
f. Critical Patient Monitoring
g. Management of Patients with Circulatory Problems and Vasoactive Drugs Usage
h. Management of Patients with Cardiac Arrest
i. Management of Patients with Arrhythmia



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j. Management of Seizure and Decrease of Consciousness
k. Pain and Sedation Management in Critical Patients
l. Critical Patient Management System in the Hospital
m. Hemorrhagic Shock
n. Blood Gas Analysis in Critical Patients
o. Distributive Shock (Sepsis and Anaphylactic Shock)

Each session lasted 40 minutes, with a 30-minute coffee break to maintain the participants' focus. Five topics were given on the first day, six topics on the second day, and the rest on the last day (7).

***3. Guided-skill group practice***

The event divided participants into six small groups. There were three skill stations, and one room comprised two small groups. Each room has medical equipment and one instructor. The instructors are Dr. Sardjito General Hospital anesthesiologists and lecturers at the Faculty of Medicine, Gadjah Mada University. Every group did a role-play to perform team-based critical care management. The group roles were leader, airway and breathing manager, circulator, and drugs and documentation handler. After finishing one station, each group will rotate to the next room and perform different cases. The cases were (7):

a. Management of Patients with Respiratory Distress
b. Oxygen Therapy and Ventilation
c. Management of Patients with Circulatory Problems and Vasoactive Drugs Usage
d. Management of Patients with Cardiac Arrest and Arrhythmia
e. Management of Seizure and Decreased Consciousness.

***4. Group (case-based) simulation exam and debriefing***

Each group took turns conducting the group exam. The anesthesiologist rated each group's performance. The case information was given step by step, depending on the participant's actions. The emergency simulation setting can be in the intensive care unit or the ward. Patient management is correct if the patient (the mannequin) is eventually stated to be alive and is judged incorrect if the patient dies.

The mannequin used in the simulation is a high-technology computerized full-body mannequin with heart rate, lung sounds, chest movement, flexible mouth and neck, and a hollow mouth-to-trachea that enabled intubation. The room consisted of a hospital bed, oxygen tube, vital sign monitor, and emergency trolley consisting of an intubation and bagging set, oxygenation cannula/mask, defibrillator machine, and emergency drugs. Furthermore, an anesthesiology resident role-played the patient's family. The simulation room was also equipped with a camera from numerous points of view so the other groups could watch and evaluate the group's performance in real-time. The instructor performed a debriefing session afterward. Debriefing is done by reviewing each group's performance by asking questions, initiating discussion, and giving feedback to all groups. All participants were also welcome to provide questions, comments, or suggestions to other groups. Furthermore, there was an announcement of the best group and the best group leader.

***5. Individual post-test***

Similar to the pre-test, the post-test consisted of 20 multiple-choice questions about emergency management. The questions were identical to the pre-test, but each ALTEM period had slightly different questions to minimize fraud.



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## Program Evaluation

### *Study design and participants*

The study utilized a cross-sectional design. The participants were medical students in their final year at the Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University, Indonesia. The exclusion criteria were students with previous participation in ALTEM, failure to complete the training, or incomplete questionnaire filling. Of the 200 participants, 114 were eligible for the study.

### *Modified Kirkpatrick model*

The program has been running since 2017, yet its effectiveness has not been objectively measured. The Kirkpatrick model was a widely recognized mode of evaluation. This model had a simple approach, only a few variables, simple evaluation criteria, and was independent of individual or environmental variables. The original Kirkpatrick consisted of 4-level measurements (8–11). Our study used a modified Kirkpatrick model with 3-level measurements.

### *Data collection and evaluation*

We distributed an online questionnaire in *Google Forms* using a modified Kirkpatrick evaluation model. The questionnaire consisted of 3 levels: level 1 (reaction), level 2 (learning), and level 3 (behavior). Level 1 measures individual perception and satisfaction regarding the program. Level 2 measures individual learning, which involves transferring knowledge and managerial skills. Level 3 assesses performance by assessing the improvement in the workplace due to previous ALTEM training. Subjects rated the extent to which they agreed with the statement on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). The answers from the questionnaires were then recapitulated and analyzed.

### *Statistical analysis*

We analyzed the data using SPSS v.26 for Windows. Before the questionnaire distribution, we examined the questionnaire's validity and reliability and concluded that the questionnaire was reliable and valid. Afterward, we conducted cross-tabulated frequencies of the variables and univariate tests for association with the chi-square statistic. We carried out correlation and multivariate ordinal regression tests where indicated. The P-value of $<0.05$ was considered significant.

### *Ethical approval*

The Institutional Review Board (IRB) granted approval on 18 May 2022 from the local IRB at the Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University (KE/FK/0589/EC/2022). Written informed consent was obtained from the research participants.

## RESULT AND DISCUSSION

A total of 114 subjects participated in the study, with 61.4% of them being women. The mean age was 23.92 ± 1.18, and most subjects did a great job in the post-test (mean score 93.90 ± 10.32). The first-level questionnaire revealed that most subjects liked and enjoyed the training (89.5%), thought the training was relevant (97.4%), considered the training applicable (86.3%), had a positive experience (98.2%), was satisfied with the instructor (84.2%), and was pleased with the skill station session (86.9%). However, certain subjects were not content with the lecturers (0.9%), training materials (7.0%), and overall training design (1.8%) (Table 1).

On level 2, we conducted a post-test to explore the subject's understanding of the emergency topics. Participants who thought this program trained protocol implementation and management algorithm of critically ill



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patients got a higher score (p = 0.002) (Table 2). On level 3, ALTEM training increased communication and teamwork skills (p <0.001) and decision-making towards critical patients (p <0.001) in the univariate analysis (Table 3). Communication and teamwork remained significantly related in the multivariate analysis (OR 7.866; p = 0005) (Table 4).

**Table 1.** Subject Perception Regarding ALTEM (level 1 Kirkpatrick questionnaire)

| Response (n = 114) | n (%) |
|---|---|
| Enjoyment of the training | |
| Neutral | 12 (10.5%) |
| Agree | 61 (53.5%) |
| Strongly agree | 41 (36.0%) |
| The training was relevant to the healthcare provider | |
| Neutral | 3 (2.6%) |
| Agree | 32 (28.1%) |
| Strongly agree | 79 (69.3%) |
| The training was easy to comprehend. # | |
| Disagree | 4 (20.2%) |
| Neutral | 23 (20.2%) |
| Agree | 62 (54.4%) |
| Strongly agree | 25 (21.9%) |
| The lessons were practical and applicable. | |
| Neutral | 7 (1.8%) |
| Agree | 39 (34.2%) |
| Strongly agree | 68 (59.6%) |
| The participant had a good experience with the program | |
| Neutral | 2 (1.8%) |
| Agree | 44 (38.6%) |
| Strongly agree | 68 (59.6%) |
| The participant was satisfied with the lecturer | |
| Strongly disagree | 1 (0.9%) |
| Neutral | 26 (22.8%) |
| Agree | 60 (52.6%) |
| Strongly agree | 27 (53.7%) |
| The participant was satisfied with the instructor | |
| Neutral | 18 (15.8%) |
| Agree | 56 (49.1%) |
| Strongly agree | 40 (35.1%) |
| The participant was satisfied with the training material | |
| Disagree | 8 (7.0%) |
| Neutral | 29 (25.4%) |
| Agree | 54 (47.4%) |
| Strongly agree | 23 (20.2%) |
| The participant was satisfied with the skill station session | |
| Neutral | 15 (13.2%) |
| Agree | 59 (51.8%) |
| Strongly agree | 40 (35.1%) |
| The participant was satisfied with the overall training design | |
| Disagree | 2 (1.8%) |
| Neutral | 22 (19.3%) |
| Agree | 62 (54.4%) |
| Strongly agree | 28 (24.6%) |

*n = the number of subjects. # = items containing the answers 'disagree' or 'strongly disagree.' There are five scales: strongly disagree, disagree, neutral, agree, and strongly agree. The scales with zero results (not chosen by the subjects) are omitted.

The study aimed to evaluate the effectiveness of the ALTEM training program in increasing the knowledge and skills of medical students of the Faculty of Medicine, Gadjah Mada University. Evaluation is needed to know the upsides and downsides of the program, which aids in improvement in the future. The modified Kirkpatrick model



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evaluated the ALTEM program in the form of a 3-level questionnaire.

**Table 2.** ALTEM Learning Assessment (level 2 Kirkpatrick questionnaire)

| Learning (n = 114) | Poor score | Fair score | Excellent score | p-value[a] |
|---|---|---|---|---|
| The program taught about leadership skills. | | | | |
| Neutral (n = 4) | 0 | 0 | 4 | 0.882 |
| Agree (n = 47) | 0 | 3 | 45 | |
| Strongly agree (n = 62) | 1 | 3 | 58 | |
| The program taught about communication and teamwork | | | | |
| Disagree (n = 1) | 0 | 0 | 1 | 0.301 |
| Neural (n = 3) | 0 | 1 | 2 | |
| Agree (n = 44) | 1 | 1 | 42 | |
| Strongly agree (n = 66) | 0 | 0 | 66 | |
| The program taught knowledge regarding emergencies. | | | | |
| Neutral (n = 2) | 0 | 0 | 2 | 0.270 |
| Agree (n = 33) | 1 | 0 | 32 | |
| Strongly agree (n = 80) | 0 | 6 | 74 | |
| The program taught about rare emergency cases. | | | | |
| Neutral (n = 6) | 0 | 1 | 5 | 0.559 |
| Agree (n = 50) | 1 | 2 | 47 | |
| Strongly agree (n = 58) | 0 | 3 | 55 | |
| The program taught about decision-making. | | | | |
| Neutral (n = 5) | 0 | 1 | 4 | 0.145 |
| Agree (n = 43) | 1 | 0 | 42 | |
| Strongly agree (n = 66) | 0 | 5 | 61 | |
| The program taught about confidence in managing critically ill patients. | | | | |
| Neutral (n = 14) | 0 | 1 | 13 | 0.546 |
| Agree (n = 49) | 1 | 1 | 47 | |
| Strongly agree (n = 51) | 0 | 4 | 47 | |
| The program facilitated the competence of the health workers in the critical areas of the hospital. | | | | |
| Neutral (n = 3) | 0 | 0 | 3 | 0.539 |
| Agree (n = 43) | 1 | 1 | 41 | |
| Strongly agree (n = 68) | 0 | 5 | 63 | |
| The program emphasized the implementation of management algorithms for critically ill patients. | | | | |
| Disagree (n = 1) | 0 | 1 | 0 | **0.002*** |
| Neutral (n = 6) | 0 | 0 | 6 | |
| Agree (n = 38) | 1 | 1 | 37 | |
| Strongly agree (n = 68) | 0 | 4 | 64 | |
| The program was efficient with comparable efficacy to other similar events | | | | |
| Neutral (n = 9) | 0 | 0 | 9 | 0.788 |
| Agree (n = 53) | 1 | 3 | 49 | |
| Strongly agree (n = 53) | 0 | 3 | 49 | |
| The program gave the participants the experience as expected | 0 | 0 | 1 | |
| Disagree (n = 1) | 0 | 1 | 5 | 0.810 |
| Neutral (n = 6) | 1 | 2 | 51 | |
| Agree (n = 54) | 0 | 3 | 50 | |
| Strongly agree (n = 53) | | | | |

[a]*Chi-square* test; *p <0.05: Significant

Level 1 revealed that ALTEM gained an overall positive response from the subjects. However, a few participants wanted more from the lecturers (0.9%), training materials (7.0%), and comprehensive training design (1.8%). Based on consumer satisfaction theory,



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satisfaction is an integration of two components. The first component is the individual emotional experience, which refers to interest, pride, and achievement regarding the service provided. It is closely related to the individual's enthusiasm and mental health condition. The second component, i.e., expectation confirmation theory, defines satisfaction as the conformity between expectation towards service and the perceived service experience. In medical education, factors affecting student satisfaction were the students' emotional experience towards the institution or program, learning experience, educational (knowledge and skill) accomplishment, and expectation fulfillment (12–15).

**Table 3.** ALTEM performance (Level 3 Kirkpatrick questionnaire)

| Perceived performance | Strongly disagree | Disagree | Neutral | Agree | Strongly agree | P-value[a] |
|---|---|---|---|---|---|---|
| The program taught about leadership skills. | | | | | | |
| Neutral (n = 2) | 0 | 0 | 1 | 1 | 0 | 0.322 |
| Agree (n = 25) | 0 | 0 | 4 | 20 | 2 | |
| Disagree (n = 29) | 0 | 0 | 5 | 16 | 8 | |
| The program taught about communication and teamwork | | | | | | |
| Disagree (n = 1) | 0 | 0 | 0 | 0 | 1 | **<0.001*** |
| Neutral (n = 1) | 0 | 1 | 0 | 0 | 0 | |
| Agree (n = 27) | 0 | 0 | 5 | 20 | 2 | |
| Strongly agree (n = 30) | 0 | 1 | 3 | 11 | 15 | |
| The program taught about rare emergency cases | | | | | | |
| Neutral (n = 3) | 0 | 0 | 0 | 1 | 2 | 0.485 |
| Agree (n = 27) | 0 | 0 | 2 | 9 | 16 | |
| Strongly agree (n = 29) | 0 | 0 | 1 | 16 | 11 | |
| The program taught about decision-making. | | | | | | |
| Neutral (n = 2) | 0 | 1 | 0 | 0 | 1 | **<0.001*** |
| Agree (n = 24) | 0 | 0 | 1 | 11 | 12 | |
| Strongly agree (n = 33) | 0 | 0 | 2 | 13 | 18 | |
| The program taught about confidence in managing critically ill patients | | | | | | |
| Neutral (n = 9) | 0 | 0 | 0 | 2 | 7 | 0.895 |
| Agree (n = 29) | 0 | 0 | 2 | 9 | 18 | |
| Strongly agree (n = 21) | 0 | 0 | 1 | 6 | 14 | |
| The program trained competence of the health workers in the critical areas of the hospital | | | | | | |
| Neutral (n = 2) | 0 | 0 | 0 | 1 | 1 | 0.992 |
| Agree (n = 24) | 0 | 0 | 1 | 11 | 12 | |
| Strongly agree (n = 33) | 0 | 0 | 2 | 14 | 17 | |
| The program emphasized the implementation of management algorithms for critically ill patients | | | | | | |
| Neutral (n = 4) | 0 | 0 | 0 | 3 | 1 | 0.635 |
| Agree (n = 23) | 0 | 0 | 1 | 8 | 14 | |
| Strongly agree (n = 32) | 0 | 0 | 2 | 12 | 18 | |
| The program is efficient with comparable efficacy to other similar programs | | | | | | |
| Neutral (n = 7) | 0 | 0 | 0 | 4 | 3 | 0.558 |
| Agree (n = 30) | 0 | 0 | 5 | 10 | 15 | |
| Strongly agree (n = 21) | 0 | 0 | 2 | 12 | 7 | |

[a]*Chi-square* test; *p <0.05: Significant



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**Table 4.** ALTEM effectiveness

| Increased performance | aOR | p-value | 95% CI |
|---|---|---|---|
| ALTEM training and increased communication and teamwork | 7.866 | **0.005*** | -2.899 s/d -0.514 |
| ALTEM training and increased decision-making skills | 0.166 | 0.684 | -1.264 s/d 0.829 |

*p <0.05: significant; CI = confidence interval; aOR = adjusted odds ratio
We analyzed the data using an ordinal regression test

In this study, 1 of 114 subjects (0.9%) reported dissatisfaction with the lecturers, and 8 of 114 participants (7.0%) reported dissatisfaction with the training material. We hypothesized that the reason for the blow was an incorrect perception regarding the ALTEM training program. ALTEM training program aimed to enhance the management skills of medical students. The participants were assumed to have a fair understanding of emergency management and have done independent study, so the lectures were brief and only contained knowledge that directly correlate or is helpful for clinical practice. Furthermore, a comprehensive discussion could be found in the ALTEM module, handed out a few days before the course. The questionnaire also did not ask about the identity of the lecturer(s) with whom the subjects feel dissatisfied, so we could not conclude whether the dissatisfaction came from one specific lecturer or overall lecturer performance. Moreover, the proportion of discontent towards the lecturers was extremely little (1/114; 0.9%), so it did not depict the perception of all participants.

A few subjects needed help understanding the materials (20.2%). According to Spencer (2003) and Ghasemi et al. (2018), the factors affecting material comprehension were the student and the teacher. The student factor includes the degree of motivation, interest in the materials, and concentration. The teacher has communication skills, especially asking questions, explaining, active listening, and sensitivity to students' verbal and nonverbal cues. The study by the Faculty of Medicine, National Autonomous University of Mexico in 2020 reported another factor affecting the student perception regarding the lecturer: the lecturer's knowledge about the materials, the treatment towards the students, the willingness of the lecturer to share their personal experience to the student, and the time spent together with the pupils (p = 0.001) (15–17).

Linton et al. (2014) found that writing could enhance students' comprehension of complex concepts (18). Writing about an idea entails the student conducting systematic thinking, which helps to connect the dots. The report could also help the students self-evaluate and increase metacognition because they could know their ability or inability to elaborate on a concept. Daou et al. (2020) compared students having peer discussions, lectures, and a combination of both. They found that the combination of peer discussion and lectures boosted understanding because the combination enforced the use of a simplified approach to elaborate complex concepts (19). Therefore, future ALTEM lectures could integrate interactive questions, writing, peer group discussion, and the lecturers' experience managing critical patients in the emergency units as additional teaching methods to enhance understanding.

Level 2 questionnaire revealed that participants who thought this program trained protocol implementation and management algorithm of critically ill patients got a higher score (p = 0.002) (Table 2). The result aligns with our program's aim to implement a critical



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patient management algorithm. Hailikari et al. (2008) reported that prior knowledge, especially procedural knowledge, significantly determined the student score ($p < 0.05$). As a result, future ALTEM studies would incorporate pre-test scores. Moreover, ALTEM pre-test and post-test quizzes would be multiple choices, consisting of medical theory and case-based essays, which could further measure the student's knowledge and managerial skills before and after training (20).

We carried out the level 3 questionnaire by comparing the learning obtained in ALTEM and the subjects' performance in the workplace. ALTEM training program was proven to improve communication and teamwork in the workplace in univariate ($p < 0.001$) and multivariate (OR 7.866; $p = 0.005$) analysis. Communication and teamwork are essential components in the healthcare system, especially regarding patient safety. Miscommunication regarding the patient status and management plan during care transition (between care areas or health worker shifts) could endanger patient safety. Moreover, ineffective communication between health workers, i.e., clinicians, pharmacists, and nurses, could cause medication errors. The fundamentals of good teamwork were that all members identified the objectives of patient treatment (including the patient himself), recognized the roles and responsibilities of himself and other team members, had effective communication, measurable process and outcome, and the leader had good leadership capability (21–24).

The lecturers explained team-based emergency management and team roles to the lecture participants. Later in the skill station session and simulation exam, the participants simulated medical management with a prior discussion with each other. The role discussion, division, and simulation helped the participants understand each member's management objectives, roles, and responsibilities and practice effective communication. The leader also had the chance to practice leadership skills. All of these contributed to the increased communication and teamwork of the subjects after the ALTEM training program.

The ALTEM training program did not significantly affect leadership ability ($p = 0.322$) or confidence in facing critical patients. Each group only did a one-time simulation in the simulation exam, meaning that only one person in each group could become the leader. The one-time simulation might contribute to a lack of perceived leadership skill enhancement by the subjects. Furthermore, the limitation of having only one simulation case per group decreased confidence and competence, particularly in managing rare cases, after the training program.

The ideal solution to increase leadership and decision-making skills is to give each participant several opportunities to lead the simulation. The multiple opportunities can be achieved by providing more instructors, rooms, and facilities so that more groups can perform simultaneously during the simulation exam.

However, a few alternatives can be considered due to time and resource limitations. One week before the course begins, each participant can be given a scenario and requested to create a short video of him (less than 5 minutes) leading the case in groups (role play). One person acts as the narrator, one person as the leader, and 2-3 persons as the team members doing the leader's instruction. The video does not need to use real medical devices or mannequins. The role play urges participants to deepen their knowledge, communication, and leadership skills. The video submission is due on the first day of the course. The instructors then grade the video and give feedback during the skill station the



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next day. Participants seen as incompetent will have more intensive drilling during the skill station (25).

Action learning (i.e., tutorial sessions) is also a feasible leadership training for short-term courses. The tutorial session consists of five to eight persons per group, guided by one instructor. The instructor presents the scenario; then, participants collaboratively explore solutions using a combination of open questions, appreciative inquiry, and diverse perspectives. The objective is to facilitate and empower individuals to speak up, train critical thinking, and foster a dynamic and participatory approach to leadership development (25).

The program was not an independent factor in increasing perceived decision-making skills in the workplace after ALTEM ($p = 0.684$). Decision-making should be made as quickly and appropriately as possible in emergencies. Case-based and timed simulation in ALTEM trains subjects to make rapid and correct decisions based on the patient's condition and medical knowledge. However, decision-making in the workplace does not only rely on the doctor's medical judgment or fundamental knowledge, but other factors also play a role, such as ethical considerations, sociocultural aspects, hospital policies, patient or family preferences, and cost-effectiveness analyses. On that account, future simulation cases should also involve the ethical, sociocultural, financial, or policy aspects so that the participants can learn to think beyond the medical aspects of treating or making a medical decision, therefore taking a more holistic approach to decision-making (21–24).

In the context of reliability, ALTEM has a manual book and checklists for instructors and is now developing simulation videos and a mobile application to standardize the program. However, there are simulation cases rated as 'very important' and 'additional' cases. The necessary cases should be simulated in every period of the ALTEM course, but the additional cases can vary. The necessary cases are taught in the lectures and skill stations, and the additional cases are written in the manual book.

Furthermore, the background of simulation cases can be tailored to address specific local medical requirements, allowing for the customization of simulation scenarios based on prevalent or critically important cases within a given medical education setting. For example, shock is one of the necessary cases in ALTEM. However, the background of the patient suffering from shock can be adjusted (e.g., heart attack, dengue fever, motor vehicle accidents, etc). Therefore, medical students living in dengue-endemic areas can be given cases of dengue shock syndrome. This adaptability ensures that ALTEM remains standardized yet flexible to medical students' competency requirements.

The assessment of learning and performance was subjective. Therefore, there was a possibility of bias. Moreover, the absence of essay-based questions in the questionnaires limited our ability to capture the underlying reasons behind subjects' responses. The study also did not include the pre-test data. Nevertheless, it is essential to highlight that this study comprehensively evaluated the effectiveness of ALTEM from various perspectives, employing a validated questionnaire and evaluation model. This approach ensures that the feedback gathered is valuable for assessing and refining the upcoming ALTEM program.

## CONCLUSION

ALTEM training program received good responses from the subjects and demonstrated



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good effectiveness in enhancing communication and teamwork. Several improvements were needed, but the overall program was a prospective initiative toward improving medical students' competence and collaboration in emergency management. We anticipate widespread acceptance and implementation across universities, envisioning a positive impact on emergency medical care throughout Indonesia.

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**Conflict of Interest**
We declare no conflicts of interest in this study.

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**Authors' Contributions**
PH, BA, RFN, AZR: study concept and design, acquisition of the data, critical revision of the manuscript for important intellectual content, obtaining funding, administrative, technical, or material support, study supervision.
CA: analysis and interpretation of the data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical expertise, administrative, technical, or material support

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Original Article

# COMPARISON OF INTRAVENOUS ADMINISTRATION OF REMIFENTANIL WITH FENTANYL FOR INCREASED BLOOD SUGAR LEVELS IN POST-CARDIAC SURGERY PATIENTS

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**ABSTRACT**

**Introduction:** The incidence of hyperglycemia in patients with heart disease undergoing cardiac surgery reaches 50% in patients without a history of Diabetes Mellitus. This condition of hyperglycemia can increase morbidity and mortality. **Objective:** This study aims to assess the effect of using the agent remifentanil intravenously 0.5-1 µg/kgBW bolus followed by maintenance at a dose of 0.05-0.1 µg/kgBW/minute intravenously compared to the use of fentanyl 3-10 µg/kgBW followed by a maintenance dose of 0.03-0.1 µg/kgBW/minute for increased blood sugar levels in patients undergoing cardiac surgery with the Cardiopulmonary Bypass (CPB) procedure. **Materials and Methods:** This study is an experimental study with a single-blind randomized controlled design. Patients will be divided into 2 groups consisting of 12 patients each, namely group R (remifentanil) received remifentanil, and group F (fentanyl) received fentanyl. Blood sugar levels will be checked before and after surgery. **Results:** The research has been conducted at Dr. Hasan Sadikin Hospital Bandung from February 2023 to May 2023**.** The average increase in blood sugar levels in the remifentanil group was 74 mg/dl, while in the fentanyl group, it was 90 mg/dl. The p-value given is 0.214. Statistical test results showed that the value of p> 0.05. **Conclusion:** This study concludes that there is no significant difference in the increase in blood sugar levels between the two groups (remifentanil and fentanyl). This can be caused by the use of opioid doses in the lower range and more complex surgical procedures in our research.

**Keywords:** Blood Sugar Levels; Cardiopulmonary Bypass; Heart Disease; Remifentanil

**ABSTRAK**

**Pendahuluan:** Angka kejadian hiperglikemia pada pasien penyakit jantung yang menjalani operasi jantung mencapai 50% pada pasien tanpa riwayat diabetes melitus. Kondisi hiperglikemia ini dapat meningkatkan angka kesakitan dan kematian. **Tujuan:** Penelitian ini bertujuan untuk menilai pengaruh penggunaan agen remifentanil secara intravena bolus 0,5-1 µg/kgBB diikuti dengan dosis rumatan 0,05-0,1 µg/kgBB/menit secara intravena dibandingkan dengan penggunaan fentanil 3-10 µg/kgBB yang diikuti dengan dosis pemeliharaan 0,03-0,1 µg/kgBB/menit untuk peningkatan kadar gula darah pada pasien yang menjalani operasi jantung dengan prosedur Pintas Jantung Paru (PJP). **Bahan dan Metode:** Penelitian ini merupakan penelitian eksperimental dengan rancangan terkontrol acak buta tunggal. Pasien akan dibagi menjadi 2 kelompok yang masing-masing terdiri dari 12 pasien, yaitu kelompok R (remifentanil) yang mendapat remifentanil dan kelompok F (fentanil) yang mendapat fentanil. Kadar gula darah akan diperiksa sebelum dan sesudah operasi. **Hasil:** Penelitian ini dilaksanakan di RSUP Dr. Hasan Sadikin Bandung pada bulan Februari 2023 sampai dengan Mei 2023. Rata-rata kenaikan kadar gula darah pada kelompok remifentanil sebesar 74 mg/dl, sedangkan pada kelompok fentanil sebesar 90 mg/dl. Nilai p yang diberikan adalah 0,214. Hasil uji statistik menunjukkan nilai p > 0,05. **Kesimpulan:** Kesimpulan penelitian ini adalah tidak terdapat perbedaan peningkatan kadar gula darah yang signifikan antara kedua kelompok (remifentanil dan fentanil). Hal ini dapat disebabkan oleh penggunaan dosis opioid dalam rentang yang lebih rendah dan prosedur bedah yang lebih kompleks dalam penelitian kami.

**Kata kunci:** Kadar Gula Darah; Pintas Jantung Paru; Penyakit Jantung; Remifentanil

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## INTRODUCTION

Cardiopulmonary bypass surgery or Heart Lung Bypass (CPB) is a procedure that is often performed in heart surgery. The act of CPB can cause an inflammatory response that increases levels of cytokines and catecholamines in plasma, resulting in hyperglycemia (1). The incidence of hyperglycemia in patients undergoing heart surgery without comorbid Diabetes mellitus reached 56.1% (2). Hyperglycemia is associated with an increase in the incidence of major side effects and mortality rate in patients undergoing heart surgery (3,4).

During the CPB procedure, the phospholipase A2 enzyme will degrade arachidonic acid which will increase inflammatory mediators such as leukotrienes, prostaglandins, and thromboxane. These mediator substances trigger activation and adhesion of neutrophils, vasoconstriction of blood vessels, platelet aggregation, and tissue damage (5). Increases in inflammatory mediators and secretion of catecholamine hormones will cause Systemic Inflammatory Response Syndrome (SIRS) which will cause insulin resistance and cause hyperglycemia which is complications that often occur after heart surgery (6,7).

Opioids are a class of drugs that are often used in surgery to control the sympathetic response during surgery and are expected to reduce surgical stress (8). One of the opioid drugs that is often used in surgery is fentanyl. Fentanyl is the most widely used opioid because it has minimal cardiovascular effects, does not cause histamine release, has a fast onset of action with a short duration of action, and is easy to use (9). Apart from fentanyl, another class of opioid drugs, remifentanil, has the same level of effectiveness as other opioids and maintains better hemodynamic stability in cardiac surgical procedures (10,11). Remifentanil is an opioid with a very short onset of action and a derivative of piperidine. Remifentanil itself has a strong analgesic effect which can reduce sympathetic stimulation and maintain pulse rate and blood pressure during surgery. Remifentanil is metabolized in plasma by nonspecific esterase with its metabolite remifentanil acid (12).

To the best knowledge of the authors, there have been no studies comparing the usefulness of fentanyl and remifentanil for cardiac surgery with CPB procedures in Indonesia. Therefore, this study aimed to compare the increased blood sugar levels in patients undergoing cardiac surgery with PJP who received fentanyl or remifentanil. We assume that the Patients who receive remifentanil therapy will experience a lower increase in blood sugar levels compared to patients who receive fentanyl therapy. To investigate this hypothesis, we compared the rate of increase in blood sugar levels in both groups of patients undergoing cardiac surgery with the CPB procedure.

## MATERIAL AND METHODS

### Study Design and Subjects

The design of this study was an experimental study done in a randomized crossover study, approved by the Ethics Committee of Dr. Hasan Sadikin Hospital Bandung, Indonesia on 23rd January 2023 with registered number LB.02.01/X.6.5/27/2023. Twenty-four patients who underwent cardiac surgery with the CPB procedure were subjects in this study. This research was conducted at the central surgical installation of Dr. Hasan Sadikin Hospital Bandung between February and May 2023.



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**Study Procedures**

After obtaining approval from the Research Ethics Committee Dr. Hasan Sadikin Hospital Bandung, patients who meet the inclusion criteria (patients aged 18 and over undergoing elective heart surgery using a heart-lung bypass machine, patients with physical status based on the American Society of Anesthesiologists (ASA) in categories I-III) are given informed consent regarding the procedure to be carried out. Drug preparation is carried out in the cardiac surgery central operating theatre pharmacy department.

Patients were divided into 2 groups, namely group R, which received remifentanil 0.5-1 µg/kgBW/minute intravenously, and group F, which received fentanyl 3-10 µg/kgBW. Drugs are divided into two types, namely induction drugs and maintenance drugs. Remifentanil 2 mg is diluted with 0.9% NaCl 40 ml to the preparation of 50 µg/ml in a 50 ml syringe, for the induction dose using a dose range of 0.5-1 µg/kgBW/minute while the maintenance dose is given at 0.05-0.1 µg/kgBW/minute in a 50 ml syringe using a syringe pump. Fentanyl medication for induction is given bolus at a dose of 3-10 µg/kgBW. Meanwhile, for maintenance, it is given at a dose of 0.03-0.1 µg/kgBW/minute, and 400 mcg fentanyl is diluted with 40 ml of 0.9% NaCl to form a preparation of 10 mcg/ml in a 50 ml syringe.

Patients who will take part in the research procedure are required to fast 6 hours before surgery. The patient received fasting replacement fluid with Ringer's lactate given at 10 cc/kgBB for 30 minutes and continued with maintenance fluid at 2cc/kgBB/hour. Then the anesthesia and surgery procedures can begin and proceed according to applicable standard operational procedures.

After the patient has an arterial line installed, the patient's blood sugar level is sampled as basic data (T1). Induction is carried out with propofol 2-3 mg/kgBW intravenously, after the patient falls asleep followed by administration of rocuronium 0.8 mg/kgBW intravenously. Additional medications given by perfusion during CPB procedures such as insulin will be noted in the study. After CPB is finished, protamine is given at a dose of 1-1.3 the dose of heparin and methylprednisolone 250 mg IV bolus. After the operation is complete, the patient's blood sugar is sampled as final data (T2).

**Data Collection**

The first data collected was blood sugar level, which was collected just before the induction of anesthesia was performed. The second data collected was blood sugar level checked after the operation had been completed.

**Statistical Analysis**

This research has a crossover design. The sample size was calculated using $\alpha$ = 0.05 and $\beta$ = 0.2 (13). A minimum number of 12 participants was required in each random sequence. Therefore, researchers estimated that a minimum total of 24 participants are needed for this study. The data was tested statistically using Statistical Product and Service Solution (SPSS) version 26.0 for Windows. Data are presented as median (interquartile range) for numeric variables and number (percentage) for categorical variables. A value of $P$ less than 0.05 is considered statistically significant.

## RESULT AND DISCUSSION

This research was conducted on 24 research subjects who underwent cardiac surgery with a cardiopulmonary bypass procedure at Dr. Hasan Sadikin Hospital Bandung in the period February 2023 to May



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2023 which has met the inclusion criteria and is not included in the exclusion criteria. Subjects were then divided into 2 groups, namely group R which used remifentanil 0.5-1 µg/kgBW bolus followed by a maintenance dose of 0.05-0.1 µg/kgBW/minute intravenously, and group F which used fentanyl 3-10 µg /kgBW bolus followed by a maintenance dose of 0.03-0.1 µg/kgBW/minute, with each group consisting of 12 research subjects.

**Table1.** Comparison of the Characteristics of Research Subjects

| Variable | Group | | p-value |
|---|---|---|---|
| | Remifentanil N=12 | Fentanyl N=12 | |
| **Age (year)** | | | |
| Mean±SD | 42 ± 12 | 41 ± 16 | 0.909[a] |
| **Sex, n (%)** | | | |
| Male | 7 (58.3) | 8 (66.7) | 1.000[c] |
| Female | 5 (41.7) | 4 (33.3) | |
| **BMI (kg/m$^2$)** | | | |
| Mean±SD | 21.9 ± 4.8 | 22.2 ± 4.7 | 0.854[a] |
| **ASA, n (%)** | | | |
| 1 | 0 | 0 | - |
| 2 | 0 | 0 | |
| 3 | 12 (100) | 12 (100) | |
| **Total operation time (minute)** | | | |
| Mean±SD | 255 ± 58 | 240 ± 52 | 0.510[a] |
| **Duration of operation-start of CPB (minute)** | | | |
| Mean±SD | 66 ± 19 | 68 ± 17 | 0.758[a] |
| **Duration of completion of CPB - completion of surgery (minute)** | | | |
| Mean±SD | 97 ± 34 | 89 ± 25 | 0.522[a] |
| **Duration of CPB** | | | |
| Mean±SD | 93 ± 21 | 83 ± 25 | 0.339[a] |
| **Aortic cross-clamp duration** | | | |
| Mean±SD | 60 ± 20 | 61 ± 22 | 0.871[a] |
| **Amount of bleeding** | | | |
| Median | 800 | 800 | 0.519[b] |
| Range (min-max) | 500 – 3000 | 500 – 1600 | |
| **Operation type, n (%)** | | | |
| CABG | 2 (16.7) | 2 (16.7) | 0.430[d] |
| MVR | 5 (41.7) | 4 (33.3) | |
| ASD Closure | 1 (8.3) | 3 (25.0) | |
| VSD Closure | 1 (8.3) | 0 (0.0) | |
| MVR+TVr | 1 (8.3) | 2 (16.7) | |
| CABG+MVR | 0 (0.0) | 1 (8.3) | |
| MVR+ASD Closure | 1 (8.3) | 0 (0.0) | |
| MVR+TVr+ASD Closure | 1 (8.3) | 0 (0.0) | |

Notes: Analysis uses [a]unpaired t-test, [b]Mann Whitney, [c]Fisher Exact, [d] Chi Square *meaning p<0,05



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**Table 2.** Comparison of Blood Sugar Levels of the Two Groups

| Variable | Group | | p-value (Remifentanil vs Fentanyl) |
|---|---|---|---|
| | Remifentanil N=12 | Fentanyl N=12 | |
| **Preoperative blood sugar levels (mg/dl)** Mean±SD | 91 ± 16 | 95 ± 14 | 0.482 |
| **Postoperative blood sugar levels (mg/dl)** Mean±SD | 164 ± 27 | 185 ± 39 | 0.137 |
| **P value (pre vs post)** | **<0,001*** | **<0,001*** | |

Notes: Analysis uses \unpaired t-test, (pre and post) uses paired t-test*meaning p<0,05

Characteristics of research subjects include age, gender, BMI, ASA, total duration of surgery, duration of surgery until the start of PJP, duration of completion of PJP until completion of surgery, length of PJP, length of aortic cross-clamping, amount of bleeding and type of operation can be seen in Table 1 and comparison blood sugar levels for both groups can be seen in Table 2. The results of statistical tests for all the research groups above showed that the P value for all variables was greater than 0.05 (p value>0.05), which means it is not significant or not statistically significant. Thus, it can be explained that there is no statistically significant difference between all variables in patient characteristics in Group Remifentanil and Group Fentanyl. There are no differences or the same in the two research groups so it can be concluded that the two groups are homogeneous and can be compared statistically.

**Table 3.** Comparison of the Increase in Blood Sugar Levels of the Two Groups

| Variable | Group | | P-value |
|---|---|---|---|
| | Remifentanil N=12 | Fentanyl N=12 | |
| **Increase in blood sugar levels** Mean±SD | 74 ± 24 | 90 ± 38 | 0.214 |

Notes: P value (Remifentanil vs Fentanyl) using unpaired t-test.*)Statistically significant (p-value < 0,05)

In the Table 3, it is found that the average increase in blood sugar levels in the remifentanil group was 74 mg/dl, and in the fentanyl group, it was 90 mg/dl. The statistical test results obtained a value of p=0.214 (p≥0.05), which means that there was no significant difference in the increase in blood sugar levels in Group Remifentanil and Group Fentanyl.

There were no significant differences in the characteristics of the research subjects between Group Remifentanil and Group Fentanyl., this shows that all samples from each group were in relatively the same range so that the two groups were homogeneous and worthy of comparison for further statistical analysis.

Based on Table 1, it is known that the average age of research subjects in group R was 42 ± 12 years, and in group F was 41 ± 16 years. The statistical test results obtained a value of p=0.909 (p≥0.05), which means that there were no significant differences in the characteristics of the research subjects based on age between group R and group F. At older ages, the ability to regulate blood sugar will decrease due to a decrease in insulin sensitivity. This is based on research by Shou which explains that the elderly population experiences a decrease in the function of the glucose transporter 4 (GLUT 4) enzyme and a decrease in insulin sensitivity. In this study, the average age of research subjects in both groups was not included in the elderly



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category so the increase in perioperative blood sugar levels can be compared (14).

The average body mass index (BMI) in group R was found to be 21.9 ± 4.8 kg/m2 and in group F the average BMI was 22.2 ± 4.7 kg/m2. The statistical test results obtained a value of p=0.854 (p≥0.05), which means that there were no significant differences in the characteristics of the research subjects based on BMI between group R and group F. Patients with a higher BMI tended to experience an increase in blood sugar levels during intraoperative. This is with research conducted by Nakadate that there is a negative correlation between BMI and insulin sensitivity (15).

In terms of total operating time, it is known that the average in group R was 255 ± 58 minutes and in group F 240 ± 52 minutes. The duration of the operation-start of CPB in group R was 66 ± 19 minutes and in group F 68 ± 17 minutes. Duration of completion of CPB - completion of surgery in group R was 97 ± 34 minutes and in group F 89 ± 25 minutes. The average CPB duration in group R was 93 ± 21 minutes and in group F 83 ± 25 minutes. The average duration of aortic cross-clamping in group R was 60 ± 20 minutes and in group F 61 ± 22 minutes. The average amount of bleeding in group R was 500 - 3000 ml and in group F 500 - 1600 ml. The CPB procedure is a procedure that is often used in cardiac surgery today. However, the CPB procedure has several disadvantages that can result in complications after surgery. This extracorporeal circulation can stimulate an inflammatory response caused by exposure of the patient's blood to the circuit of the CPB machine. Aortic cross-clamp time (ACCT) and cardiopulmonary bypass time are associated with increased morbidity and mortality after cardiac surgery, which is related to myocardial injury, ischemia, and inflammatory response. Therefore, the results of post-operative cardiac surgery can be influenced by the length of cardiac surgery and the CPB procedure. This is based on research conducted by Madhavan that a longer CPB procedure can increase the risk of postoperative complications (16).

The surgical procedures carried out in this study were divided into three large groups, namely valve replacement surgery, Coronary Artery Bypass Graft, and septal closure. Valve replacement surgery was the most common surgical procedure performed in both groups, namely 5 cases (41.7%) in group R and 4 cases (33.3%) in group F, CABG surgery in both groups amounted to 2 cases (16.7%), surgery closure of the septum hole in group R amounted to 2 cases (16.7%) and in group F there were 3 cases (25%), the remaining cases studied included two valve replacement operations, CABG with valve replacement, closure of the septum hole and valve replacement. This is different from the surgical procedures carried out by Lee where the type of surgery in all research samples was valve replacement surgery (17). Meanwhile, in this study the surgical procedures carried out were more diverse with several surgical procedures covering two groups of surgical procedures.

The results of this study also showed that after surgery, the average increase in blood sugar levels in group R was 164 mg/dl, and in group F was 185 mg/dl. The statistical test results obtained a value of p=0.137 (p≥0.05) indicating that there was no significant difference in blood sugar levels after surgery between group R and group F.

Blood sugar levels in group R and group F seen from each group before surgery and after surgery showed a significant difference (p<0.001), this shows that there was a significant influence on the treatment given to group R and group F. Previous research



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conducted by Umpierrez in the GLUCO-CABG study also explained that the incidence of hyperglycemia is something that often occurs in patients undergoing cardiac surgery with an incidence of more than 50% in patients without a history of diabetes mellitus (18). This can be caused by tissue damage that occurs during cardiac surgery using the CPB procedure.

Research conducted by Lee shows that remifentanil is more effective in reducing cytokines in cardiac surgery accompanied by PJP procedures. This is indicated by an increase in IL-6 and IL-8 levels which is lower than in the group of patients who used the drug fentanyl. Lee divided 2 groups of patients who received the opioid remifentanil with an induction dose of 0.5-1.0 µg/kg and a maintenance dose of 0.05-0.1 µg/kg/min with a group of patients who received the opioid fentanyl with an induction dose of 3-10 µg/kg and a maintenance dose 0.03-0.1 µg/kg/min (17). In research conducted at Dr. Hasan Sadikin General Hospital, the induction dose in group R was 1.0 µg/kg and the maintenance dose was in the lower range, namely 0.05 µg/kg/min and the induction dose was in the lower range, namely 3 µg/kg and the average maintenance dose is 0.05 µg/kg/min where the use of this dose takes into account the patient's hemodynamic condition. Apart from that, the depth of anesthesia in this study was also not assessed, which allowed inadequate sedation and opioid medication to be given so that the stress response due to surgical trauma continued and there was an increase in postoperative blood sugar levels.

Another difference in patient characteristics is the type of surgical procedure performed, where this study involved valve replacement surgery, CABG, septal closure, and a combination of surgical procedures. Meanwhile, in Lee's research, the surgical procedure involved only valve replacement. This also influences research outcomes where various surgical procedures will trigger wider tissue damage and cause a higher sympathetic response.

Some limitations of this research are that the study did not look at postoperative outcomes such as length of treatment in the intensive care room, complications after surgery, mortality rate, and the number of samples in this study was 24 with each group of 12 patients, so this will affect the statistical calculations on this research.

## CONCLUSION

There was no significant difference in the increase in blood sugar levels after surgery in the group receiving the opioid remifentanil and the opioid fentanyl. This could be because the number of samples in this study was 12 patients in each group. It is hoped that future research can involve a larger sample size so that it can represent the population. Apart from that, the use of doses with different ranges will certainly affect different research outcomes in each group. Various types of surgery also influence the outcome of the operation where this study involved valve replacement surgery, CABG, septal closure, and a combination of surgical procedures.

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### Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this article.



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**Authors' Contributions**
IT, DT, RW planned the study and contributed to data collection and analysis. All authors have reviewed and approved the final manuscript.

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Original Article

# INVESTIGATION OF HEART RATE VARIABILITY AND THE REQUIREMENT FOR VASOPRESSORS RELATIONSHIP DUE TO HYPOTENSION IN PATIENTS UNDERGOING CAESAREAN SECTION WITH SPINAL ANESTHESIA

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## ABSTRACT

**Introduction:** The most common effect of spinal anesthesia applied in cesarean section operations is hypotension. It is very important to prevent hypotension due to fetal bradycardia, acidosis, and maternal effects. **Objective**: This research was conducted to predict and prevent maternal hypotension in pregnant women undergoing elective cesarean section with spinal anesthesia by measuring heart rate variability parameters about hypotension. **Materials and Methods:** The study included pregnant women aged 18-45 with ASA 2 classification who underwent elective cesarean section with spinal anesthesia. Using the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' device and its smartphone application, 102 volunteer pregnant patients were monitored for 5 minutes in the recovery unit, and their data were recorded. After the administration of spinal anesthesia, patients who exhibited a decrease in systolic blood pressure of 20% or more from their baseline values received intravenous ephedrine in 10 mg bolus doses at each instance of low blood pressure measurements. Patients who received a total of 20 mg or more ephedrine doses or more as needed were designated as 'Group 1,' while patients who received less than 20 mg or no ephedrine were classified as 'Group 2.' **Results:** This study was completed with a total of 102 pregnant patients With 46 patients in Group 1 and 56 patients in Group 2, the relevant parameters that showed a statistically significant difference between patient groups were subjected to ROC analysis for predicting hypotension. It was determined that patients with high HF POWER and TOTAL POWER values had a greater need for vasopressors due to hypotension following spinal anesthesia ($p<0.05$). **Conclusion:** In the research, these values are believed to have the potential to predict hypotension in patients undergoing cesarean sections with spinal anesthesia.

**Keywords:** Heart Rate Variability; Hypotension; Childbirth Complications; Pregnant; Spinal Anesthesia

## ABSTRAK

**Pendahuluan:** Efek paling umum dari anestesi spinal yang diterapkan pada operasi sesar adalah hipotensi. Sangat penting untuk mencegah hipotensi karena bradikardia janin, asidosis, dan efek maternal. Tujuan: Penelitian ini dilakukan untuk memprediksi dan mencegah hipotensi maternal pada wanita hamil yang menjalani operasi sesar elektif dengan anestesi spinal dengan mengukur parameter variabilitas detak jantung terkait hipotensi. **Bahan dan Metode:** Penelitian ini melibatkan wanita hamil berusia 18-45 tahun dengan klasifikasi ASA 2 yang menjalani operasi sesar elektif dengan anestesi spinal. Menggunakan perangkat 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' dan aplikasi *smartphone* nya, 102 pasien hamil sukarelawan dipantau selama 5 menit di unit pemulihan, dan data mereka dicatat. Setelah pemberian anestesi spinal, pasien yang menunjukkan penurunan tekanan darah sistolik sebesar 20% atau lebih dari nilai awal mereka menerima ephedrine intravena dalam dosis bolus 10 mg pada setiap pengukuran tekanan darah rendah. Pasien yang menerima total dosis ephedrine sebanyak 20 mg atau lebih atau lebih sesuai kebutuhan dianggap sebagai 'Kelompok 1,' sedangkan pasien yang menerima kurang dari 20 mg atau tidak ada ephedrine diklasifikasikan sebagai 'Kelompok 2.' **Hasil:** Penelitian ini diselesaikan dengan total 102 pasien hamil. Dengan 46 pasien di Kelompok 1 dan 56 pasien di Kelompok 2,



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parameter yang relevan yang menunjukkan perbedaan yang signifikan secara statistik antara kelompok pasien dikenai analisis ROC untuk memprediksi hipotensi. Ditemukan bahwa pasien dengan nilai HF POWER dan TOTAL POWER yang tinggi memiliki kebutuhan yang lebih besar untuk vasopresor akibat hipotensi setelah anestesi spinal (p<0,05). **Kesimpulan:** Dalam penelitian ini, hasil-hasil tersebut diyakini memiliki potensi untuk memprediksi hipotensi pada pasien yang menjalani operasi sesar dengan anestesi spinal.

**Kata Kunci:** Variabilitas Denyut Jantung; Hipotensi; Komplikasi Persalinan; Hamil; Anestesi Spinal

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## INTRODUCTION

Spinal anesthesia is frequently preferred in cesarean section procedures due to its ease of application, rapid onset of action, and advantages such as reduced intraoperative blood loss compared to general anesthesia. Hypotension, one of the complications of spinal anesthesia, occurs in one-third of pregnant women. Intraoperative hypotension, associated with serious complications in the mother such as perioperative acute kidney injury and myocardial ischemia, has been noted to have adverse neurological effects on the fetus in the first hours after birth and can lead to fetal acidemia (1). Therefore, predicting and preventing significant hypotension with unwanted effects on the pregnant woman and the fetus is of paramount importance for morbidity and mortality.

In the literature, numerous studies aim to predict and intervene early in intraoperative hypotension following cesarean section under spinal anesthesia. However, these studies have often been insufficient in predicting hypotension or have used methods that lack clinical convenience (2–4).

### Heart Rate Variability Measurements

Even at a regular rhythm, there is a few milliseconds difference between each heartbeat, known as 'heart rate variability' (HRV). HRV is an important parameter that demonstrates the interaction between cardiac and cerebral systems and is used to obtain detailed information about the autonomic nervous system's control of the heart.

The likelihood of developing hypotension due to spinal anesthesia is higher in patients with pre-existing autonomic dysfunction. Some studies have suggested that hypotension observed in cesarean sections under spinal anesthesia in pregnant women can be predicted using parameters related to HRV, but there are also conflicting results from other studies (5).

This research aims to predict significant hypotension that may occur after the administration of spinal anesthesia in pregnant women undergoing elective cesarean section by measuring heart rate variability using a non-invasive device that is clinically convenient. This approach seeks to identify patients at risk of hypotension in advance, allowing for early intervention to reduce the duration and severity of hypotension.

## MATERIALS AND METHODS

### Ethical Approval and Study Design

This study was initiated after obtaining ethical approval from the Erciyes University Non-Invasive Clinical Research Ethics Committee (2022/698). The study is a non-interventional descriptive observational study with a post-hoc analysis investigating the relationship between heart rate variability and



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the need for vasopressors due to hypotension in patients undergoing cesarean section between October 2022 and March 2023 in the operating theater unit of Kayseri Erciyes University Hospital.

**Study Participants**

The study included pregnant women aged 18-45 with ASA 2 classification, who were scheduled for elective cesarean section. Patients with hypertension or any other heart disease during pregnancy, those using medications that could affect heart rate, those undergoing other intraoperative anesthetic techniques, those with contraindications for spinal anesthesia, those who experienced significant blood loss before or during the operation, and those for whom the use of ephedrine was contraindicated were excluded from the study.

**Data Collection and Analysis**

For the study, the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' device, which provides heart rate variability measurements through digital pulse wave analysis from the fingertip, was ordered from abroad and obtained for use. Subsequently, the device's existing smartphone application was installed on the research phone. 102 volunteer pregnant patients who had no exclusion criteria and underwent cesarean section under spinal anesthesia in the operating room of Erciyes University between October 2022 and March 2023 were included in the sample after obtaining their consent. All the patients were monitored with the device in the recovery unit at rest. Heart rate variability and parameters were calculated using the data obtained from 5-minute measurements, based on studies indicating correlations between measurements obtained from 24-hour electrocardiographic records and calculations from 5-minute measurements (6). All data were recorded in the phone application without grouping for each patient.

Patients taken to the operating table underwent standard monitoring, including ECG, non-invasive blood pressure, and saturation. All measurements were performed with patients in the supine position. Fluid loading was performed with approximately 1000 ml of crystalloid solution before the procedure and continued with crystalloid infusion during the operation. Patients without the need for intraoperative sedation were included in the study.

**Spinal Anesthesia Procedure**

Baseline systolic blood pressure values measured before the operation were recorded as 'pre-procedural values' for each patient. Spinal anesthesia was provided with a dose of 0.5% hyperbaric bupivacaine calculated according to the patient's height, using the formula (0.06 x patient's height in cm = bupivacaine dose in mg), administered through a Quincke 25-gauge spinal needle at the L3-4 intervertebral space with the patient in a sitting position, head down (7). A pin-prick test was applied to measure the sensory block level and patients who did not reach the T6 level within 20 minutes or developed a block at levels higher than T4 were excluded from the study. Patients' blood pressure and pulse were noted at specified stages: before spinal anesthesia (pre-procedure), immediately after spinal anesthesia (0 minutes), 1 minute after spinal anesthesia (1 minute), 3 minutes, 5 minutes, 15 minutes, and 30 minutes after spinal anesthesia.



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### Definition of Hypotension

In this study, a decrease of 20% or more in the baseline systolic blood pressure values measured before the procedure, as measured before the operation, was considered hypotension, following routine practice in the operating room, and ephedrine was administered in intravenous bolus doses of 10 mg for patients with low blood pressure measurements. High-dose ephedrine was defined as the intravenous administration of 20 mg or more of ephedrine during the operation. Patients receiving a total of 20 mg or more of ephedrine during the operation were included in 'Group 1', while patients receiving less than 20 mg or no ephedrine were classified as 'Group 2'.

### Data Analysis

The data obtained were evaluated using the IBM SPSS 25.0 statistical package program. Descriptive statistics were presented as unit count (n), percentage (%), mean ± standard deviation (mean±sd), median (M), minimum (min), and maximum (max) values. Data distribution was assessed using Q-Q plots, Shapiro-Wilk tests, and histogram graphics. Parametric data were analyzed using Student's t-test for normally distributed data, while non-parametric data were analyzed using the Mann-Whitney U test. Group differences were analyzed using Student's t-test for parametric data, the Mann-Whitney U test for non-parametric data, and ROC analysis. The study was conducted with a 95% confidence interval and a 5% margin of error, and a p-value of less than 0.05 was considered statistically significant.

## RESULTS AND DISCUSSION

### Descriptive Statistical Analysis Results Between Patient Groups

In this study, 102 patients were included, with 46 (45.1%) in Group 1 and 56 (54.9%) in Group 2. The ages of Group 1 patients ranged from 19 to 44 years, with a mean age of 28.24±5.47 years, while Group 2 patients' ages ranged from 18 to 45 years, with a mean age of 31.32±6.50 years. Based on the measurements conducted with the device before the operation, Mann-Whitney U Test results revealed statistically significant differences between Group 1 and Group 2 patients in HRV and time-related measurements, including the root mean square of successive differences between normal heartbeats (RMSSD), the standard deviation of the R-R intervals of normal sinus beats (SDNN), the natural logarithm (LN) and the percentage of adjacent the number of pairs of successive NN (R-R) intervals that differ from each other by more than 50 ms (pNN50%). Regarding frequency domain measurements, statistically significant differences were observed between the groups in TOTAL POWER, Low Frequency (LF) / High Frequency (HF), LF POWER, and HF POWER values. Furthermore, there was a statistically significant difference in the ages of patient groups ($p<0.05$) (Table 1).

The average baseline systolic blood pressure values measured before the operation, the average systolic blood pressure values measured during the intraoperative periods, and the average total ephedrine dosage administered throughout the operation following spinal anesthesia were calculated for the patients. Out of the 102 patients participating in the study, 46 patients received ephedrine doses of 20 mg or higher, while 56



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patients received ephedrine doses lower than 20 mg or no ephedrine at all. Based on the measurements conducted in both groups, statistically significant differences were observed in the averages of systolic blood pressure values and the total ephedrine doses administered to patients during the measurements performed at 1st, 3rd, and 5th minutes after spinal anesthesia (p<0.05) (Table 2).

**Hypotension ROC analysis with TOTAL POWER**

In the ROC analysis conducted to assess the predictive power of TOTAL POWER for post-spinal anesthesia hypotension in pregnant women, the AUC (95%) value was calculated as 0.905 (0.848-0.963). The cut-off value was determined as 984.07, with a sensitivity of 83% and specificity of 17% (p 0.0001) (Table 3) (Figure 1).

**Table 1.** Statistical Analysis Results Between Patient Groups

| Variable | Group 1 (n=46) | | | Group 2 (n=56) | | | z | u | p-value* |
|---|---|---|---|---|---|---|---|---|---|
| | Mean±SD | Min. | Max. | Mean±SD | Min. | Max. | | | |
| **Age** | 28.24±5.47 | 19.00 | 44.00 | 31.32±6.50 | 18.00 | 45.00 | -2.432 | 927 | 0.015 |
| **HRV** | 56.87±4.71 | 46,00 | 67.00 | 47.75±7.39 | 27.00 | 60.00 | -6.311 | 351 | 0.000 |
| **RMSSD** | 42.24±13.30 | 19.87 | 78.34 | 24.50±10.29 | 5.84 | 50.32 | -6.318 | 348.5 | 0.000 |
| **SDNN** | 56.30±16.10 | 31.45 | 126.73 | 39.33±13.22 | 16.48 | 87.04 | -5.542 | 464 | 0.000 |
| **LN** | 3.70±0.30 | 2.99 | 4.36 | 3.10±0.48 | 1.8 | 3.9 | -6.383 | 339 | 0.000 |
| **pNN50%** | 16.28±12.95 | 3.00 | 48.00 | 4.66±4.58 | 0.00 | 17.00 | -6.009 | 397 | 0.000 |
| **MEANRR** | 674.80±100.16 | 472.49 | 932.00 | 644.11±94.60 | 454.43 | 863.52 | -1.244 | 1103 | 0.213 |
| **TOTAL POWER** | 1813.82±991.03 | 448.19 | 4809.79 | 628.87±384.51 | 126.44 | 1744.61 | -7.122 | 229 | 0,000 |
| **LF/HF** | 1.53±0.96 | 0.18 | 3.88 | 3.55±3.82 | 0.37 | 22.48 | -4.422 | 630.5 | 0.000 |
| **LF POWER** | 971.30±599.41 | 266.85 | 3240.53 | 434.12±267.61 | 90.74 | 1071.72 | -5.568 | 460 | 0.000 |
| **HF POWER** | 842.52±677.79 | 181.34 | 4081.77 | 194.68±168.77 | 17.98 | 890.36 | -7.445 | 181 | 0.000 |
| **LF PEAK** | 0.09±0.03 | 0.04 | 0.15 | 0.09±0.09 | 0.04 | 0.70 | -1.323 | 1091.5 | 0.186 |
| **HF PEAK** | 0.24±0.08 | 0.15 | 0.45 | 0.25±0.10 | 0.15 | 0.48 | -0.475 | 1217.5 | 0.635 |

**Mann-Whitney U Test* SD: Standard deviation

**Hypotension ROC analysis with HF POWER**

In the ROC analysis conducted to assess the predictive power of HF POWER for post-spinal anesthesia hypotension in pregnant women, the AUC (95%) value was calculated as 0.925 (0.876-0.975). The cut-off value was determined as 327.05, with a sensitivity of 85% and specificity of 15% (p 0.0001) (Table 3) (Figure 2).



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As a result of the significance analyses conducted, the relevant parameters were subjected to ROC analysis. The ROC analysis of TOTAL POWER and HF POWER values revealed that they could be decisive parameters in predicting hypotension in terms of sensitivity and specificity. The intergroup values were found to be significant in the analysis of the average TOTAL POWER and HF POWER values of Group 1 and Group 2 patients, and high sensitivity was observed in the ROC analysis.

**Table 2.** Average of SBP (Systolic Blood Pressure) Values and Total Amount of Ephedrine Administered Between Patient Groups

| | Group 1 (N=46) | Group 2 (N=56) | p-value |
|---|---|---|---|
| **Average of Baseline SBP** | 127,66 ± 12,8 | 124,54 ± 11,43 | 0.202 |
| **Average SBP at 0-Minute Post-Spinal** | 114,41 ± 16,04 | 122,91 ± 20,09 | 0.022 |
| **Average SBP at 1 Minute Post-Spinal** | **94,33 ± 15,01** | **118,33 ± 15,25** | **<0,01** |
| **Average SBP at 3 Minutes Post-Spinal** | **89,74 ± 15,26** | **115,49 ± 16,30** | **<0,01** |
| **Average SBP at 5 Minutes Post-Spinal** | **99,13 ± 16,69** | **116,91 ± 19,2** | **<0,01** |
| **Average SBP at 15 Minutes Post-Spinal** | 112,3 ± 11,59 | 116,58 ± 12,04 | 0.060 |
| **Average SBP at 30 Minutes Post-Spinal** | 115,83 ± 11,08 | 115,11 ± 11,37 | 0.803 |
| **Average Total Amount of Ephedrine Administered** | **23,04 ± 4,65** | **2,36 ± 4,29** | **<0,01** |

Notes: Mean±Standard deviation. Systolic blood pressure values were calculated in mmHg and the amount of ephedrine administered was calculated in mg. SBP: systolic blood pressure

**Table 3.** Hypotension ROC analysis with TOTAL POWER and HF POWER

| | AUC (%95) | cut-off | p-value | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|
| **TOTAL POWER** | 0,905(0,848-0,963) | 984,07 | 0,00 | 0,83 | 0,17 |
| **HF POWER** | 0,925(0,876-0,975) | 327,05 | 0,00 | 0,85 | 0,15 |

Notes: AUC – Area under the curve

In cesarean-section surgeries, the desired outcome of anesthesia is maternal comfort and safety, along with fetal well-being and the maintenance of vital fetal functions without depression (1). In a study utilizing the 'Hypotension Prediction Index' (HPI) for preventing intraoperative hypotension, the guidance of the index did not meet the expectations of significantly reducing intraoperative hypotension (8). In an article related to the predictability of intraoperative hypotension, it was noted that artificial intelligence programs could accurately predict hypotension, but they did not improve clinical outcomes. It was suggested that with the development of 'Augmented Intelligence' programs, the cause of hypotension, including surgical manipulations, could be determined.



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These programs could guide clinicians regarding the choice of interventions, such as intravenous fluid replacement, vasoactive agents, or inotropic drugs, aiming to prevent hypotension (9).

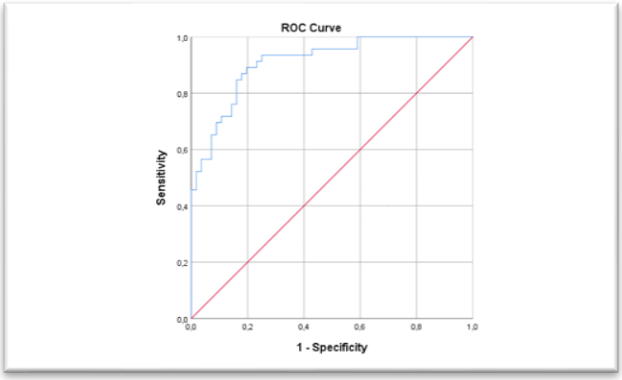


**Figure 1.** ROC analysis of TOTAL POWER in predicting hypotension

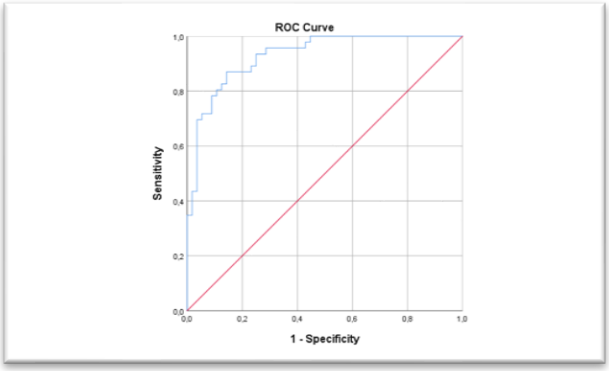


**Figure 2.** ROC analysis of HF POWER in predicting hypotension

One effective method for preventing hypotension following spinal anesthesia in obstetrics is the administration of ephedrine. Some studies on spinal anesthesia for cesarean delivery have defined a systolic blood pressure drop of 20% or more from baseline as 'hypotension' (3). Yeh, Chang, and Tsai (2020) characterized a 20% drop in systolic blood pressure measured as baseline as a 'hypotension criterion' and administering ephedrine at 20 mg or more as 'high-dose ephedrine' (10). Kang et al. found that the use of ephedrine was essential for preventing maternal hypotension and had a minimal impact on umbilical artery pH. They also suggested the use of 20 mg prophylactic ephedrine infusion for the prevention of maternal hypotension (11). In this study, the usage of ephedrine was considered a predictor of significant hypotension and was used as a criterion for grouping patients.

Some studies have suggested that heart rate variability measurements are related to hypotension following spinal anesthesia in cesarean surgeries. Hanss et al. found in their studies in 2005 and 2006 that patients with higher sympathetic tone were particularly sensitive to hypotension following spinal anesthesia, and an LF/HF ratio greater than 2.5 was indicative of severe hypotension in pregnant women (9,10). In Bishop et al.'s study from 2017, the LF/HF ratio was identified as an optimal threshold with a value of 2.0 for predicting obstetric spinal hypotension, indicating that heart rate variability analysis techniques have significant potential for predicting and managing hypotension (5). However, in this study, the LF/HF value showed negative significance but did not demonstrate the desired sensitivity in the ROC analysis.

Thomas et al. stated in 2019 that parameters such as SDNN, LF POWER, HF POWER, and LF/HF ratio were essential in predicting the health of the autonomic nervous system (12). In a study conducted by Frandsen et al. in 2022, they found that low TOTAL POWER and HF values measured on the day of surgery were indicative of intraoperative



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hypotension under general anesthesia (13). Eller in 2007 stated that TOTAL POWER and HF values were associated with atherosclerosis (14). Vinayagam et al. reported in their studies in 2019 that variables like SDNN and RMSSD were independently associated with hypotension and could be useful in predicting hypotension following spinal anesthesia (15). In Shehata et al.'s research from 2019, HRV was not predictive for hypotension in preeclamptic pregnant women (16).

This study is limited to patients undergoing cesarean section in the operating room unit of Erciyes University Hospital between October 2022 and March 2023and it is acknowledged that patients may vary in terms of mental stress and anxiety. Despite warning patients to "remain calm" during heart rate variability measurements before entering the operating room, it is unlikely that all patients will be equally unaffected by these factors.

## CONCLUSION

This study suggests that elevated TOTAL POWER and HF POWER values, measured by the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV,' indicate a higher likelihood of requiring vasoactive agents for hypotension after spinal anesthesia during cesarean surgery. Despite being an indirect measure of autonomic activity, this device offers a practical means of predicting hypotension in routine cesarean operations. Implementing interventions like preoperative fluid replacement and positioning adjustments for high HF POWER and TOTAL POWER values could mitigate intraoperative hypotension severity. Future research with a larger patient cohort and artificial intelligence integration aims to enhance predictive accuracy for vasoactive agent requirements during elective cesarean surgeries.

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None.

**Conflict of Interest**
None of the authors in the study have any conflict of interest.

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**Authors' Contributions**
All authors have contributed to all processes in this research.

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Case Report

# PULSED RADIOFREQUENCY ON SPHENOPALATINE GANGLION AS THE INTERVENTIONAL PAIN MANAGEMENT IN CLUSTER HEADACHE SECONDARY TO SPHENOID MENINGIOMA

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## ABSTRACT

**Introduction:** Cluster headache is one of the neurovascular headaches characterized by severe recurrent unilateral pain distributed around the orbit and accompanied by autonomic symptoms such as lacrimation, conjunctival injection nasal congestion or rhinorrhea, edema of the eyelid, sweating, and miosis. The attack usually lasts for 15 to 180 minutes. The possible mechanism of cluster headache is through the trigeminal-autonomic reflex. Management of the cluster headache is divided into pharmacological therapy including abortive and prophylaxis, as well as interventional pain management like deep brain stimulation, occipital nerve stimulation, and radiofrequency of the sphenopalatine ganglion. **Objective:** This report aims to demonstrate the effectivity of pulsed radiofrequency sphenopalatine ganglion on cluster headaches secondary to meningioma. **Case Report:** A 47-year-old female consulted the pain clinic with a chief complaint of profound facial pain for a year. The patient also reported autonomic symptoms such as rhinorrhea and lacrimation. The patient was diagnosed with meningioma and already treated with conventional therapy such as gabapentine, carbamazepine, omeprazole, and mecobalamin. Due to the location of meningioma which causes the tumor inoperable. The patient complained of constant and worsening pain, therefore pulsed radiofrequency on sphenopalatine ganglion was chosen to treat the patient. The patient reported relief of pain ever since. **Discussion:** Among the consequences and benefits, pulsed radiofrequency is the choice of interventional pain management. Possibly the pain from the compression of the greater palatine nerve, intervention on the sphenopalatine will cause relief of the pain. Pulsed radiofrequency on sphenopalatine ganglion was reported successful in alleviating the pain of the patient. **Conclusion:** Pulsed radiofrequency of the sphenopalatine ganglion successfully alleviates the pain of the cluster headache due to meningioma. However, further study with a bigger population is recommended to see the efficacy of interventional pain management objectively.

**Keywords:** Intervention Pain Management; Pulsed Radiofrequency; Secondary Cluster Headache; Sphenoid Meningioma; Sphenopalatine Ganglion

## ABSTRAK

**Pendahuluan:** Nyeri kepala cluster merupakan nyeri kepala neurovaskuler yang ditandai dengan nyeri unilateral berat rekuren yang berada di daerah orbita dan adanya gejala otonom seperti lakrimasi, injeksi konjungtiva, kongesti nasi atau rhinorrhea, edema pada kelopak mata, berkeringat dan miosis. Serangan umumnya berdurasi 15 menit sampai dengan 2 jam. Mekanisme yang mendasari kemungkinan disebabkan refleks trigeminal otonom. Manajemen nyeri kepala kluster dibagi menjadi terapi farmakologis yaitu abortif dan profilaksis serta terapi intervensi nyeri seperti *deep brain stimulation, occipital nerve stimulation* dan radiofrekuensi pada ganglion spenopalatin. **Tujuan:** Studi ini bertujuan untuk demonstrasi efektivitas *pulsed radiofrequency* ganglion spenopalatin pada nyeri kepala kluster akibat meningioma. **Laporan Kasus:** Perempuan 47 tahun dikonsultasikan pada klinik nyeri dengan keluhan utama nyeri kepala hebat selama 1 tahun. Pasien menyebutkan adanya gejala otonom seperti rinorea dan lakrimasi. Pasien terdiagnosis meningioma dan mendapat terapi konvensiopnal seperti gabapentin, carbamazepine, omeprazole, dan mecobalamin akibat lokasi meningioma yang menjadi kasus yang tidak dapat dilakukan pembedahan. Adanya nyeri yang konstan dan memburuk, radiofrekuensi berdenyut pada ganglion spenopalatin menjadi pilihan untuk terapi pasien. Pasien melaporkan nyeri berkurang setelah dilakukan intervensi. **Diskusi:** Menimbang keuntungan dan kerugian manajemen intervensi nyeri lainnya, PRF merupakan pilihan manajemen intervensional nyeri. Radiofrekuensi berdenyut dilaporkan berhasil mengurangi nyeri pada pasien. **Kesimpulan:** *Pulsed radiofrequency* pada ganglion spenopalatin



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berhasil mengurangi nyeri kepala kluster akibat meningioma. Namun dibutuhkan dilakukan studi lebih lanjut untuk melihat efektivitar terapi secara objektif.

**Kata kunci:** Manajemen Nyeri Intervensi; Radiofrekuensi Berdenyut; Nyeri Kepala Kluster Sekunder; Meningioma Sphenoid; Ganglion Spenopalatin

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## INTRODUCTION

Cluster headache is one of the neurovascular headaches which usually triggered by vasodilators such as alcohol or nitroglycerin (1). The characteristic of cluster headache is severe recurrent unilateral pain usually distributed around the orbit. The symptoms are usually accompanied by autonomic cranial symptoms such as lacrimation, conjunctival injection, nasal congestion or rhinorrhea, edema of the eyelid, sweating, and miosis. The duration of the attack is from 15 minutes to 180 minutes (2). In August 2007, a meta-analysis found during 1-year prevalence, the number of cluster headaches ranged from 3 to 150/100,000 cases. The sex ratio on cluster headaches differs according to the type of cluster headaches and the age of the onset. During the age of onset under 50 years old, both episodic and chronic cluster headaches happened to males more likely than females. Meanwhile, on the age of onset of 50 years old, the distribution differed, episodic cluster headaches were more likely to happen to males, while chronic cluster headaches were more likely to happen to females (3).

Cluster headache possibly caused by activation of trigeminal-autonomic reflex. The trigeminal-autonomic reflex is a connection in the brainstem that connects between the trigeminal nerve and facial cranial nerve parasympathetic outflow. The reflex is usually triggered by the stimulation of the trigeminovascular pathway. Through the sphenopalatine ganglion, the reflex is also activated through the parasympathetic outflow from the superior salivatory nucleus, and the cranial nerve which causes vasodilatation and parasympathetic activation (3). Other than the primary cause, cluster headaches are also caused by other etiologies such as nasopharyngeal carcinoma, sphenoidal meningioma, carotid artery dissection, vertebral artery dissection, pituitary adenoma, or aneurysm (KOU) (4).

Management of cluster headaches varied from conservative to interventional management. Conservative therapy from abortive therapy such as the use of oxygen, ergotamine, or sumatriptan injection. The use of verapamil is still widely applied for prophylactic therapy. When the conservative therapy is ineffective, and the pain recurrent the clinician should start to consider interventional management like radiofrequency of the ganglion pterygopalatine (PPG), Occipital nerve stimulation (ONS), or deep brain stimulation (DBS) (5).

In this study, we reported the case of secondary cluster headache due to sphenoid meningioma. Due to the tumor being inoperable, we need to gather the physicians to alleviate the pain. This report aims to demonstrate the effectivity of pulsed radiofrequency sphenopalatine ganglion on cluster headaches secondary to meningioma.



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## CASE REPORT

A 47-year-old female was consulted at the pain clinic for interventional pain management. The patient came with a chief complaint of profound facial pain. The pain has already been felt since one year ago but has worsened in the last two months. The pain was located in the right ocular area and radiated through the back of the head. Recently, the pain also radiated through the back of the neck. The quality of the pain was constant, and sharp stabbing. The pain was triggered while the patient prayed, looked up, woke up, and closed her eyes. The pain is constant during the day, but when triggered the pain worsens for 15 to 30 minutes.

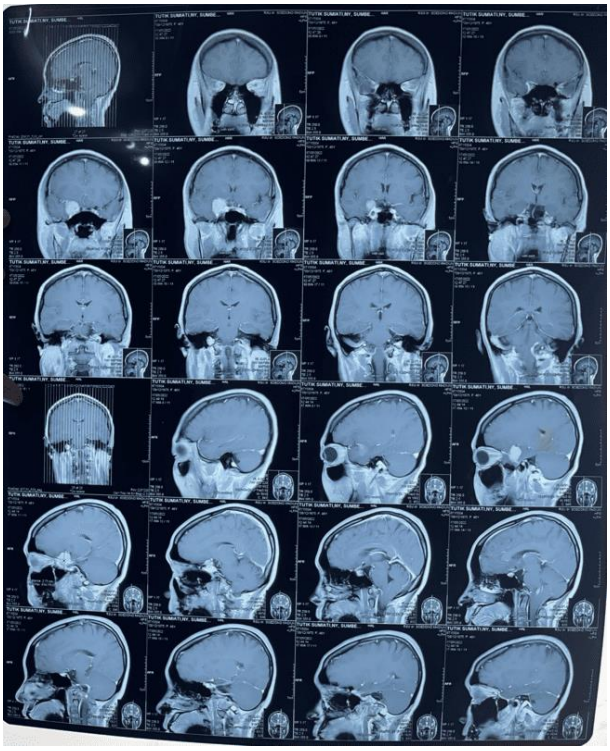

**Figure 1.** Coronal and Sagittal View MRI of the Patient

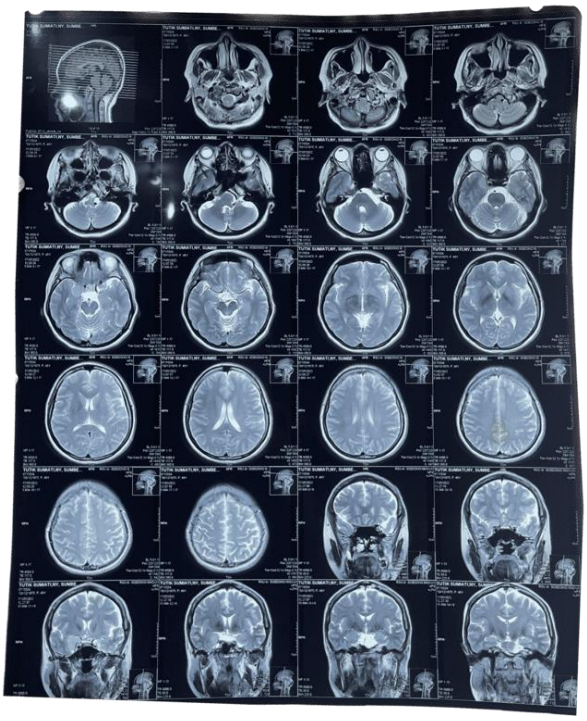

**Figure 2.** Coronal and Axial View MRI of the Patient

The patient first comes to the ophthalmologist due to the ocular pain, there are no visual disturbances, double vision, tunnel vision or floaters. The patient was cleared because of no apparent disturbances in her vision.

The patient was prescribed hyaluronic acid eyedrops. The pain did not subside, then the patient went to the neurologist and was diagnosed with migraine due to unilateral headache. The patient was given ibuprofen but still the pain has not subsided.

The patient was taken to MRI and found a meningioma on the right super-sellar which pressed the dextrous optic chiasm with the size 1.9 x 2.5 x 2.7cm. The patient has a history of three-month birth control injections for fourteen years. Before the patient was referred to the neurosurgeon, the neurologist was prescribing gabapentin, phenobarbital, and dexamethasone.



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The patient was referred to the neurosurgeon and prescribed mecobalamine, gabapentin, carbamazepine, and omeprazole. Due to the location of the meningioma, the management taken was conventional and nothing invasive. The neurosurgeon then referred to the pain clinic for interventional pain management.

When asked the Numeric Rating Scale (NRS) from 0 to 10, with 0 being pain-free and 10 being the worst facial pain in her life, the patient answered the scale was 7-9. The pain disturbed her daily activities such as bathing, eating, and her quality of sleep. During the attack, the patient also experienced autonomic symptoms such as rhinorrhea, and lacrimation (epiphora). The patient had no history of hypertension, diabetes, or allergy.

The vital signs of the patient were compos mentis with a total Glasgow coma score (GCS) of fifteen. Blood pressure was 120/80 mmHg, with 79 beats per minute, regular. The temperature was 36 degrees Celsius, and the respiratory rate was 16 times per minute.

The patient was given sphenopalatine ganglion block for the pain intervention. The empiric therapy given included bedrest, slight head up thirty degrees, ringer acetate (RA) solution 1500cc/24hours, fentanyl drip 100mcg/kolf of RA solution, tramadol administered per oral twice daily, amitriptyline per oral twice administered twice daily, ondansetron 40mg injection administered twice daily intravenous, and topazole 40mg injection administered twice daily intravenous.

The patient also did a diagnostic procedure to confirm the sensitivity of the sphenopalatine ganglion block beforehand. The patient was prepared in a supine position with an extending cervical spine. The transnasal approach will be done with a cotton tip applicator, therefore needed to measure the estimated depth of the cotton tip applicator by measuring the opening of the nares to the mandibular notch below the zygoma. The applicator was soaked with lidocaine 1% and then inserted into the nares parallel to the zygoma, angled laterally until it lays on the nasopharyngeal mucosa posterior to the middle nasal turbinate. Then the second applicator was applied slightly posteriorly and cranially to the initial applicator. The patient well responded to the diagnostic block by confirming the current NRS was 1-2, which has proven sensitive to future intervention.

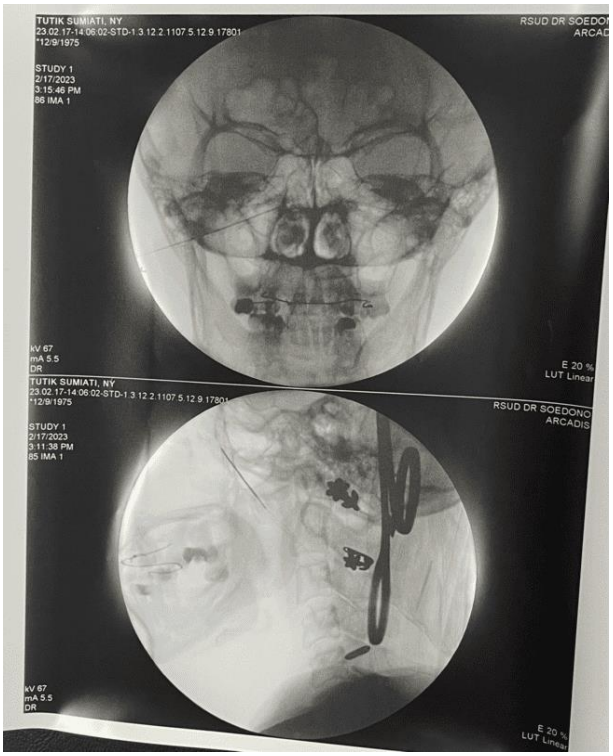


**Figure 3.** Fluoroscopy Imaging of the Intervention

The intervention began with positioning the patient supine on the operation table. The area of the intervention which is the zygoma area disinfected with betadine and alcohol and later



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covered with sterile draping. The intervention was guided by fluoroscopy and positioned both AP and lateral projection. The local anesthetized by lidocaine 1% infiltrated around the injection area until wheal was formed. The needle is inserted by inferior to the zygomatic arch and directed medially in coaxial view until the zygomatic arch is passed. Then needle slightly redirected the cephalad into the pterygopalatine fossa. The depth of the needle was later confirmed by the AP projection of the fluoroscopy.

The stimulation began with sensory stimulation at 0.15Hz 2.5mV then followed by motoric stimulation at 5mV. The pulsed radiofrequency was used with 10 Ampere with 2 mV with four cycles of four minutes at 42 degrees Celsius. The bleeding caused by this procedure was minimal.

Following the procedure, the patient only felt pain in the injection area, which is still and locally anesthetized using lidocaine 1%. Patients did not experience epistaxis, transient anesthesia or hypoesthesia, lacrimation of the eye, or local or retroorbital hematoma.

The patient was prescribed paracetamol three times a day for the anti-inflammation, amitriptyline twice a day as the prophylactic therapy, and tramadol twice a day as needed for the painkiller.

The day after the procedure, said the patient the pain was abruptly lessened. The NRS was between 1-2 on the dextrous area. The patient felt comfortable with the daily activities. And the pain is still constant with NRS 1-2 until day 5 after the procedure. Patients were followed after 10 months post interventional pain management, and the NRS still constant in 1-2. The patient is still able to tolerate the pain and the pain does not interfere with her daily activities.

## DISCUSSION

Meningioma can cause several alterations in the physiology of the brain such as increased intracranial pressure, compression of pain-sensitive structures (dura, blood vessels, periosteum), secondary to difficulty with vision, extreme hypertension (part of cushing triad), and also psychogenic due to stress from loss of functional capacity (5). A study conducted by Hadidchi, et al (6), states 40% of meningioma showed the symptom of meningioma-associated headache, with tension-type headache as the most likely type shown. The characteristic of the headache is mostly dull, with NRS 4-6, without trigger, and bilateral. These findings are in contrast with the patient due to the characteristic of the pain sharp, with NRS 7-9, trigger-involved and unilateral.

According to the International Classification Headache Society (7), cluster headache is described as severe unilateral pain usually located orbital, supraorbital, and temporal and lasts between 15 and 180 minutes. The autonomic symptoms such as ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead, and facial sweating, miosis, ptosis, and/or eyelid edema and or agitation usually accompany the cluster headache. This type of headache matches our finding in this report, in which the patient complained of sharp pain in the right orbital area with lacrimation and rhinorrhea. The patient also felt symptoms for approximately 9 months. This complaint matches the ICHS criteria for chronic cluster headaches (7).



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Prevalence of the cluster headaches is about 0.1% worldwide, which mostly happens to males. Due to the rare incidence of cluster headaches, the incidence of cluster headache-secondary to meningioma becomes rarer. Secondary cluster headaches are usually caused by nasopharyngeal carcinoma, sphenoidal meningioma, carotid artery dissection, vertebral artery dissection, pituitary adenoma, or aneurysm (4). With the MRI confirmation, the patient has meningioma located on suprasellar dextra. Possibly the patient had a secondary cluster headache due to the meningioma.

The position of the meningioma itself possibly induces the cluster headache. With the MRI, the position of the meningioma on this patient posteriorly to the orbital fissure which presses the greater palatine nerves. The greater palatine nerve is one of the sensory fibers of the sphenopalatine ganglion which supplies the sensation of the palate, and mucus membrane and also the sympathetic vidian nerve passing through the SPG which is distributed later to the nose, palate, and lacrimal gland, this possibly explained the symptoms of rhinorrhea and lacrimation of the patient (8). This theory aligned with a systematic review in 2020, which showed secondary cluster headaches associated with 37.7% vascular pathologies and 32.5% due to tumor pathologies including brain mass-like lesions (9).

The cluster headache pathophysiology includes the trigeminal system, parasympathetic system, and hypothalamus mediated. The trigeminal system plays a role where there is a trigeminal nococervical complex that modulates and transmits potentially painful stimuli from the face and head to the brain (8). Study (10) showed evidence of mast cells in all grade meningioma, mostly in high grade. With the activation of mast cells, it will release multi-potent molecules, one of them is histamines (11). Histamine works as a vasoactive substance, which will cause vasodilatation. The patient already felt the pain for almost 10 months without remission, which according to the IHS diagnosed with chronic cluster headache. Due to the location of the meningioma, the neurosurgeon decides the tumor is inoperable, which according to the studies before shows complete relief of pain after tumor resection (12,13). Treated with conventional therapy like carbamazepine, mecobalamine, and gabapentine for 10 10-month periods the patient admitted there was no significant difference in pain levels. The patient also complained two weeks recently, that the pain had worsened Therefore, this suggests the therapies are ineffective for this patient and need to consider possible interventional pain management.

The patient was done diagnostic block transnasal with lidocaine 1% and proven to relieve the pain with confirming from VAS 7-9 to VAS 1-2. Relief of the pain confirms the patient might be sensitive to the sphenopalatine ganglion block. The intervention was done with pulsed radiofrequency at 42 Celsius and four cycles of 120 seconds. The patient later confirmed the relief of the pain until the tenth month after the intervention follow-up. These findings aligned with studies before (14,15).

Sphenopalatine ganglion is hypothesized to play a role in the pathophysiology of trigeminal autonomic cephalgia (TAC) which includes cluster headache. The sphenopalatine ganglion parasympathetic effect mechanism is through the afferent signals from cranial vessels and dura mater get relayed through the trigeminal ganglion and then end in the trigeminal cervical complex.



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These signals then activate the superior salivatory nucleus then show sympathetic activity which correlates with the symptoms shown in patients such as rhinorrhea, and lacrimation (16).

Intervention pain management on sphenopalatine ganglion such as neural block, continuous radiofrequency, pulsed radiofrequency, and electrical stimulation was proven significant to relieve the patient pain on cluster headache (2,16–18). The SPG nerve block provides a positive result, and the side effect is typically local, which is a bitter taste and numbness of the throat. However, one study showed the need for repetitive intervention to reach long-term pain relief. The evidence of nerve block pain management is mostly case reports and case series, but there are few randomized controlled studies. Continuous radiofrequency or some called radiofrequency ablation, tends to have a longer-lasting effect than SPG nerve block. The side effects of CRF are more complex than the nerve block. Temporary paresthesia in the upper gums and cheeks which last for 3-6 weeks, and permanent hypoesthesia over the cheek and the palate, which disappeared within 3 months (18). CRF mechanism to alleviate the pain is via ablating the nociceptive nerve fibers, exposing the nerve to high temperatures (70- 90 Celsius degree) continuously. This mechanism is probably the reason why there are such profound uncomfortable side effects due to the damage to the nerve itself (19). The neurostimulation of SPG proved efficient for treating cluster headaches (18), but the utilities and infrastructure are unavailable.

Our rationale for choosing PRF laid on the main mechanism of the pulsed radiofrequency is neuromodulation. The neuromodulation process alters the excitability of c-fibers, which are commonly involved in neuropathic pain syndromes (19,20). PRF is also shown evident in some immune activity-pain pathways. The study showed PRF pain management resulted in decreased microglial activity, which is one of the neuropathic pain pathways. PRF also modulates inflammatory cytokines such as IL-6, IL-17, IFN-gamma, IFR8, and TNF-alpha, which mediate neuropathic pain (20). The other mechanisms include adjustment of the inner structure axons, gene expression, and inhibition of extracellular signal-regulated kinase (19). Studies have shown the increase of *c-fos* immunoreactive neurons in the superficial lamine of the dorsal horn three hours after application, meanwhile on conventional radiofrequency the enhancement starts on day seven after the intervention. This enhancing *c-fos* immunoreactive will form prepodinorphin which acts as endogenous analgesia. *c-fos* neuron also acts as an inhibitory interneuron that reduces nociception (21,22). Enhancement of *c-fos* is also inversely correlated with the excitability of C fibers which attenuates the neuropathic pain (19).

This intervention in pain management is also supported by the other study (15,23), which shows the long-term efficacy of the SPG PRF. Small prospective studies of 6 patients with chronic short-lasting unilateral neuralgiform headache with conjunctival injection and tearing accompanied by cranial autonomy symptoms showed that SPG PRF is considered a safe and effective treatment. Three patient patients experienced worsening head pain for two to four weeks after the procedure. However, the authors explained this is a common and high percentage due to the small population of the study (24).



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There are currently no reports on interventional pain management for cluster headaches secondary to meningioma with SPG PRF due to the rarity of the cases.

The study conducted by Ho and Elahi, 2014 (25) showed successful interventional pain management of cluster headaches secondary to sphenoid meningioma through SPG-CRF. The patient also reported NRS after the intervention pain management is 2-3, and able to wean off all of the narcotics drugs. Although the result of SPG PRF may vary possibly due to different parameters such as frequency, pulse width, temperature, time, cannula, and active tip size; varies tissue types like sympathetic ganglia, peripheral nerves, and DRG; and varies of species such as humans versus rodents (20). The incomplete pain relief in this case was hypothesized due to the presence of the inoperable meningioma still But, according to the patient, she was satisfied with the result and felt significant comfort than before the interventional pain management. She also did daily activity comfortably even at the 10 monthly follow up.

The limitations of this study is the lack of routine monthly follow-up to the pain clinic, and due to the rarity of the cases, future research needs to be done in a larger population and a longer time to determine the effectiveness of the SPG PRF on cluster headache secondary to meningioma pain management.

## CONCLUSION

From this study, pulsed radiofrequency on sphenopalatine ganglion block on cluster headache secondary meningioma can be an option whether the conventional therapy is already ineffective. This result needs further study which requires a bigger sample size, and a longer period of follow-up to conclude a more objective result.

**Acknowledgment**
None.

**Conflict of Interest**
The authors declare no conflict of interest

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**Authors' Contributors**
All authors have contributed to all processes in this research.

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Case Report

# PERIOPERATIVE MANAGEMENT OF MARFAN SYNDROME IN PREGNANCY AND CONGESTIVE HEART FAILURE

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**ABSTRACT**

**Introduction:** A mutation in fibrillin-1 (FBN1) leads to the autosomal dominant condition known as Marfan Syndrome (MFS). The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. Due to a greater frequency of maternal problems and fetal involvement, pregnancy with Marfan syndrome (MFS) provides challenges to healthcare professionals and patients and requires special treatment. **Objective:** This study aimed to analyze the perioperative management of Marfan syndrome in pregnancy and congestive heart failure (CHF). **Case report:** A 27-year-old primigravida with 38-39 weeks gestation presented with a referral letter with a diagnosis of G1P0A0 with scoliosis and peripartum cardiomyopathy. The patient complained of shortness of breath accompanied by cold sweat since the second trimester of gestation. Physical examination revealed the presence of arachnodactyly and spine deformity. The patient underwent an emergency cesarean section with general anesthesia. Breathing problem appeared the next day after cesarean section, the patient was intubated in the ICU. Chest X-ray depicted bilateral pulmonary edema. A mechanical ventilator was set up and fluid restriction had been done. The patient was extubated after showing breathing improvement in the second week in the ICU. **Discussion:** The diagnosis of MFS in this patient was defined based on the revised Ghent Nosology. MFS with spine deformity causes breathing problems because of the altered geometry of the thoracic cavity. MFS in pregnancy may worsen the breathing problem due to autotransfusion that leads to pulmonary edema. A mechanical ventilator with a specific setting accompanied by fluid restriction is recommended to reduce the fluid overload in the lungs. **Conclusion:** Mechanical ventilators with specific settings and fluid restriction are effective perioperative management to reduce pulmonary edema on MFS in pregnancy and congestive heart failure.

**Keywords:** Cardiovascular disease; Marfan Syndrome; Perioperative management; Pregnancy; Preventable death.

**ABSTRAK**

**Pendahuluan:** Mutasi pada fibrillin-1 (FBN1) menyebabkan kondisi dominan autosom yang dikenal sebagai Sindrom Marfan (MFS). Kehamilan dengan MFS dapat meningkatkan morbiditas dan mortalitas terkait kehamilan dan persalinan. **Tujuan:** Laporan kasus ini akan menganalisa manajemen perioperatif Marfan Syndrome dengan gravida dan gagal jantung kongestif. **Laporan kasus:** Seorang wanita 27 tahun dengan hamil 38-39 minggu dengan diagnosis G1P0A0 dan skoliosis dan gagal jantung. Pasien mengeluh sesak disertai keringat dingin sejak trimester 2. Pemeriksaan fisik ditemukan araknodaktili dan deformitas tulang belakang. Kemudian dilakukan *section caesarea* segera dengan anestesi total. Sehari pasca operasi, pasien mengeluh sesak dan diputuskan untuk dilakukan intubasi di ICU. Rontgen thorax menunjukkan edema paru bilateral. Dilakukan pengaturan ventilator yang tepat dan restriksi cairan. Pasien di ekstubasi pada minggu kedua di ICU setelah menunjukkan perbaikan pernafasan. **Diskusi:** Penegakan diagnosis MFS pada pasien ini berdasarkan Nosologi Ghent yang telah direvisi. MFS yang disertai dengan kelainan tulang belakang dapat menimbulkan masalah pernafasan akibat berubahnya bentuk dan lapang rongga dada. MFS pada kehamilan juga memperparah masalah penafasan akibat autotransfusi yang dapat menyebabkan edema paru. Pengaturan ventilator yang disesuaikan dengan derajat keparahan ARDS serta restriksi cairan yang tepat dapat mengurangi penumpukan cairan pada paru. **Kesimpulan:** Pengaturan ventilator yang spesifik dan restriksi cairan yang tepat merupakan manajemen perioperative yang efektif untuk mengatasi edema paru pada MFS dengan gravida dan gagal jantung kongestif.

**Keywords:** Penyakit Kardiovaskular; Sindroma marfan; Manajemen perioperatif; Kehamilan; Kematian yang dapat dicegah.

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## INTRODUCTION

A mutation in fibrillin-1 (FBN1) leads to the autosomal dominant condition known as Marfan Syndrome (MFS). This syndrome has various manifestations including aortic aneurysm that can be followed by ectopia lentis, aortic dissection, and other systemic abnormalities. Cardiovascular abnormalities findings, such as progressive aneurysm of the aortic root are considered the highest mortality risk for Marfan Syndrome (MFS). The progressive aneurysm of the aortic root could lead to aortic dissection and rupture if the corrective surgery was not performed (1). The diagnosis of MFS depends on specific clinical criteria (updated Ghent nosology), although this can be complicated because aspects of the disease change based on the patient's age, while others are seen regularly in the general population, with significant phenotypic diversity. Certain manifestations of MFS also overlap with other connective tissue diseases (2).

Although MFS is an uncommon condition (1:5.000), the prevalence is estimated to be substantially higher among athletes, particularly in sports where height and longer limbs provide them a significant advantage. Voley ball is one of the examples, which is classified as a moderate dynamic and a low static sport (3). However, this does not rule out the possibility that it will occur in pregnant women. Goland described AoD in 29 of 39 cases of pregnancy-related difficulties, including the ascending aorta (19 cases), descending aorta (8 cases), or both (2 cases). Eight of these women had not been diagnosed with MFS before the emergence of aortic issues. (5).

“These patients need anesthesia treatment either for heart surgery or other operations. Patients who are diagnosed with cardiac disease should be referred to a higher center with adequate monitoring facilities and professionals for peripartum and perinatal care. The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. The anesthesiologist has to understand the history of the patient and possible side effects of the surgical procedure, this aims to assess the risks and suitable anesthesia treatment for the patient.” (6). Because of a greater prevalence of maternal problems and fetal involvement in pregnancy with Marfan syndrome (MFS), healthcare professionals and patients face unique obstacles (4). Therefore, in this case report, the authors will conduct an analysis of the perioperative management of Marfan syndrome in pregnancy and congestive heart failure (CHF).

## CASE REPORT

A 27-year-old primigravida with 38-39 weeks gestation presented to the emergency obstetrics and gynecology department of Dr. Soedono General Hospital with a referral letter from Dolopo General Hospital. The patient was referred with G1P0A0 with scoliosis and peripartum cardiomyopathy. The patient complained of persistent uterine contraction for the past two days. The patient was referred from the previous hospital due to pulmonary edema and a high risk of cardiovascular disease. The patient complained of shortness of breath accompanied by cold sweat since the second trimester of gestation. Shortness of breath gets worse with activity and doesn't get better with lying down. Previously, the patient had been receiving treatment since she was 11 years old due to her complaint of shortness of breath. It was suspected by the doctor at that time that the patient had a heart condition and scoliosis, so



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she had to take regular medication forever. However, the patient did not take medication regularly. The patient has no history of allergies and surgery.

The patient appeared short of breath and was first seen with a thin and tall stature with a sunken chest. Physical examination revealed the presence of arachnodactyly and spine deformity. The patient's consciousness is *compos mentis*, blood pressure was 128/94 mmHg, and the pulse was increasing to 118 beats per minute. The patient had a temperature of 37,5ºC, oxygen saturation of 98% (in 3 liters per minute of the nasal cannula), and was tachypneic with a respiratory rate of 34 breaths per minute. The obstetric examination resulted in a fundal height of 26 cm and a fetal heart rate of 124 beats per minute. Cervical exam revealed ± 1 cm dilated, 25% effaced, and -1 station. Chest X-ray showed normal lungs and heart radiographic appearance and severe thoracolumbar scoliosis with right convexity.

Complete blood count test showed Hemoglobin 11.2 g/dL, platelets $371x10^3/\mu L$, Hematocrite 43.1%, total leucocytes count $10.53x10^3/\mu L$, erythrocytes count 5.69 juta/cm, MCV 75.7 fL, MCH 22.5 pg, MCHC 29.7 g/dl. The coagulation test showed PT 8.7 second (Control 11.9) and APTT 26.5 The liver function test showed albumin 2.94 g/dl (N 3.5-5), SGOT 20 U/L (N 8-31), SGPT 18 U/L (N 6-31). The kidney function test showed blood urea 6 mg/dl (N 10-20), and creatinine 0.56 mg/dl (N 0.6-1.1). A random blood glucose test showed 112 mg/dl (N 136-145). The electrolytes blood test showed natrium 132 mmol/L (N 136-145), calium 4.90 mmol/L (N 3.5-5.1), and calcium ION 1.03 mmol/L (N 1.12-1.32). The immunological test showed anti-HIV non-reactive and HbsAg Negative.

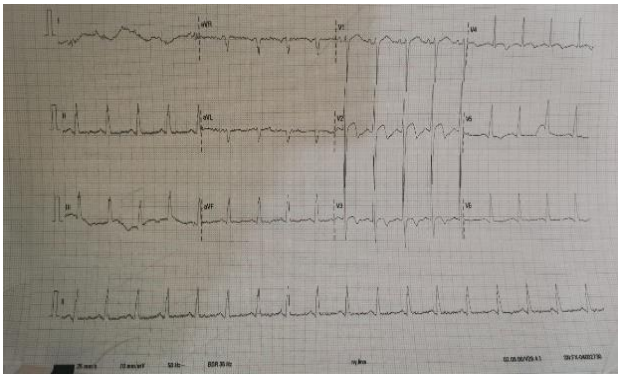

**Figure 1.** The Electrocardiography Showed Sinus Rhythm and Left Ventricle Hypertrophy

## Treatment

The patient was diagnosed with G1P0A0, 38/39 weeks inpartu *latent phase* with scoliosis dan peripartum cardiomyopathy. The patient had planned an emergency cesarean section with general anesthesia. There was no problem during the surgery and the patient was moved to the maternity ward in stable condition. Post SC treatment was Ringer Lactate infusion of 20 drops per minute, Ketorolac injection of 30 mg/8 hours, and Ondancetron injection of 4 mg/8 hours.

## Result and Follow-Up

The next day after the C-Section procedure, the patient complained of shortness of breath and then was given 3 liters/minute oxygenation with a nasal cannula. The complaint was getting worse that night, and the anesthesiologist decided to undergo intubation for indications of persistent shortness of breath due to suspicion of pulmonary edema. The patient was then referred to the Intensive Care Unit (ICU) to have a ventilator which was set to BIPAP $FiO_2$ 70%, PEEP 5 $cmH_2O$, PIns 8 cmH2O, PSupp 8 $cmH_2O$. Mean Arterial Pressure (MAP) was maintained above 65 mmHg and a fluid deficit of 2000-4000 cc per day. Echocardiography and chest X-ray were planned for the next day. Intravenous drugs were prescribed by the anesthesiologist;



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Aminofluid infusion 500cc/ 24 hour, nutritional milk on nasogastric tube 6x100cc, Cefotaxime injection 1gr/8hr, Pantoprazole injection 40mg/12hr, Paracetamol 500mg/8hr (if needed), Dobutamin on syringe pump 4mcg/hr, Vasoconstrictor on syringe pump 50nn/hr, Furosemide injection 10mg/hr. Cripsa 2,5mg/24hr and Caralan 5mg/12hr were given as oral medications.

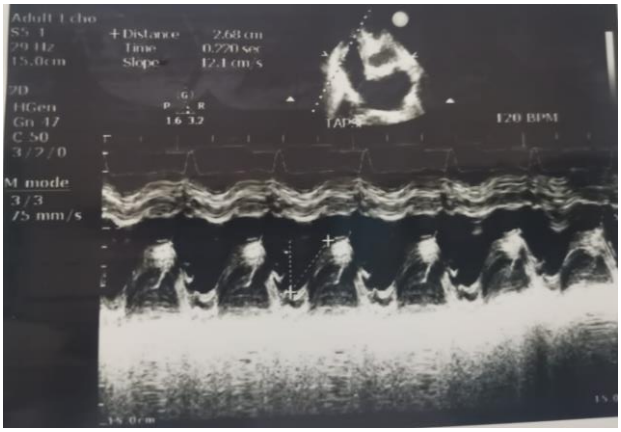

**Figure 2.** Echocardiography

Echocardiography revealed the systolic function of the Left Ventricle (LV) was normal with an Ejection Fraction (EF) of 56% and the diastolic function of the LV was impaired relaxation. The function of the Right Ventricle (RV) was normal. The result of blood gas examination showed that pH 7.33, PCO2 70 mmHg, PO2 149 mmHg, Bicarbonate (HCO3) 37.6 mmol/L, Excess Base (EB) 9.5 mmol/L, Oxygen Saturation (SO2) 99.0%, and temperature 36,0 ºC

On the sixth day of follow-up in the ICU, the shortness of breath was diminished and the condition showed improvement in breathing. Another anteroposterior chest X-ray was planned for further evaluation and the result showed normal lungs and heart radiographic appearance and severe thoracolumbar scoliosis with right convexity.

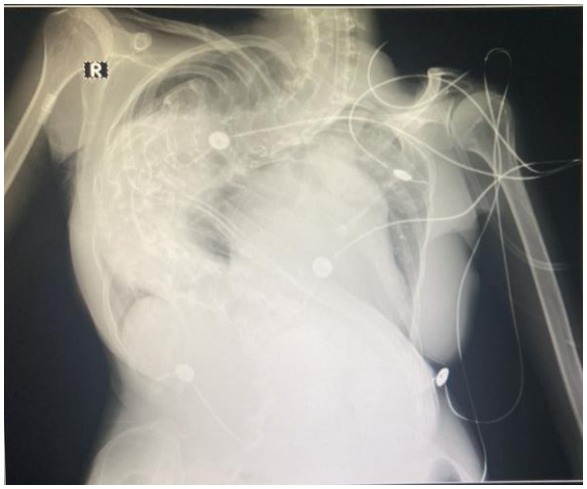

**Figure 3.** Chest X-ray Depicting Bilateral Pulmonary Edema

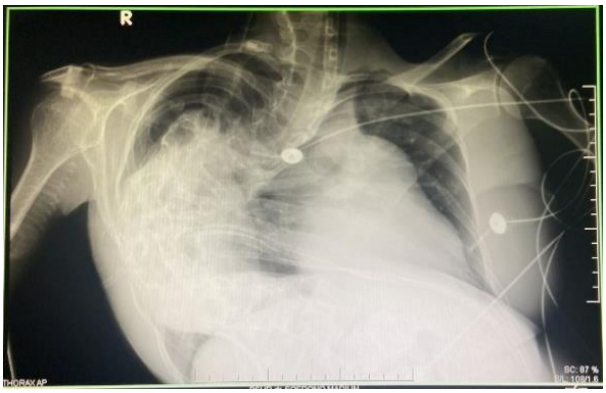

**Figure 4.** Radiological evaluation Chest X-rays on the sixth day in the ICU

After the evaluation, ventilator weaning was demonstrated gradually and MAP was maintained above 60 mmHg. On day 14 in ICU, the patient's condition showed improvement, and shortness of breath was completely diminished so that the patient could be extubated and moved to the High Care Unit (HCU) for monitoring, then moved to the maternity ward for 5 days before discharge.

## DISCUSSION

New diagnostic guidelines for patients with or without a family history of Marfan syndrome have been provided in the 2010 revised Ghent nosology. In the absence of an established family history of Marfan's



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syndrome, the diagnosis might be made using one of the following methods:

1. Regardless of the presence or absence of systemic features, the diagnosis of Marfan syndrome can be made in the presence of aortic root dilatation or dissection and ectopia lentis, unless there are indications for Sphrintzen-Goldberg syndrome (SGS), Loeys-Dietz syndrome (LDS), or vascular Ehlers-Danlos syndrome (vEDS).
2. The presence of aortic root dilatation or dissection and FBN1 mutation) is sufficient to establish the diagnosis even when ectopia lentis is absent.
3. The presence of aortic root dilatation or dissection with no ectopia lentis and FBN1 status is either unknown or negative, the diagnosis of Marfan syndrome is confirmed by the presence of other systemic findings (≥7 points, according to the new scoring system). However, signs suggestive of SGS, LDS, or vEDS should be ruled out and suitable alternative genetic tests (TGFBR 1/2, collagen biochemistry, COL3A1, and other relevant genetic tests when indicated) should be performed.
4. Before diagnosing Marfan syndrome in the presence of ectopia lentis without aortic root dilatation or dissection, an FBN1 mutation previously associated with aortic disease must be identified. If the FBN1 mutation is not linked to cardiovascular illness, the patient should be labeled as having "ectopia lentis syndrome" (7).

In this case, the physical examination of this patient revealed a sunken chest/pectus deformity, arachnodactyly, and spinal deformity as severe thoracolumbar scoliosis. Ectopia lentis as one of the clinical signs of MFS appeared in this patient accompanied by high myopia. The diagnosis of MFS can be established by the following clinical signs according to Ghent Nasology diagnostic criteria with a total systemic score of 10 (8).

The patient has severe thoracolumbar scoliosis. This is one of the musculoskeletal manifestations caused by the abnormalities of the connective tissues as a result of the mutation of FBN1. The musculoskeletal manifestations in MFS include spinal deformities, chest wall deformities, and low back pain. This patient suffered from breathing difficulty because of her severe scoliosis. Scoliosis affects the geometry of the chest and reduces the three-dimensional range of motion of the thoracic cage and spine during breathing. This may result in reduced lung capacities, limited diaphragmatic excursion, and inefficiency of the chest wall muscles (9).

Mechanical ventilation may help to overcome the breathing problem. Another breathing problem in this patient came from bilateral pulmonary edema that was caused by autotransfusion in pregnancy. Approximately ±20-30% of blood volume enters the circulation as the result of uterine contractions (10). There is an increase in cardiac output of 60 to 80% and also an increase in peripheral resistance in the lungs (10). The presence of MFS prompted the occurrence of pulmonary edema. The connective tissues in the lungs become looser and the movement of fluid from intravascular to interstitial becomes faster rather than the condition without MFS (9).

A mechanical ventilator was used in this case to reduce the pulmonary edema and to overcome the breathing problem. The severity of acute respiratory distress syndrome (ARDS) caused by pulmonary edema needs to be considered before setting up the ventilator. According to the severity, ARDS is classified into three based on the following criteria (11):

1. Mild: 200 mm Hg < Pao2/Fio2 ratio ≤ 300 mm Hg with positive end-expiratory



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pressure (PEEP) or continuous positive airway pressure ≥ 5 cm H2O.
2. Moderate: 100 mm Hg < Pao2/Fio2 ratio ≤ 200 mm Hg with PEEP ≥ 5 cm H2O.
3. Severe: Pao2/Fio2 ratio ≤ 100 mm Hg with PEEP ≥ 5 cm H2O

In this case, the patient was classified into moderate ARDS, and the following recommendations for mechanical ventilator-specific settings are:

1. ARDS should be started at lower tidal volumes (6 mL per kg) instead of at traditional volumes (10 to 15 mL per kg),
2. Higher positive end-expiratory pressure values (12 cm $H_2O$) should be considered for initial mechanical ventilation in patients with ARDS,
3. Prone positioning for 12 to 16 hours per day,
4. Prophylaxis for venous thromboembolism should be given to all patients,
5. Enteral feeding should be initiated if a patient is anticipated to be on a ventilator for 72 hours,
6. Spontaneous breathing trials guided by a ventilator liberation (weaning) protocol should be initiated once a patient with ARDS begins to improve. (11)

Fluid therapy, in addition to the ventilator setting, must be explored in this patient. The goal is to maintain tissue perfusion, integrity, and function while restoring intravascular volume to maximize hemodynamic parameters. (12). It is matched with Malbrain's statement that also recommend the ROSE concept of fluid balance therapy, which shows the relationship between positive fluid balance and overload fluid in critically ill patients (13).

The administration of loop diuretic drugs in this case may reduce fluid overload. The mechanism of action of the drug is by inhibiting the co-transporter Na+/2Cl-/K+ in the thick ascending loop of Henle where one-third of the filtered sodium will be reabsorbed. This process can decrease sodium and chloride reabsorption and increase diuresis (14). Loop diuretic drugs may increase the synthesis of prostaglandins which cause kidney and venous dilation. This effect will indirectly reduce pulmonary wedge pressure. Loop diuretic drugs may also decrease electrolytes such as potassium, magnesium, calcium, and chloride. Furosemide can be given 20-40 mg twice a day with a maximum dose of 600 mg per day (14).

Patients with heart failure should avoid excessive fluid intake, according to European Society of Cardiology (ESC) guidelines. For severe heart failure, a fluid restriction of 1.5–2 liters per day is advised. Fluid restriction has been shown to have a favorable effect. Fluid restrictions of 1000 cc per day with explicit instructions or 2000 cc per day without specific instructions can improve quality of life. Fluid restriction is not always recommended for all patients with heart failure, but this therapy can be considered for patients with poor quality of life, low adherence to medication, and decompensated heart failure with or without hyponatremia. Fluid restriction can be adjusted based on body weight at 30 ml/kg/day (15).

## CONCLUSION

Marfan Syndrome is an inherited disorder that affects connective tissue. The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. During pregnancy, many changes occur in the cardiovascular system, one of which is autotransfusion. This condition may cause an increase in cardiac output which leads to pulmonary edema and respiratory failure. A mechanical ventilator with specific settings and fluid restriction can be used to reduce the clinical symptoms.



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Case Report

# COMBINED SPINAL-EPIDURAL ANESTHESIA WITH ISOBARIC ROPIVACAINE 0.375% FOR INGUINAL HERNIA SURGERY IN A HEART FAILURE PATIENT WITH EJECTION FRACTION OF 36%

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## ABSTRACT

**Introduction:** Heart failure is a condition caused by myocardial abnormalities that interfere with the fulfillment of the body's metabolism. It is one of the primary causes of high perioperative morbidity and mortality rates, and its management presents a challenge to anesthesiologists. **Objective:** To demonstrate combined spinal-epidural anesthesia with isobaric ropivacaine 0.375% for inguinal hernia repair surgery in a heart failure patient with an ejection fraction of 36%. **Case Report:** A 53-year-old man presented with a complaint of a lump on his left groin accompanied by pain with a visual analog scale (VAS) pain score of 3/10 three days before admission. The patient was also known to often complain of shortness of breath and chest palpitations when lying down at night and during strenuous activity. Based on the examination, the patient was then diagnosed with reducible left lateral inguinal hernia and heart failure with LVEF 36%. Subsequently, the patient was scheduled for elective herniotomy-hernioraphy surgery under low-dose combined spinal-epidural anesthesia. Spinal anesthesia was performed with isobaric ropivacaine 0.375% and fentanyl 25 µg in a total volume of 3.5 ml at the L3-L4 intervertebral space. Epidural anesthesia was performed with isobaric ropivacaine 0.375% and fentanyl 25 µg in a total volume of 8 ml at the L2-L3 intervertebral space. After 10 minutes, the sensory block reached the T6 level, but the motor block was only partial (Bromage 1). A continuous infusion of isobaric ropivacaine 0.1875% 1 ml/hour was administered through the epidural catheter to control postoperative pain. During surgery and hospitalization, the patient's hemodynamic condition remained stable. **Conclusion:** Combined spinal-epidural anesthesia with isobaric ropivacaine 0.375% can provide adequate anesthesia with relatively stable hemodynamics, thus making it safe for inguinal hernia repair surgery in heart failure patients with reduced ejection fraction.

**Keywords:** Combined Spinal-Epidural Anesthesia; Isobaric Ropivacaine 0.375%; Inguinal Hernia; Heart Failure; Case Report; Anesthesia Management

## ABSTRAK

**Pendahuluan:** Gagal jantung adalah penyakit yang disebabkan oleh abnormalitas miokardium yang mengganggu pemenuhan metabolisme tubuh. Kondisi ini menjadi salah satu penyebab utama tingginya angka morbiditas dan mortalitas perioperatif sehingga penatalaksanaannya menghadirkan tantangan bagi ahli anestesi. **Tujuan:** Untuk memaparkan penggunaan kombinasi anestesi spinal-epidural dengan ropivacaine isobarik 0.375% untuk operasi perbaikan hernia inguinalis pada pasien gagal jantung dengan fraksi ejeksi 36%. **Laporan Kasus:** Seorang pasien laki-laki berusia 53 tahun datang dengan keluhan terdapat benjolan pada lipatan paha sebelah kiri disertai nyeri dengan skor nyeri *visual analog scale* (VAS) 3/10 sejak tiga hari sebelum masuk rumah sakit. Pasien juga diketahui sering mengeluhkan sesak napas disertai dada yang berdebar-debar saat berbaring di malam hari dan saat beraktivitas berat. Berdasarkan pemeriksaan, pasien kemudian didiagnosis dengan hernia inguinalis lateralis kiri yang dapat direduksi dan gagal jantung dengan LVEF 36%. Selanjutnya, pasien dijadwalkan untuk menjalani operasi herniotomi-herniorafi elektif dengan kombinasi anestesi spinal-epidural dosis rendah. Anestesi spinal dilakukan dengan ropivacaine isobarik 0.375% dan fentanil 25 µg dalam volume total 3.5 ml pada *intervertebral space* L3-L4. Anestesi epidural dilakukan dengan ropivacaine isobarik 0.375% dan fentanil 25 µg dalam volume total 8 ml pada *intervertebrale space* L2-L3. Setelah 10 menit, blok sensorik tercapai hingga T6, tetapi blok motorik hanya parsial (Bromage 1). Infus kontinu ropivacaine isobarik 0.1875% 1 ml/jam diberikan melalui kateter epidural untuk mengontrol nyeri pascaoperasi. Selama operasi dan perawatan di rumah sakit kondisi hemodinamik pasien tetap stabil. **Kesimpulan:** Kombinasi anestesi spinal-epidural dengan ropivacaine isobarik 0.375% dapat menghasilkan



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anestesi yang adekuat dengan hemodinamik yang relatif stabil sehingga aman untuk operasi perbaikan hernia inguinalis dari pasien gagal jantung dengan fraksi ejeksi berkurang.

**Kata Kunci:** Kombinasi Anestesi Spinal-Epidural; Ropivacaine Isobarik 0.375%; Hernia Inguinalis; Gagal Jantung; Laporan Kasus; Manajemen Anestesi

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## INTRODUCTION

Heart failure reflects a complicated disorder of the heart caused by functional or structural damage of the myocardium. This disorder reduces the capacity to fill the ventricles or expel blood into the systemic circulation, leading to an inability to fulfill the body's metabolic demands. In general, heart failure can be classified based on the level of left ventricular ejection fraction (LVEF), including heart failure with reduced ejection fraction (HFrEF), ejection fraction <40%; heart failure with mildly reduced ejection fraction (HFmrEF), ejection fraction 41-49%; and heart failure with preserved ejection fraction (HFpEF), ejection fraction ≥50%. The incidence of heart failure reaches 64 million cases worldwide, and many of these cases require non-cardiac surgery, including inguinal hernia repair. On the other hand, heart failure itself is one of the risks of increased perioperative morbidity and mortality (1–3).

Whenever heart failure patients require surgical procedures, the decision to perform surgery is often a challenge for anesthesiologists. Reports suggest the likelihood of death during elective surgery in individuals with heart failure rises by up to 14%. This is because anesthesia and the surgical procedure itself can potentially worsen the heart failure condition. Therefore, anesthesiologists should be able to determine the appropriate type of anesthetic technique and perioperative management to minimize the risk of cardiac complications during surgery. Combined spinal-epidural anesthesia has become an increasingly common approach to providing anesthesia in patients with complex medical conditions, such as heart failure. It can provide precise sensory and motor blocks in the area to be operated on while allowing for better management of hemodynamic changes that may occur during surgery (4,5).

However, the use of combined spinal-epidural anesthesia in the context of inguinal hernia surgery in patients with heart failure and reduced ejection fraction has yet to be widely described in the literature. Therefore, this case report aims to present the use of combined spinal-epidural anesthesia with isobaric ropivacaine 0.375% for inguinal hernia repair surgery in a heart failure patient with an ejection fraction of 36%.

## CASE REPORT

A 53-year-old male farmer presented to the emergency department with a one-year history of a lump on the left groin that had been in and out. Three days before admission, the patient began complaints of pain, especially when the lump came out. In addition, the patient also often complained of shortness of breath when lying down at night and during strenuous activity accompanied by chest palpitations. The patient denied any complaints of nausea, vomiting, difficulty defecating, or farting. The patient's previous medical history included a heart attack five years ago and uncontrolled hypertension. The patient denied having diabetes mellitus but was a heavy smoker and had quit since the heart attack. The patient was previously treated by a cardiologist



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with atorvastatin 20 mg, sacubitril-valsartan 50 mg, bisoprolol 2.5 mg, spironolactone 25 mg, and furosemide 40 mg, each once daily.

On preoperative physical examination, the patient appeared moderately ill; weight 65 kg; height 160 cm; Glasgow Coma Scale (GCS) E4V5M6; patent airway; maximal mouth opening; Mallampati II; free neck motion; no short neck or mandibular protrusion; vital signs: blood pressure 149/75 mmHg, pulse rate 69 beats/min, body temperature 36.7 °C, respiratory rate 16 breaths/min, and SpO2 97% in room air. Respiratory and cardiovascular examinations were normal, with no wheezing, rhonchi, murmurs, or S3 gallop. Abdominal examination showed a flat abdominal wall with no ascites. Auscultation showed normal peristalsis of 12 times/min. The percussion examination sounded tympanic throughout the abdominal field. Palpation revealed no mass or muscular defense, and the borders of the spleen and liver could not be identified. The lump that came out on the left groin can be repositioned, and there is pain when pressed with a visual analog scale (VAS) pain score of 3/10.

Preoperative laboratory and blood gas analysis results are presented in Table 1 and Table 2. Anterior-posterior (AP) chest X-ray demonstrated cardiomegaly with a cardiothoracic ratio (CTR) of 67% (Figure 1). A 12-lead electrocardiographic (ECG) indicates sinus rhythm, heart rate of 75 beats/min, left axis deviation (LAD), and left ventricular hypertrophy (LVH). Furthermore, an echocardiographic investigation showed mild aortic regurgitation, left ventricular dilatation (LVIDd 7.18 cm), decreased left ventricular systolic function (LVEF 36% with Teich), impaired left ventricular diastolic function (DT 246 ms, E/A 0.6, E/E' 15.7, PCWP 21 mmHg), and normal right ventricular function (TAPSE 2.1 cm). Segmental LV analysis showed mid-anterior basal kinetics, normokinetics of other segments, and eccentric LVH.

**Table 1.** Preoperative Laboratory Test Results

| Parameters | Value | Parameters | Value |
|---|---|---|---|
| **Hb** | 13.3 g/dl | **ALT** | 23 U/L |
| **NLR** | 4.96 | **Albumin** | 4 g/dl |
| **WBC** | 8.1 x $10^3$/uL | **Random blood glucose** | 104 mg/dl |
| **HCT** | 38.8% | **Na** | 140.3 mmol/L |
| **Platelets** | 427 x $10^3$/uL | **K** | 3.7 mmol/L |
| **PT** | 11.4 secs | **Cl** | 107.6 mmol/L |
| **APTT** | 30.1 secs | **Serum creatinine** | 1 mg/dl |
| **AST** | 14 U/L | **BUN** | 12 mg/dl |

**Table 2.** Preoperative Blood Gas Analysis Results

| Parameters | Value | Parameters | Value |
|---|---|---|---|
| **Temperature** | 36 °C | **TCO2** | 31 mmol/L |
| **FiO2** | 0.21 | **HCO3** | 30 mmol/L |
| **Ca** | 1.14 mmol/L | **Hb** | 12.5 g/dl |
| **pH** | 7.52 | **SO2** | 96% |
| **pO2** | 72 mmHg | **AaDO2** | 32 mmHg |
| **pCO2** | 35.8 mmHg | **Na** | 143 mmol/L |
| **BE** | 7.1 | **K** | 3.5 mmol/L |



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Based on the examination, the patient was diagnosed with a reducible left lateral inguinal hernia and planned for elective herniotomy-hernioraphy surgery with low-dose combined spinal-epidural anesthesia. On pre-anesthesia evaluation, the patient was labeled with American Society of Anesthesiologists (ASA) Physical Status III, Revised Cardiac Risk Index for Pre-Operative Risk (RRCI) 3 with an estimated risk of a major adverse cardiac event in 30 days of 15%, New York Heart Association (NYHA) Class II, and estimated metabolic equivalents of task (MET) score ≥ 4.

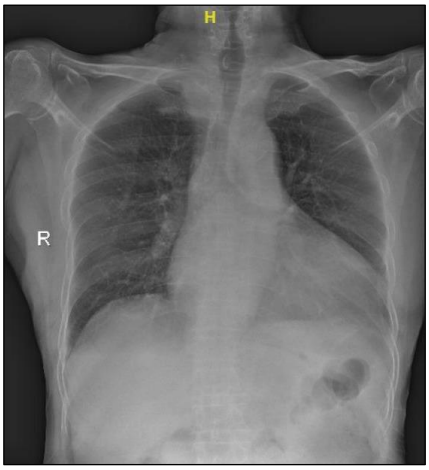


**Figure 1.** Preoperative Chest X-Rays

The surgery was performed one week after the hospital admission. Before the surgery, the patient was fasted for 6 hours, and the medication given by the cardiologist was continued during the perioperative period. ECG, heart rate, SpO2, and blood pressure were closely monitored in the operating room. The patient was positioned sitting, and the hanging-drop technique was used to identify the epidural space at the L2-L3 intervertebral space with a median approach. Then, the epidural catheter was inserted to a depth of 12 cm. Spinal anesthesia was carried out at the L3-L4 intervertebral space through a paramedian approach using a 27G Quincke needle. Next, a test dose was performed through the epidural catheter with epinephrine 1:100.000 1 ml plus lidocaine 2% 2 ml. Then, isobaric ropivacaine 0.375% plus fentanyl 25 µg in a total volume of 3.5 ml was injected into the subarachnoid space. Epidural anesthesia was administered with isobaric ropivacaine 0.375% plus fentanyl 25 µg in a total volume of 8 ml. Sensory block was achieved up to the level of T6 segment at the 10th minute as checked by pinprick test. However, the motor block was not entirely achieved as the patient could still move his knee slightly during intraoperative (Bromage 1).

The surgical procedure lasted 75 minutes and went smoothly, with a relatively stable hemodynamic status without the support of vasopressor or inotropic agents (Figure 2). During surgery, 500 ml of 6% hydroxyethyl starch (HES) was infused, and the patient was given 5 liters/minute of oxygen using a simple mask. The patient was then transferred to the intensive care unit (ICU) shortly after the surgical procedure. Estimated blood loss and urine output were 30 ml and 100 ml, respectively. To control postoperative pain, a continuous infusion of isobaric ropivacaine 0.1875% 1 ml/hour was given through an epidural catheter plus an intravenous injection of metamizole sodium 1 gram three times a day. The patient's hemodynamic condition remained stable during the ICU stay, with no adverse events or complications related to anesthesia and surgical procedures. After two days of hospitalization in the ICU, the epidural catheter was removed, and oxygen administration was changed to 4 liters/minute via nasal cannula. Finally, the patient was transferred to a regular inpatient room and discharged the following day.



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## DISCUSSION

Inguinal hernia repair is one of the most common surgical procedures performed by surgeons globally, with over 20 million patients operated on each year. Current guidelines recommend that hernia repair be tailored according to expertise, resources, and factors related to the patient's condition, including comorbidities such as heart disease (6). Comorbid heart disease is a medical condition that significantly contributes to illness and death in individuals having non-cardiac surgery. More precisely, the percentage of patients who die within 30 days following surgery is notably greater among individuals with heart failure (9.3%) compared to those with atrial fibrillation (6.4%) and coronary heart disease (2.9%). Furthermore, the mortality rate of patients with heart failure was also markedly higher in patients with LVEF <40% compared to those with normal LVEF (7).

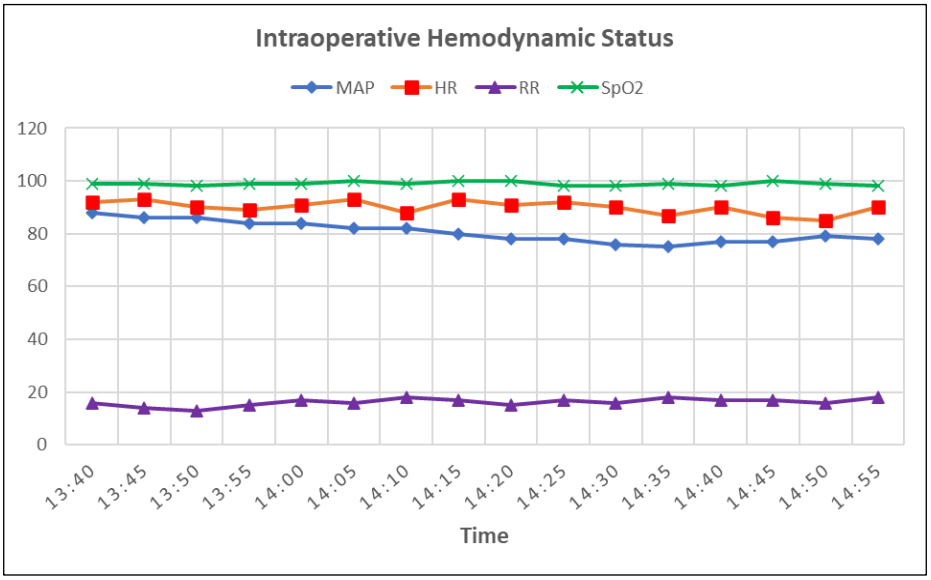


**Figure 2.** Intraoperative Hemodynamic Status

Effective pain management is a crucial aspect of caring for surgical patients. Additionally, it is important to note that pain is a contributing factor to the occurrence of postoperative myocardial ischemia. This is because the associated tachycardia can shorten the diastolic phase and diminish the supply of blood flow to the myocardium (7). There is no consensus on which anesthetic technique should be used in inguinal hernia surgery. The most widely used anesthetic technique for inguinal hernia surgery is general anesthesia (almost 80%), as it can facilitate laparoscopy by relaxing the abdominal muscles, allowing additional procedures, such as laparotomy or bowel resection, and securing the airway. However, general anesthesia tends to be contraindicated in patients with cardiac disease, as induction of anesthesia and intubation are often associated with hemodynamic instability. Regardless of how tight blood pressure control is in the preoperative period, not a few hypertensive patients experience hypotension in response to anesthetic induction agents, followed by hypertension due to increased catecholamine secretion in response to intubation or surgical procedures (5,8,9).

Over the past few years, the use of spinal anesthesia has recently become a popular anesthetic technique for lower abdominal and inguinal hernia surgery. However, the use of this technique is often associated with the



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incidence of hypotension and bradycardia. These conditions are mainly caused by arterial and venous vasodilation due to excessive sympathetic block accompanied by activation of cardioinhibitory receptors that disrupt sympathovagal balance and increase parasympathetic tone. Therefore, to overcome this, modification of anesthetic techniques, adjustment of the dose and type of drugs used, and preloading colloidal fluids before starting anesthesia can be done (10,11). In this case, we performed a combined spinal-epidural anesthesia technique with isobaric ropivacaine 0.375%. Sensory block was achieved up to the T6 level, but motor block was only partially achieved. This implies that a low dose of ropivacaine is sufficient to produce the anesthetic block required for hernia surgery. In addition, our patient was preloaded with 500 ml of 6% HES. Furthermore, the patient was also asked to continue treatment from a cardiologist during the perioperative period as recommended by the 2014 American Heart Association guidelines (7).

Ropivacaine is a long-acting local anesthetic. It has the same pharmacokinetic and pharmacodynamic features as bupivacaine by reversibly inhibiting sodium ion entry into nerve fibers, but with lower cardiovascular toxicity. It is also less lipophilic than other local anesthetics, such as bupivacaine, and has a lower ability to reach large myelinated motor fibers. As a result, it tends to act on nociceptive fibers A, B, and C rather than motor fibers, resulting in minimal motor block (12). Based on a clinical trial by Mohtadi et al., which compared the use of spinal anesthesia with ropivacaine 0.5% 3.5 ml plus fentanyl 25 µg and ropivacaine 0.5% 3.5 ml plus sufentanil 2.5 µg, it was indicated that there was no significant difference in the duration of analgesia and motor block. Nevertheless, the group treated with ropivacaine plus fentanyl exhibited superior hemodynamic stability and a lower incidence of pruritus compared to the group given ropivacaine with sufentanil (13).

Meanwhile, another study by Wang and Xu compared the use of combined spinal-epidural anesthesia with ropivacaine 0.1% 2-3 ml and epidural anesthesia with ropivacaine 0.5% 3 ml for labor analgesia (each group also received a continuous infusion of ropivacaine 1% 10 ml plus sufentanil 0.3-0.4 µg/ml in 100 ml normal saline at a rate of 5 ml/hour via an epidural catheter), showed that the combined spinal-epidural anesthesia group had significantly lower VAS pain scores during labor than the epidural anesthesia group. In addition, the incidence of side effects, such as nausea, vomiting, and pruritus, was also significantly lower in the combined spinal-epidural anesthesia group (14).

Currently, combined spinal-epidural anesthesia has been widely used for lower abdominal surgery. With low-dose combined spinal-epidural anesthesia, anesthesia can be done by administering small amounts of local anesthetic drugs into the subarachnoid space, followed by continuous infusion into the epidural space. Spinal anesthesia can provide rapid sensory and motor block onset and sufficient muscle relaxation. Meanwhile, an epidural catheter insertion allows titration and extension of anesthesia and analgesia, especially for postoperative pain control. This technique facilitates the adjustment of the block to the appropriate level, resulting in better hemodynamic stability and a decreased occurrence of hypotension. As a result, this decreased the requirement for vasopressors and inotropic drugs (15). Therefore, the use of low-dose combined spinal-epidural anesthesia may be an option for a safe and effective anesthetic modality in patients with heart failure who are



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typically contraindicated with other anesthetic modalities.

The goals of anesthetic management in patients with cardiac disease consist of preventing tachycardia, maintaining normovolemia, preventing increased afterload, and avoiding drug-induced myocardial depression. Neuraxial anesthesia can be used as the primary anesthetic or in combination with general anesthesia for patients with cardiac disease. Several factors, including the presence of other medical conditions, the type of surgery, and the patient's preference, play a crucial role in assessing the advantages and disadvantages of neuraxial anesthesia (16). Since this is a case report, the main limitation of this study is that we only included one patient, making our findings difficult to generalize to a broader population. In addition, the absence of a comparator also makes it impossible to compare outcomes between those exposed and unexposed.

## CONCLUSION

This case report demonstrates that combined spinal-epidural anesthesia with isobaric ropivacaine 0.375% is feasible and safe to use in a heart failure patient with an ejection fraction of 36% undergoing inguinal hernia repair surgery as it can provide adequate analgesia and good hemodynamic stability without side effects, and thus can be an option for patients with similar conditions. However, further studies with a randomized controlled trial (RCT) design and larger samples are still needed to confirm these findings.

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### Conflict of Interest

The authors declare that there is no conflict of interest.

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### Authors' Contribution

**Muhammad Isra Rafidin Rayyan, Salman Sultan Ghiffari, Achmad Hariyanto** – conceptualization, data collection, data analysis and interpretation, and manuscript preparation; **Achmad Wahib Wahju Winarso, Haris Darmawan, Ichlasul Mahdi Fardhani** – supervision, critical review, and final approval of the manuscript.

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Systematic Review

# AIMS65 SCORING SYSTEM FOR PREDICTING CLINICAL OUTCOMES AMONG EMERGENCY DEPARTMENT PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING

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## ABSTRACT

**Introduction:** Several scoring systems were developed for early risk stratification in Upper Gastrointestinal Bleeding (UGIB) patients. AIMS65 score is a scoring system that only consists of five parameters, it might be used in daily clinical practice because of rapid and easy to calculate within 12 hours of admission. **Objective:** To evaluate the AIMS65 scoring system as a predictor of mortality, rebleeding events, need for endoscopic therapy, blood transfusion, and ICU admission for all causes of UGIB. **Methods:** We conducted a systematic review on PubMed, ScienceDirect, ProQuest, and Cochrane Library databases from the 2012 to 2022 publication period. We included either prospective or retrospective cohort studies that reported UGIB with all kinds of aetiologies who presented in the emergency department (ED), reported discriminative performance for each outcome, and reported the optimal cut-off of AIMS65. The primary measurement of discriminative performance for clinical outcomes includes mortality, rebleeding incidents, need for endoscopic therapy, blood transfusion, and ICU admission. **Results:** We identified 351 published studies, of which 20 were included in this study. Most of the studies reported discriminative performance for predicting mortality, which amounts to about 18 out of 20 studies. Rebleeding prediction was reported in 11 studies, need for endoscopic therapy in 5 studies, blood transfusion in 7 studies, and ICU admission in 2 studies. Most of the studies reported fair to excellent discriminative performance for predicting mortality, but in contrast for predicting rebleeding, the need for endoscopic therapy, blood transfusion, and ICU admission. Cut-off values≥ 2 are frequently reported to distinguish between high-risk and low-risk patients in mortality. **Conclusion:** AIMS65 can be applied to patients with UGIB in ED for predicting mortality, but not applicable for predicting rebleeding events, the need for endoscopic therapy, blood transfusion, and ICU admission. It enhances early decision-making and triage for UGIB patients.

**Keywords:** AIMS65; Upper Gastrointestinal Bleeding (UGIB); Health Emergency Preparedness; Systematic Review.

## ABSTRAK

**Pendahuluan:** Beberapa sistem skoring dikembangkan untuk stratifikasi risiko dini pada Pasien Perdarahan Gastrointestinal Bagian Atas (PSCBA). Skor AIMS65 adalah sistem skoring yang hanya terdiri dari lima parameter, dapat digunakan dalam praktik klinis sehari-hari karena cepat dan mudah dihitung dalam waktu 12 jam setelah admisi. **Tujuan:** Untuk mengevaluasi sistem penilaian AIMS65 sebagai prediktor mortalitas, kejadian perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU untuk semua penyebab PSCBA. **Metode:** Kami melakukan tinjauan sistematis melalui basis data *PubMed*, *ScienceDirect*, *ProQuest*, dan *Cochrane Library* dari periode publikasi 2012 hingga 2022. Kami memasukkan studi kohort prospektif atau retrospektif yang melaporkan UGIB dengan semua jenis etiologi yang dilaporkan di unit gawat darurat (UGD), melaporkan kemampuan diskriminatif untuk setiap hasil, dan melaporkan batas optimal AIMS65. Pengukuran utama kinerja diskriminatif untuk hasil klinis mencakup angka mortalitas, kejadian perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU. **Hasil:** Kami mengidentifikasi 351 penelitian yang dipublikasikan, 20 di antaranya diinklusi dalam penelitian ini. Sebagian besar penelitian melaporkan kinerja diskriminatif dalam memprediksi kematian, yaitu pada 18 dari 20 penelitian. Prediksi perdarahan ulang dilaporkan dalam 11 penelitian, kebutuhan terapi endoskopi dalam 5 penelitian, transfusi darah dalam 7 penelitian, dan admisi ke ICU dalam 2 penelitian. Sebagian besar penelitian melaporkan kinerja diskriminatif yang cukup baik hingga sangat baik dalam memprediksi angka kematian, namun berbeda dalam memprediksi perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU. Nilai batas ≥ 2 sering dilaporkan untuk membedakan antara pasien berisiko tinggi dan pasien berisiko rendah dalam hal kematian. **Kesimpulan:** AIMS65 dapat diterapkan pada pasien PSCBA di IGD untuk memprediksi mortalitas, namun tidak dapat diterapkan untuk memprediksi kejadian perdarahan ulang, kebutuhan terapi



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endoskopi, transfusi darah, dan admisi ke ICU. Ini dapat meningkatkan pengambilan keputusan dini dan triase untuk pasien dengan PSCBA.

**Kata Kunci:** AIMS65; Pasien Pendarahan Gastrointestinal Bagian Atas (PSCBA); Kesiapsiagaan Darurat Kesehatan; Tinjauan Sistematis.

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## INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a medical emergency case located between the oral cavity to the proximal treitz ligament. UGIB is clinically presented by haematemesis, coffee-ground emesis, and melena. Despite the improvement of overall mortality and morbidity rates in developing countries because of advanced diagnosis and treatment, the mortality rate of UGIB around the world in the past decade unchanged and varied between 3–14% (1). Patients with UGIB can present in either stable condition or requiring rapid management, such as resuscitation, blood transfusion, ICU admission, and endoscopic therapy depending on the clinical assessment of the patient. Endoscopy has an important role in the diagnostic and therapeutic of UGIB (2). Because of limited competent operators and equipment in all health facilities, most patients with UGIB do not receive rapid endoscopic intervention. Endoscopic procedures also have risks such as perforation and discomfort to patients so several considerations are needed to decide whether the patient needs an endoscopy or not (3).

The existing scoring system is considered helpful for physicians in the emergency department (ED) to enhance decision-making. A scoring system is able to guide earlier treatment or care for patients above the cut-off which is considered as a high risk, thus leading to improvements in mortality and morbidity rates (4,5). Several scoring systems were developed for early risk stratification in UGIB patients, such as the Glasgow Blatchford Score (GBS), Rockall Score, and AIMS65 (4,6). The Rockall Score requires an endoscopic component so it cannot be used for pre-endoscopic triage. The GBS and AIMS65 scoring systems are possible to overcome these problems because the prognostic parameters do not require endoscopic examination, but the GBS system has limitations compared to AIMS65 when used in clinical practice because it weighted each parameter so the outcome was often over-evaluated when calculated (7).

AIMS65 score is a more recent scoring system compared to the two others which only consists of 5 parameters, such as albumin levels, INR, changes in mental status, blood pressure, and age > 65 years old. It might be used in daily clinical practice because of rapid and easy to calculate within 12 hours of admission (7,8). As such, this systematic review aims to identify the AIMS65 scoring system for its ability to predict the prognosis including mortality rebleeding events, the need for therapy including endoscopic therapy, blood transfusion, and ICU admission for all causes of upper gastrointestinal bleeding based on predictive accuracy.

## MATERIAL AND METHOD

### Search Strategy

The literature search was conducted on four databases, including PubMed, ScienceDirect, ProQuest, and Cochrane Library with a publication period ranging from 2012 to 2022 using keywords related to "AIMS65" and "Upper Gastrointestinal Bleeding". Only studies written in English and



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full-text access articles were considered in this systematic review.

### Eligibility Criteria

This study was conducted using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). We only included articles that match our eligibility criteria based on PICOS: (i) Population: all-cause UGIB patients admitted to the emergency department; (ii) Intervention: AIMS65 score; (iii) Comparison: not applicable; (iv) Outcomes: mortality, rebleeding, endoscopic therapy, blood transfusion, and ICU admission (v) Study design: a prospective or retrospective cohort. The analyzed variables were the discriminative performance of AIMS65 for each outcome, and the optimal cut-off should be reported to distinguish between low and high-risk patients. We excluded the AIMS65 score which validated variceal or non-variceal bleeding only. Furthermore, we exclude studies that measure discrimination ability for composite clinical outcomes. Two reviewers independently screened the titles and abstract based on inclusion and exclusion criteria, the discrepancies are solved by consensus and involve a third reviewer when needed. PICOS framework for inclusion studies can be seen in Table 1.

**Table 1.** PICOS framework

| | |
|---|---|
| **Population** | All-cause UGIB patients admitted to the emergency department |
| **Intervention** | AIMS65 score |
| **Comparison** | Not applicable |
| **Outcome** | Mortality, rebleeding, endoscopic therapy, blood transfusion, ICU admission |
| **Study design** | Cohort |

### Data Extraction and Quality Assessment

The following data were extracted from each study: publication date, study design, sample size, and optimal cut-off, and we also extracted all performances of the score in terms of discrimination ability or AUC. The AUC thresholds to judge predictive ability have been described by other researchers: excellent (AUC ≥0.90); good (AUC ≥0.80 and <0.90); fair (AUC ≥0.70 and <0.80); and poor (AUC <0.70) (9). Calibration, sensitivity, specificity, positive predictive value, and negative predictive value were also reported if available. The extracted data from each study will be conducted for narrative synthesis. All included studies will be assessed by two independent reviewers. The risk of bias and concern for applicability were assessed using a Prediction-model Risk of Bias Assessment Tool (PROBAST). PROBAST was developed to assess the quality of primary studies on multivariable models in a systematic review. This tool evaluated the risk of bias using four domains (participants, predictor, outcome, and analysis) and concern for applicability using three domains (participants, predictor, outcome) then finally judged by criteria of 'low', 'high', and 'unclear'.

## RESULTS AND DISCUSSION

### Search Result

We identified 351 published studies in the initial literature search. From a total of 72 articles selected for full-text review, we only included 20 studies that reported optimal cut-off and discrimination ability of AIMS65 scores for predicting mortality, rebleeding, endoscopic therapy, blood transfusion, and ICU admission to conduct this systematic review. PRISMA flowchart for the selection studies process can be seen in Figure 1.

### Study and Sample Characteristics

Total of 20 studies, 10 prospective cohort (6,10–18), 9 retrospective cohort (7,19–26), and 1 both prospective and retrospective cohort



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(27). The population ranged between 129 to 4019. The studies recruited from several countries with a median age between 52 to 71 years old. All of the studies recruited only assessed ED patients and reported the discrimination ability of AUC. No study reported the calibration measurement for the clinical outcome of AIMS65 scores. Eighteen of the studies evaluate the accuracy of predicting mortality. Detailed characteristics of included studies can be seen in Table 2.

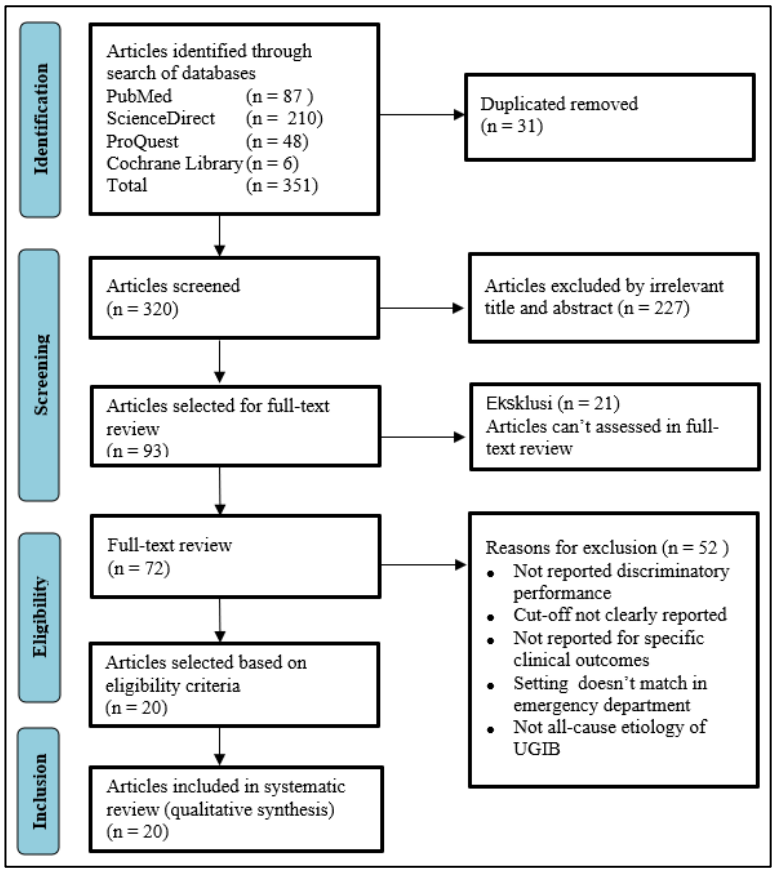


**Figure 1.** PRISMA flowchart

**Table 2.** Characteristics of Included Studies

| First author, year | Design | Eligibility Criteria | Sample size | Male (%) | Median Age (IQR) Mean Age ± SD | Optimal Cut-off | Outcome |
|---|---|---|---|---|---|---|---|
| **Hyett et al. 2013** | Retrospective, single-center | UGIB based on ICD-9 codes | 278 | 150 (54%) | 63 (IQR 50–77) | (≥2) | Inpatient mortality |
| **Thandassery et al. 2015** | Retrospective, single-center | UGIB patients who underwent endoscopic evaluation within 12 hours; above 14 years of age | 251 | 193 (76.8 %) | 52 (IQR 15–84) | (≥2) | Blood transfusion, endoscopic therapy, ICU admission, rebleeding, mortality |
| **Abougergi et al. 2016** | Prospective, multicenter | Patients with UGIB either at the time of presentation to the hospital or if developed UGIB as an inpatient | *298* | 197 (66%) | 64 (IQR 52–75) | ≥4 | In-hospital mortality, 30-day mortality, in-hospital rebleeding, 30-day rebleeding |



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| First author, year | Design | Eligibility Criteria | Sample size | Male (%) | Median Age (IQR) Mean Age ± SD | Optimal Cut-off | Outcome |
|---|---|---|---|---|---|---|---|
| **Martı´nez-Cara et al. 2016** | Prospective, single center | UGIB patients who underwent endoscopy; all patients received pantoprazole 80 mg iv as an initial bolus followed by a continuous infusion of 120 mg for the first 24 hours | 309 | 214 (69.3 %) | 64.6 ± 16.7 | (≥1)<br>(≥2) | In-patient mortality,<br>Endoscopic therapy, blood transfusion, 6-month mortality |
| **Robertson et al., 2016** | Retrospective, single-center | UGIB based on ICD-10 codes | 424 | 279 (66%) | 71 (IQR 15–93) | (≥2)<br>(≥3) | In-hospital rebleeding,<br>ICU admission, blood transfusion, in-hospital mortality |
| **Zhong et al. 2016** | Prospective, single center | Acute UGIB. Recurrent episode of UGIB; admission to the hospital and developed AUGIB for unrelated disease excluded | 320 | 198 (61.9 %) | 63 (IQR 42–79) | (≥2) | In-hospital mortality, in-patient rebleeding |
| **Lau et al. 2016** | Prospective, single center | UGIB patients who are not admitted to the hospital ward were excluded. | 129 | 79 (61.2 %) | 65.1 ± 21 | (≥1) | In-patient mortality, blood transfusion |
| **Zhao et al. 2017** | Retrospective, single-center | UGIB patients above 65 years of age; endoscopic evaluation within 24 hours | 293 | 170 (58%) | 72.4 ± 6.3 | (≥2) | In-patient mortality, rebleeding |
| **Kalkan et al. 2017** | Retrospective, single-center | Patient with the presence of overt endoscopic stigmata of UGIB; above 60 years of age | 335 | 202 (60%) | 72.9 ± 9 | (≥2.5) | 30-day mortality, rebleeding |
| **Stanley et al. 2017** | Propsektif, International multicenter | Patient with evidence of UGIB defined by haematemesis, coffee-ground vomiting, melaena. A patient who developed UGIB while an inpatient for another reader were excluded | 3012 | 1750 (58%) | 65 (IQR 24–90) | (≥2)<br>(≥1) | 30-day mortality, Endoscopic therapy |
| **Tang et al. 2018** | Retrospective, *single-center* | UGIB patients above 14 years of age. Patients who had been followed up for less than 30 days and were diagnosed other than UGIB were excluded | 395 | 274 (69/4 %) | 65 (IQR 50–77) | (≥2.5) | 30-day mortality |
| **Gu et al. 2018** | Retrospective, single-center | UGIB patients who did not receive endoscopy examination as they had severe clinical symptoms and needed emergent clinical treatment | 799 | 612 (77.22 %) | 57.46 ± 18.04 | (≥2) | In-hospital mortality |
| **Shafaghi et al. 2019** | Retrospective, single-center | UGIB patients above 18 years of age. Patients who didn't undergo endoscopy were excluded | 563 | 345 (61.3 %) | 60.53 ± 18.62 | (≥2) | In-patient mortality, 30-day mortality, endoscopic intervention, blood transfusion |
| **Redondo-Cerezo et al. 2020** | Prospective, single center | UGIB patients were followed for 6 months after their discharge | 547 | 367 (67.1 %) | 64.1 ± 16.4 | (≥2)<br>(≥1) | 30-day mortality<br>7-day rebleeding, endoscopic therapy |



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| First author, year | Design | Eligibility Criteria | Sample size | Male (%) | Median Age (IQR) Mean Age ± SD | Optimal Cut-off | Outcome |
|---|---|---|---|---|---|---|---|
| **Saffouri et al. 2020** | Prospective, international multicenter | UGIB patients who developed upper GI bleeding as inpatients were | 3012 | 1746 (58%) | 65 (IQR 24–90) | (≥1) | Blood transfusion |
| **Liu et al. 2020** | Prospective, multicenter | UGIB patients non-trauma; above 18 years | 1072 | 779 (72.67 %) | 61.41 ± 1577 | (≥0.5) | 90-day mortality, 90-day rebleeding |
| **Lu et al. 2020** | Retrospective, single-center | UGIB patients who are hospitalized within 48 hours of endoscopy; non-AUGIB cause death | 284 | 197 (69.4 %) | 64 (IQR 50–73) | (≥2) | In-hospital mortality |
| **Sachan et al. 2021** | Prospective, single center | UGIB patients above 18 years of age | 268 | 222 (82.8 %) | 48.49 ± 13.23 | (≥2) | 8-week mortality, rebleeding, blood transfusion |
| **Chang et al. 2021** | Prospective, single center | UGIB patients above 18 years of age. Patients who had a history of UGIB in the previous 3 months or had undergone endoscopy at another institution before admission were excluded | 337 | 247 (73.3 %) | 61.1 ± 16.5 | (≥3) | In-hospital mortality |
| **Laursen et al. 2021** | Prospective and Retrospective, multicenter | Patients with acute UGIB are defined as presenting with haematemesis, coffee-ground vomiting, or melaena. | 4019 | 2703 (67.25 %) | 65 (IQR 30) | (≥2) | 30-day rebleeding |

## Quality Assessment

All of the studies reported low concerns of applicability due to included studies having similar result in the review question. The analysis is the most common biased domain because the most studiesdo not report the calibration measurement of the AIMS65 score to predict clinical outcomes, therefore the judgment for all included studies is identified as high risk of bias. Quality assessment using PROBAST can be seen in Table 3.

## Outcomes: Mortality prediction

From 20 studies that reported the discriminative performance of AIMS65 scores for predicting mortality, it was acceptable in general because the AUC showed ≥ 0.7 in most studies with a range from 0.65 to 0.955. 4 studies reported excellent discriminative performance, 5 studies reported good discriminative performance, 10 studies reported good discriminative performance, and only 3 studies reported poor discriminative performance. A total of 11 had data on sensitivity and specificity, ranging from 38% to 100% and 24% to 95.76%, respectively. PPV and NPV were available in 4 studies, ranging from 5.8% to 12% and 91% to 100%, respectively. Included studies were reported with various optimal cut-offs ranging from ≥ 0.5 to ≥ 4 with a frequently reported was ≥ 2. Mortality was reported on various follow-ups such as inpatient, in-hospital, 30-day, 8-week, 90-day, and 6-month. The predictive ability of AIMS65 to predict mortality can be seen in Table 4.

## Outcomes: Rebleeding prediction

A total of 11 studies evaluated discriminative performance for rebleeding incidence. The AUC for rebleeding events prognosis ranged from 0.491 to 0.86.



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**Table 3.** Quality assessment by PROBAST

| Author | Risk of Bias | | | | Applicability | | | Overall | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Risk of bias | Applicability |
| (19) | + | ? | ? | - | + | + | + | - | + |
| Thandassery et al., 2015 | + | ? | ? | - | + | + | + | - | + |
| Abougergi et al., 2016 | + | + | + | - | + | + | + | - | + |
| Martı´nez-Cara et al., 2016 | + | + | + | - | + | + | + | - | + |
| Robertson et al, 2016 | + | + | ? | - | + | + | + | - | + |
| Zhong et al., 2016 | + | + | + | - | + | + | + | - | + |
| Lau et al., 2016 | + | + | - | - | + | + | + | - | + |
| Zhao et al., 2017 | - | ? | - | - | + | + | + | - | - |
| Kalkan dkk., 2017 | - | + | - | - | + | + | + | - | - |
| Stanley et al., 2017 | + | - | + | - | + | + | + | - | + |
| Tang et al., 2018 | + | + | + | - | + | + | + | - | + |
| Gu et al., 2018 | + | - | + | - | + | + | + | - | + |
| Shafaghi et al., 2019 | + | - | ? | - | + | + | + | - | + |
| Redondo-Cerezo et al., 2020 | + | + | ? | - | + | + | + | - | + |
| Saffouri et al., 2020 | + | - | ? | - | + | + | + | - | + |
| Rao et al., 2020 | - | - | + | - | + | + | + | - | + |
| Liu et al., 2020 | + | + | + | - | + | + | + | - | + |
| Lu et al., 2020 | + | ? | ? | - | + | + | + | - | + |
| Sachan et al., 2021 | + | + | + | - | + | + | + | - | + |
| Chang et al., 2021 | + | + | ? | - | + | + | + | - | + |
| Laursen et al., 2021 | + | ? | + | - | + | + | + | - | + |

*PROBAST = Prediction model Risk Of Bias Assessment Tool, ROB; risk of bias

*1, risk of bias for participants; 2, risk of bias for predictor; 3, risk of bias for outcome; 4, risk of bias for analysis; 5, concern applicability for participants; 6, concern applicability for predictor; 7, concern applicability for outcome

*(+) indicates low ROB/low concern regarding applicability; (−) indicates high ROB/high concern regarding applicability; and (?) indicates unclear ROB/unclear concern regarding applicability.

There is only one study that reported fair and good discrimination performance with optimal cut-offs≥ 2 and ≥ 2.5, respectively.The remaining studies reported poor discriminative performance with optimal cut-off ranging from ≥ 0.5 to ≥ 3. Sensitivity and specificity were available in 6 studies, and they ranged from 57%-78.9% and 35.52% - 89.4%, respectively. PPV and NPV were available only in 1 study with the value of 14.25% and 92.29%. Follow-up time for rebleeding varies in all studies, such as inpatient, in-hospital, 7-day, 30-day, and 90-day. The predictive ability of AIMS65 to predict rebleeding can be seen in Table 5. postoperative pain between the experimental and placebo groups.

**Outcomes: Need for endoscopic therapy prediction**

Five studies consistently found the poor discriminative performance of AIMS65 scores for predicting the need for endoscopy therapy with the AUC ranging from 0.48 to 0.63. Three studies reported optimal cut-off was ≥ 1 and two studies reported optimal cut-off was ≥ 2. Of 5 studies, only 2 studies included sensitivity and specificity, those 2 studies also reported PPV and NPV. The predictive ability of AIMS65 to predict the need for endoscopic therapy can be seen in Table 6.

**Outcomes: Need for blood transfusion**

Seven studies reported blood transfusion prediction with the AUC ranged from 0.57 to 0.72. Only 2 optimal cut-offs were reported for blood transfusion specifically ≥ 1 and ≥ 2. Two studies reported fair discrimination performance with different optimal cut-offs of ≥ 1 and ≥ 2 respectively. Five remaining studies reported poor discrimination for rebleeding events. The predictive ability of AIMS65 to predict blood transfusion can be seen in Table 7.



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**Table 4.** Predictive Ability of AIMS65 to Predict Mortality

| Study | Optimal Cut-off | Follow-up | AUC and Category | Sensitivity/ Specificity (%) | PPV/ NPV (%) |
|---|---|---|---|---|---|
| Hyett et al. | ≥2 | Inpatient mortality | 0.93 (95% CI, 0.89–0.96) (Excellent) | 83/48 | NS |
| Thandassery et al. | ≥2 | NS | 0.74 (95% CI, 0.63–0.85) (Fair) | NS | NS |
| Abougergi et al. | ≥4<br>≥4 | In-hospital mortality<br>30-day mortality | 0.85 (95% CI, 0.81–0.89) (Good)<br>0.74 (95% CI, 0.70–0.79) (Fair) | NS<br>NS | NS<br>NS |
| Martı´nez-Cara et al. | ≥1<br>≥2 | Inpatient mortality<br>6-month mortality | 0.76 (95% CI, 0.68–0.83) (Fair)<br>0.74 (95% CI, 0.66–0.82) (Fair) | 100/24<br>38/89 | 12/100<br>31/91 |
| Robertson et al. | ≥3 | Inpatient mortality | 0.80 (95% CI, 0.69–0.91) (Good) | 72/77 | NS |
| Zhong et al. | ≥2 | In-hospital mortality | 0.786, 95% CI, 0.670-0.903) (Fair) | NS | NS |
| Lau et al. | ≥1 | Inpatient mortality | 0.83 (95% CI, 0.67–0.99) (Good) | 100/48 | 5.8/100 |
| Zhao et al. | ≥2 | Inpatient mortality | 0.833 (95% CI, 0.785–0.874) (Good) | 96/54 | NS |
| Kalkan et al. | ≥2.5 | 30-day mortality | 0.88 (Good) | 79.6/89.2 | NS |
| Stanley et al. | ≥2 | 30-day mortality | 0.78 (95% CI, 0.75–0.81) (Fair) | 65.8/76.2 | 18/96.6 |
| Tang et al. | ≥2.5 | 30-day mortality | 0.907 (95% CI, 0.874–0.934) (Excellent) | 70.73/95.76 | NS |
| Stokbro et al. | ≥1 | 30-day mortality | 0.74 (Fair) | NS | NS |
| Gu et al. | ≥2 | In-hospital mortality | 0.91 (95% CI, 0.84–0.98) (Excellent) | NS | NS |
| Shafaghi et al. | ≥2 | Inpatient mortality | 0.675 (95%CI 0.545–0.806) (Poor) | 57.1/79.5 | NS |
| Redondo-Cerezo et al. | ≥2 | 30-day mortality | 0.75 (95% CI, 0.69–0.81) (Fair) | NS | NS |
| Liu et al. | ≥0.5 | 90-day mortality | 0.672 (95% CI, 0.624–0.721) (Poor) | 87.18/36.44 | 14.39/ 95.87 |
| Lu et al. | ≥2 | In-hospital mortality | 0.955 (95%CI, 0.923–0.976) (Excellent) | NS | NS |
| Sachan et al. | ≥2 | 8-week mortality | 0.725 (95%CI, 0.656–0.794) (Fair) | 80.3/53.9 | NS |
| Chang et al. | ≥3 | In-hospital mortality | 0.747 (95% CI, 0.630–0.863) (Fair) | NS | NS |
| Laursen et al. | ≥2 | 30-day mortality | 0.65 (95% CI, 0.62–0.69) (Poor) | NS | NS |

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

**Table 5.** Predictive Ability of AIMS65 to Predict Rebleeding

| Study | Optimal Cut-off | Follow-up | AUC and Category | Sensitivity/ Specificity (%) | PPV/ NPV (%) |
|---|---|---|---|---|---|
| Hyett et al. | ≥2 | Inpatient rebleeding | 0.63 (95% CI, 0.57–0.69) (Poor) | 57/73 | NS |
| Thandassery et al. | ≥2 | NS | 0.53 (95% CI, 0.40–0.66) (Poor) | NS | NS |
| Abougergi et al. | ≥3<br>≥3 | In-hospital rebleeding<br>30-day rebleeding | 0.69 (95% CI, 0.63–0.74) (Poor)<br>0.63 (95% CI, 0.57–0.69) (Poor) | NS<br>NS | NS<br>NS |
| Robertson et al. | ≥2 | In-hospital rebleeding | 0.61 (95% CI, 0.51–0.70) (Poor) | 76/44 | NS |
| Zhong et al. | ≥2 | Inpatient rebleeding | 0.735 (95% CI, 0.667-0.802) (Fair) | NS | NS |
| Zhao et al. | ≥2 | NS | 0.646 (95% CI, 0.588–0.700) (Poor) | 74/52 | NS |
| Kalkan et al. | ≥2.5 | NS | 0.86 (Good) | 75.5/89.4 | NS |
| Shafaghi et al. | ≥2 | 30-day rebleeding | 0.491 (95% CI 0.369–0.614) (Poor) | NS | NS |
| Redondo-Cerezo et al. | ≥1 | 7 day-rebleeding | 0.64 (95% CI, 0.59–0.68) (Poor) | NS | NS |
| Liu et al. | ≥0.5 | 90-day rebleeding | 0.585 (95% CI, 0.537–0.634) (Poor) | 78.29/35.52 | 14.25/9 2.29 |
| Sachan et al. | ≥2 | NS | 0.626 (95% CI, 0.546–0.707) (Poor) | 78.9/48.3 | NS |

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)



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**Outcomes: Need for ICU admission**

Discriminative performance for ICU admission was only presented in 2 studies, Thandassery et al reported an AUC for ICU admission to be 0.61, and Robertson et al (x) reported an AUC of 0.74 for ICU admission. All of the studies reported optimal cut-off was ≥ 2. Only Robertson et al reported sensitivity and specificity of about 88% and 47%. The predictive ability of AIMS65 to predict ICU admission can be seen in Table 8.

**Discussion**

We conducted a systematic review to assess the predictive accuracy of AIMS65 as pre-endoscopic risk scoring in emergency department's UGIB patients for mortality, rebleeding, need for endoscopic therapy, blood transfusion, and ICU admission. AIMS65 is a scoring system developed by Saltzman et al. on 29.222 patients to predict inpatient mortality in UGIB patients (8). A total of 20 studies included in this systematic review reported a various follow-up time to predict mortality indicating that AIMS65 had an acceptable discriminative performance in most studies. Hyett et al. reported excellent discriminative performance for inpatient mortality using optimal cut-off ≥ 2. This is not surprising even though the accuracy showed better performance than the derived study because AIMS65 was established for that (19). Zhao et al using the same optimal cut-off reported good discrimination for inpatient mortality for elderly UGIB patients above 65 years in which they had at least one comorbid, and also reported in non-survival patients they had significantly lower hemoglobin levels (21). Lau et al. and Martı´nez-Cara et al. reported good and fair discriminative performance for inpatient mortality using cutoff ≥ 1 (11,13).

Martı´nez-Cara et al. also reported fair discriminative performance for 6-month mortality using cut-off ≥ 2. Extending time to follow-up was considered because patients with UGIB could challenge the precarious clinical balance of frail patients, such as patients with cirrhotic and cardiovascular diseases with the result that cause delayed death (11). Robertson et al. using cut-off ≥ 3 showed good discriminative performance in predicting inpatient mortality (20). Zhong et al. and Gu et al. reported good and excellent discriminative performance using cut-off ≥ 2 in predicting in-hospital mortality in the Chinese population (12,24). Chang et al. reported fair discriminative performance using cut-off ≥ 3 in predicting in-hospital mortality and specified that AIMS65 showed significant predictive accuracy in variceal bleeding than non-variceal bleeding (18). Abougergi et al. reported discriminative performance ≥ 0.7 using optimal cut-off ≥ 4 not only for in-hospital mortality but also for 30-day mortality (10).

**Table 6.** Predictive Ability of AIMS65 to Predict the Need for Endoscopic Therapy

| Study | Optimal Cut-off | AUC and Category | Sensitivity/ Specificity (%) | PPV/NPV(%) |
|---|---|---|---|---|
| Thandassery et al. | ≥2 | 0.48 (95% CI, 0.39–0.56) (Poor) | NS | NS |
| Martı´nez-Cara et al. | ≥1 | 0.62 (95% CI, 0.56–0.68) (Poor) | 87/28 | 45/76 |
| Stanley et al. | ≥1 | 0.63 (95% CI, 0.60–0.65) (Poor) | 79.7/38.7 | 25.9/87.6 |
| Shafaghi et al. | ≥2 | 0.562 (95% CI, 0.487–0.637) (Poor) | NS | NS |
| Redondo-Cerezo et al. | ≥1 | 0.59 (95% CI, 0.54–0.64) (Poor) | NS | NS |

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)



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**Table 7.** Predictive Ability of AIMS65 to Predict Blood Transfusion

| Study | Optimal Cut-off | AUC and Category | Sensitivity/ Specificity (%) | PPV/NPV(%) |
|---|---|---|---|---|
| Thandassery et al. | ≥2 | 0.60 (95% CI, 0.51–0.67) (Poor) | NS | NS |
| Martı´nez-Cara et al. | ≥1 | 0.71 (95% CI, 0.65–0.77) (Fair) | 88/37 | 69/64 |
| Robertson et al. | ≥2 | 0.72 (95% CI, 0.67–0.77) (Fair) | 71/63 | NS |
| Lau et al. | ≥1 | 0.57 (95% CI, 0.43–0.68) (Poor) | 60.9/48.1 | 20.3/8.5 |
| Shafaghi et al. | ≥2 | 0.674 (95% CI 0.628–0.721) (Poor) | NS | NS |
| Saffouri et al. | ≥1 | 0.692 (95% CI, 0.663–0.720) (Poor) | NS | NS |
| Sachan et al. | ≥2 | 0.643 (95% CI, 0.574–0.711) (Poor) | 68.1/55.4 | NS |

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

**Table 8.** Predictive Ability of AIMS65 to Predict ICU Admission

| Study | Optimal Cut-off | AUC and Category | Sensitivity/ Specificity (%) | PPV/NPV(%) |
|---|---|---|---|---|
| Thandassery et al | ≥2 | 0.61 (95% CI, 0.52–0.70) (Poor) | NS | NS |
| Robertson et al. | ≥2 | 0.74 (95% CI, 0.68–0.80) (Fair) | 88/47 | NS |

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

Stanley et al. (n = 3012) is the only study that collected data from six countries. The study reported fair discriminative performance for 30-day mortality using cut-off ≥ 2 and stated that AIMS65 scores had a lack of measurement for albumin that led to an underestimation of the accuracy of AIMS65 scores to identify low-risk patients. Redondo-Cerezo et al. using a similar cut-off reported fair discriminative and stated that low albumin levels might be a surrogate marker of severe comorbidities that lead to adverse outcomes (6,14). Kalkan et al. and Tang et al. used a cut-off ≥ 2.5 in predicting 30-day mortality.

Kalkan et al. reported good discriminative performance in which the population included in those studies only ≥ 60 years old, It also stated that increased risk of mortality was associated with serum albumin, hemoglobin level, multiple medications, and creatinine level, age, and comorbidity in which multiple medications and elevated creatinine level was an independent risk factor for mortality (22). Sachan et al. reported fair discriminative performance in 8-week mortality using cut-off ≥ 2. This study reported the most common etiology for UGIB was variceal bleeding, replacing peptic ulcer disease in most studies that reported the etiology of all-cause UGIB. Thandassery et al. using optimal cut-off≥ 2 reported the mortality incidence of AIMS65 in scores 0, 1, 2, 3, and 4 are about 3%, 7.8%, 20%, 36%, and 40%, respectively (7,17).

Despite most included studies reporting fair to excellent discriminative performance for mortality, three studies reported poor discriminative performance. Shafaghi et al. using a cut-off value ≥ 2 for inpatient mortality stated although albumin is an independent risk factor that is included in the variable, the albumin threshold is not the best to get one point in AIMS65 scores. This study reported that 41.14% of patients in the non-survival group had albumin ranging between 3 to 3.5 so changing the Albumin threshold to 3 to 3.5 in AIMS65 increased its discriminative performance to predicting mortality from 0.67 to 0.72 (25). Liu et al using cut-off ≥ 0.5 for 90-day mortality stated that AIMS65 had a lower discriminative performance compared with



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ABC scores (0.672 vs 0.722) but had a sensitivity higher than ABC score (87.18% vs 76.07%) (16). The largest international multicenter cohort by Laursen et al. in 2021 (n=4019) collected data from Israel, Spanyol, and Italy showed poor discriminative performance in predicting 30-day mortality in the Italian population in a setting with the largest population in this study. This condition affects the overall discriminative performance of AIMS65 scores in this study. The lower predictive accuracy of AIMS65 in the Italian cohort may be explained by a high proportion of cirrhotic in high-risk patients about 21% (27).

Accuracy of scores for predicting rebleeding events showed fair and good discriminative performance by Zhong et al. and Kalkan et al. Kalkan et al. stated that AIMS65 using a cut-off score ≥ 2.5 predicted rebleeding with 75.5% sensitivity and 89.4% specificity (12,22). However, the remaining studies reported poor discriminative performance for rebleeding events. Studies using cut-off value ≥ 2 with sensitivity and specificity reported are Hyett et al. about 57% and 73%, Robertson et al about 76% and 44%, Zhao et al. about 74% and 52%, and Sachan et al. about 78.9% and 48.3%. It showed inconsistent sensitivity and specificity that led to hesitation for its predictive ability in terms of discriminative performance (17,19–21).

Thandassery et al. using a similar cut-off reported that rebleeding events are not linear with increases in scores. Scores 0, 1, 2, 3, and 4 are reported around 6.1%, 10.9%, 15%, 4%, and 20%, respectively. The need for endoscopic therapy showed poor discriminative performance in all included studies. Martı´nez-Cara et al stated that AIMS65 is an optimal scoring for low-risk patients, especially if the goal is to avoid endoscopy. It was caused by 16 patients with AIMS65 scores of 0 still needing endoscopic therapy. Thandassery et al. reported no significant difference between low-risk (< 2) and high-risk (≥ 2) patients in need of endoscopic therapy (26.1% vs 21.8%). This study also reported about 37 patients with a score of 0 and 15 patients with a score of 1 still required endoscopic therapy. Most studies are concerned about biases because the need for endoscopic therapy is carried out due to early endoscopic examination by a physician (7,11).

Blood transfusions showed fair discriminative only in two studies. Martı´nez-Cara et al. using optimal cut-off ≥ 1 stated about 30% of non-survival patients had cardiovascular disease, which may affect the need for blood transfusion. Lau et al using optimal cut-off ≥ 1 showed poor discrimination performance. It may be explained because hemoglobin level is not included as a variable component that led to an inability to predict the need for blood transfusion. Blood transfusion requirements, as an endpoint for UGIB, have an essential role in resuscitation rather than intervention. It may raise questions as to whether the need for blood transfusion should be included as an endpoint (11,13). ICU admission was only reported in 2 studies with different discriminative performances. Robertson et al. showed fair discriminative performance (AUC 0.74) and reported that patients managed in the general ward who required ICU admission are about 56 (13.2%) patients. Thandassery et al. showed poor discriminative performance (AUC 0.61). It is also stated although significant difference in the number of low-risk and high-risk patients in ICU admission (16.8% vs 38.2%, p=0.001), the study reported 11 (8.3%) patients with a score of 0 and 22 (34.3%) patients with a score 1 underwent admission to ICU. ICU admission



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has an important role in the management of UGIB patients in critical condition or requires close monitoring to improve their quality of life, while low-risk patients on AIMS65 scores do not avoid the chances admitted to ICU (7,20).

A good scoring system shows a good fit between the probabilities calculated using the scoring system and the outcomes observed. Discriminative performance is an essential indicator of predictive accuracy to overcome a lack of accuracy using sensitivity or specificity only. A cut-off for each scoring system is also important to distinguish low-risk and high-risk in predicting clinical outcomes (28). Unfortunately, cut-off values were reported almost differently for each included study. The reason for the inconsistent cut-off value from the studies included is difficult to explain. However, this condition might be due to some differences in those studies such as participant's ethnicity, UGIB etiology, use of medical treatment before endoscopy, time of endoscopy, and adherence to the guidelines regarding endoscopic therapy (23,24).

This systematic review shows a lack of evidence for discriminative performance ranging from fair to excellent in predicting rebleeding events, the need for endoscopic treatment, blood transfusion, and ICU admission. AIMS65 only showed sufficient evidence of fair to excellent discriminative performance in predicting mortality. It is clinically important because knowing which patients are at a true high risk of mortality can help to guide limited resources such as emergency endoscopy or ICU beds. AIMS65 included variables that are easily remembered, obtained, and less subjective. Furthermore, the variables are non-weighted and easy to calculate within 12 hours as part of the initial evaluation in ED. This is very potent to ensure objective assessment and applicable to enhance decision-making than individual clinical judgment only as an early risk stratification assessment (2,4,7).

All studies included in this study were conducted in the Emergency Departments, so it fits in line with the main objective of this review. We also determined, especially for clinical outcomes that it might be favorable to consider it as decision-support rather than composite outcomes. To our knowledge, this review is among the few that systematically synthesize on specific topic of AIMS65 score in patients with UGIB. Additionally, all included studies were very recent and publicized from 2012 to 2022.

However, this study has some limitations. First, the clinical outcomes of the need for intervention are limited to the need for endoscopic therapy, blood transfusion, and ICU admission. Surgery and radiology may be considered as clinical outcomes for this study. Second, lack of studies that reported long-term mortality or rebleeding events. There is only one study that reported mortality for 6 months. Another limitation is all included studies do not report calibration performance in analysis. Knowing that the included studies were designed as a validation study, recent impact analysis studies are needed to evaluate the usefulness of the score in a clinical setting in terms of patient satisfaction or resource/time allocation.

## CONCLUSION

In conclusion, AIMS65 is a simple, non-dependent-to-endoscopic examination, and easily calculated, so it is practical for UGIB cases in the emergency department. AIMS65 showed fair to excellent evidence in predicting mortality, but the evidence for predicting rebleeding events, the need for endoscopic



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therapy, blood transfusion, and ICU admission, says otherwise. However, AIMS65 still has a critically important role in early decision-making and triage for UGIB patients.

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**Conflict of Interest**

The authors declared that there is no conflict of interest in this study.

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**Authors' Contributor**

All authors have contributed to several processes in this study.

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Up to six authors, list all the authors.

- Yi Q, Li K, Jian Z, Xiao Y. Risk factors for acute kidney injury after cardiovascular surgery: Evidence from 2,157 cases and 49,777 controls - A meta-analysis. Cardio Renal Med. 2016; 6: 237–50

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- Amini S, Najafi MN, Karrari SP, Mashhadi ME, Mirzaei S, Tashnizi MA, et al. Risk factors and outcome of acute kidney injury after isolated cabg surgery: A prospective cohort study. Brazilian J Cardiovasc Surg. 2019; 34(1): 70–5.

***2. A book***

McKnight CL, Burns B. Pneumothorax. In: StatPearls. StatPearls Publishing; 2021.

**3. *Homepage/Web site***

Ikatan Dokter Anak Indonesia. Rekomendasi Ikatan Dokter Anak Indonesia: Asuhan Nutrisi Pediatrik (Pediatric Nutrition Care). Paediatric. 2011; 3(2): 5–6.

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