

Research Article

Comparison of Early Goal-Directed Therapy versus Standard Care in Sepsis

Ziaullah¹, Salman Khan^{2*}, Amin ul Haq³, Amin Ullah⁴, Mohammad Shafiq⁵, Abdul Jabbar⁶

^{1,3}Associate Professor, Medicine Department, Saidu Group of Teaching Hospital, Swat, Pakistan.

^{2*}Assistant Professor, Medicine Department, Saidu Group of Teaching Hospital, Swat, Pakistan.

^{4,6}Professor, Medicine Department, Saidu Group of Teaching Hospital, Swat, Pakistan.

⁵Senior Registrar, Medicine Department, Saidu Group of Teaching Hospital, Swat, Pakistan.

Corresponding Author: Dr. Salman Khan

Assistant Professor, Medicine Department, Saidu Group of Teaching Hospital, Swat, Pakistan.

Email: salman67kmc@gmail.com

Received: 23-03-2026, Revised: 12-05-2026, Accepted: 18-05-2026

ABSTRACT

Background: Despite great progress in critical care management, sepsis continues to be a leading cause of morbidity and mortality globally.

Objective: To assess the effectiveness of EGDT versus standard care on clinical outcomes in those with a sepsis diagnosis.

Materials and Methods: A randomized controlled trial was done at Medicine Department, Saidu Group of Teaching Hospital, Pakistan, between September 2025 to February 2026. A total of 120 adult patients diagnosed with sepsis were enrolled and equally divided into two groups. Data were analyzed using SPSS version 26.

Results: The clinical characteristics at the beginning were similar for both groups. The EGDT group demonstrated significantly improved mean arterial pressure (72.4 ± 6.5 mmHg vs 68.2 ± 7.1 mmHg), higher lactate clearance (38.5% vs 26.9%), shorter ICU stay (6.4 ± 2.1 days vs 8.2 ± 3.0 days), and lower septic shock progression (18.3% vs 36.7%). There was significantly less mortality in the EGDT group (13.3%) than in the standard care group (28.3%).

Conclusion: Early Goal-Directed Therapy was found to be effective compared to standard care in achieving physiologic stabilization, preventing complications, and reducing mortality in sepsis patients.

Keywords: Sepsis, Early Goal-Directed Therapy, Standard Care, Septic Shock, Mortality, Critical Care.

INTRODUCTION

Sepsis is still one of the most important causes of death and critical illness throughout the world and is a major clinical problem even in the era of critical care medicine. It is a host response to infection where the affected organ function becomes critical and may progress to septic shock if treatment is not started timely. The emphasis in the past 20 years has been on improving the effectiveness of early treatment to reduce the mortality rate of those who have been diagnosed with sepsis, and to improve the outcome for patients. The one of the most important advances in the management of septic shock is the systematic optimization of hemodynamic parameters in the early treatment of septic shock, known as Early Goal-Directed Therapy (EGDT). In recent years, the paradigm of treatment in critical care has expanded beyond EGDT to a more personalized and biomarker-guided approach for optimizing patient-centered outcomes and applications in precision medicine (1). The principles of Early

Goal-Directed Therapy have transformed the way sepsis is treated, and the early use of fluid resuscitation, vasopressors, transfusion of blood if needed, and continuous monitoring of physiological parameters in the first few hours of septic shock has changed all that.

The main purpose of EGDT is to restore tissue perfusion rapidly and prevent the onset of irreversible organ damage. Overall, systematic evidence of the effectiveness of EGDT has shown significant improvements in the management of septic shock, especially in terms of early hemodynamic stabilization and reduced mortality in certain populations. There is a continued debate, however, regarding the effectiveness of EGDT versus standard care protocols (2) and differences in adherence to protocols, health care delivery systems, and patient variables still exist. Protocolized resuscitation strategies (PRS) have slowly been integrated into the world-wide treatment cascades for sepsis. Attempts have been made to measure any benefits of the standardized

interventions versus clinician-directed treatment. Clinical comparison has shown that EGDT is a useful tool for early physiologic optimization, but that it can have variable effects depending upon the timing of the intervention, the severity of the disease and the institutional resources. The results highlight the need for ongoing assessment of structured resuscitation protocols in different health care environments to establish their clinical utility and effectiveness in improving survival of septic shock patients (3).

In addition to resuscitation techniques, there is increasing evidence that Early Goal-Directed Therapy (EGDT) can be used in conjunction with other supportive care measures by a multidisciplinary team to increase the likelihood of recovery and minimize the risk of complications from sepsis. A number of trials have been conducted that have demonstrated the advantages of the combined strategy on clinical outcomes when compared to careful nursing care. The benefits of hemodynamic optimization protocols can be maximized by optimizing the nursing care including close monitoring, early recognition of complications, and individual supportive therapy. The models of integrated treatment illustrate the evolving treatment paradigm of sepsis and the need for a multi-disciplinary approach to critical care (4). Economics is another barrier to implementing advanced sepsis management in healthcare systems. The costs of structured interventions like Early Goal-Directed Therapy are also very relevant as critical care is often scarce, especially in low- and middle-income countries. Cost analyses of the implementation of EGDT have suggested that while the protocolisation of EGDT may result in the increased consumption of resources in the short term, the successful implementation of EGDT may be associated with improved outcomes and reduced consumption of prolonged intensive care, thus creating a more cost-effective approach. Healthcare policy makers must be aware of the economic aspect of sepsis interventions to ensure that interventions are effectively delivered in critical care settings and are sustainable in a healthcare institution (5). The key to critical care management now is hemodynamic optimization and full supportive therapy. The nurse-led, goal-directed management interventions for sepsis with pulmonary disease (such as pneumonia) have been shown to be associated with several benefits. The effect of structured pulmonary rehabilitation in critical care management has

been linked to better prognosis and recovery in septic critically ill patients (6).

Timely administration of antimicrobial therapy is one of the key components in the management of sepsis. A delay in the delivery of antimicrobial agents has always been associated with poor prognosis and mortality in patients with septic shock. Studies comparing the timing of antimicrobial use in the context of Early Goal-Directed Therapy have reinforced the need for early measures of infection control along with hemodynamic stabilization. Standardised resuscitation combined with early antimicrobial treatment could be synergistic and improve survival and delay the onset of multiple organ dysfunction syndrome in severely ill patients (7). While the principles of EGDT are now widely accepted, there is increasing evidence that there are subgroups of septic shock with different responses to treatment. In addition, secondary analyses of multicenter international trials have suggested that the therapeutic benefits of EGDT might be dependent upon patient characteristics, disease severity, and baseline physiology. This variation highlights the need for individualized treatment options in place of the prescribed application of protocol. Identification of patient populations that are most likely to benefit from more aggressive resuscitation strategies is one of the major research priorities in critical care (8).

The principles of goal-directed therapy have also been demonstrated to be applicable to other therapeutic areas such as optimization of surgical care and perioperative medicine. Hemodynamic algorithms used to guide individualized fluid administration and cardiovascular support have been shown to be effective in lowering postoperative complications such as surgical site infections. These observations lend physiological support to the concept of goal-directed therapy, and suggest that goal-directed approaches to tissue perfusion may be useful in multiple settings and circumstances of hemodynamic instability and activation of systemic inflammatory responses (9). The principles of Early Goal-Directed Therapy have also been embraced in the treatment of septic shock in children, with emphasis on physiologic monitoring and customizing resuscitation targets. A number of advanced monitoring strategies have been evaluated in clinical trials in children treated with EGDT with the aim of improving therapeutic precision, and these strategies have proven to be feasible. These pediatric studies are useful in informing adaptation of structured

sepsis interventions in various patient groups and age groups (10).

The advances made over the years have influenced the current goal-directed resuscitation strategies. Comparisons of intermittent and continuous oxygen saturation monitoring during the treatment of septic shock in the context of EGDT have identified the importance of physiologic monitoring as an essential part of the care of septic shock. More responsive clinical decisions and increased efficiency of resuscitative efforts given to the critically ill patient can be achieved with optimized monitoring approaches (11). The ideas of goal-directed therapy have expanded to cardiac surgery, where perioperatively optimized hemodynamics in the individual have been shown to be effective in improving outcome. In comparative analyses of the various individualized goal-directed therapies, the more general clinical implications of precision cardiovascular management strategies and their potential to be applied to more severely ill patients with septic conditions are emphasized (12).

Another important context that affects current delivery of sepsis care is the implementation of sepsis bundle protocols in EDs. Sepsis care bundles have been adopted as a common metric of quality care across health systems, and early recognition and a defined pathway of action can significantly impact outcomes. A bundle of implementation strategies may improve protocol compliance and facilitate early initiation of evidence-based therapeutic interventions in the early treatment of sepsis (13). Goal-directed nurse-led physiotherapy interventions were also found to have a positive impact in older patients with sepsis-associated pulmonary complications. The incorporation of supportive care for rehabilitation in the standard care for sepsis can increase functional recovery and decrease morbidity in more severely affected populations. The findings of the study are consistent with the growing emphasis of the use of multimodal therapy in addition to hemodynamic resuscitation (14).

The treatment optimization strategies are also affected by specific infectious etiologies of sepsis. Nurse-led goal-directed pulmonary interventions in patients with multidrug-resistant organisms associated with pulmonary infections has been shown to have better prognosis and better recovery results. The findings indicate that there is a need for specific supportive care measures, which need to be integrated into a broader treatment plan for

sepsis, as an important part of treatment (15). Goal directed hemodynamic optimization has also been helpful in high risk surgical patients undergoing abdominal surgery. Goal directed therapy in the perioperative period remains a topic for randomized clinical trial evidence of personalized cardiovascular management strategies aimed at minimizing periop complications and optimizing physiological stability. Optimization strategies used during the perioperative period can provide valuable lessons to be applied to patient management strategies in sepsis (16).

Treatment of sepsis continues to be one of the most controversial and critical areas of fluid management. Fluid therapy is directed towards a goal that is designed to give enough fluid for tissue perfusion and not cause fluid overload or organ dysfunction. A systematic review of the evidence-based fluid optimization strategies has revealed important renal and overall physiological effects in patients in critical condition. Optimizing fluids in sepsis treatment continues to be an essential element in the quest for better treatment results (17). In the last few years, new technologies have also modified the approach to sepsis resuscitation, such as bedside imaging and ultrasound-guided interventions. The benefits of critical care ultrasound-led fluid resuscitation compared to the more traditional Early Goal-Directed Therapy approaches point to potential for more personalized and physiologically responsive fluid resuscitation decisions using advanced imaging modalities. Further study is still required to compare EGDT with traditional treatment to determine the optimal treatment between the various healthcare settings for survival and for minimizing sepsis-associated morbidity, as the management of sepsis is moving towards precision medicine-based approaches (18).

Objective: To investigate whether Early Goal-Directed Therapy is more effective than standard care in clinical outcomes, hemodynamic stabilization, and mortality in patients with sepsis who were diagnosed in a tertiary care hospital.

MATERIALS AND METHODS

Study Design: Randomized Controlled Trial.

Study Setting: Medicine Department, Saidul Group of Teaching Hospital, Pakistan.

Study Duration: September 2025 to February 2026.

Sample Size: There were 120 patients with sepsis who were enrolled in the study. The two

groups of patients were evenly matched, with 60 patients in the Early Goal-Directed Therapy group and 60 patients in the standard group.

Sampling Technique: Non-probability consecutive sampling technique was used for participant recruitment.

Inclusion Criteria: The study included all adult patients (age 18 years or older) who presented to the emergency department (ED) or intensive care unit (ICU) with clinically diagnosed sepsis who met the sepsis diagnostic criteria. Both male and female patients were enrolled irrespective of socioeconomic background. Patients or their legal guardians who gave informed written consent to participate in the study were included.

Exclusion Criteria: Patients under 18 years old, pregnant women, patients with a terminal malignancy, severe chronic liver disease, end-stage renal failure on maintenance dialysis, advanced heart failure, immunocompromised status (HIV infection), and those transferred from another health service facility after initial sepsis resuscitation for more than six hours were excluded. People who declined consent and patients having incomplete clinical information were also excluded.

METHODS

Eligible patients, who fulfilled the criteria of the study, were enrolled and randomized into two

groups using a computer-generated method after obtaining ethical approval from the institutional review committee. Early Goal-Directed Therapy (EGDT) was administered to Group A, which involved protocolized fluid resuscitation, administration of vasopressors as needed, mean arterial pressure (MAP) monitoring, urine output monitoring, and serum lactate and central venous parameter monitoring within the first six hours of treatment. Group B was treated for sepsis with routine hospital clinical practice without the need to adhere to resuscitation goals specified in the protocol. Data were collected on a structured data collection form and included baseline demographic data, comorbidities, Sequential Organ Failure Assessment (SOFA) scores, serum lactate levels, length of intensive care unit stay, use of vasopressor support, mechanical ventilation, and in-hospital mortality. The data were analyzed statistically in SPSS version 26. Data were analyzed using an independent sample t-test and a chi-square test, with the value of $p \leq 0.05$ set as the cut-off for statistical significance.

RESULTS

A total of 120 patients with sepsis were studied. Sixty patients were allocated to the Early Goal-Directed Therapy (EGDT) group and 60 to the standard care group.

Table 1. Baseline Demographic and Clinical Characteristics

Variables	EGDT Group (n=60)	Standard Care (n=60)	P-value
Mean Age (years)	55.8 $\pm$ 13.4	56.9 $\pm$ 12.7	0.641
Male Gender, n (%)	34 (56.7%)	36 (60.0%)	0.711
Female Gender, n (%)	26 (43.3%)	24 (40.0%)	0.711
Baseline SOFA Score	8.1 $\pm$ 2.3	8.4 $\pm$ 2.1	0.472
Initial Serum Lactate (mmol/L)	4.7 $\pm$ 1.4	4.8 $\pm$ 1.5	0.783
Diabetes Mellitus, n (%)	22 (36.7%)	24 (40.0%)	0.705
Hypertension, n (%)	28 (46.7%)	30 (50.0%)	0.714

No statistically significant differences were observed in baseline demographic variables

between the two groups ($p > 0.05$), indicating comparable clinical profiles before intervention.

Table 2. Hemodynamic and Laboratory Outcomes

Variables	EGDT Group	Standard Care	P-value
Mean Arterial Pressure at 6 Hours (mmHg)	72.4 $\pm$ 6.5	68.2 $\pm$ 7.1	0.002
Lactate Clearance (%)	38.5 $\pm$ 10.8	26.9 $\pm$ 9.7	<0.001
Urine Output (mL/kg/hr)	1.1 $\pm$ 0.3	0.8 $\pm$ 0.2	0.001
Vasopressor Requirement, n (%)	18 (30.0%)	29 (48.3%)	0.041

Patients receiving EGDT demonstrated significantly improved hemodynamic stabilization and metabolic recovery. Lactate

clearance was substantially higher in the EGDT group compared with standard care.

Table 3. Clinical Outcomes

Outcomes	EGDT Group	Standard Care	P-value
ICU Stay (days)	6.4 ± 2.1	8.2 ± 3.0	0.001
Mechanical Ventilation Required	17 (28.3%)	26 (43.3%)	0.087
Renal Dysfunction	9 (15.0%)	18 (30.0%)	0.048
Septic Shock Progression	11 (18.3%)	22 (36.7%)	0.024

The EGDT group showed shorter ICU stays and lower progression toward septic shock. Renal

dysfunction incidence was also significantly reduced among patients managed with EGDT.

Table 4. Mortality Outcomes

Outcome	EGDT Group	Standard Care	P-value
Survivors	52 (86.7%)	43 (71.7%)	0.043
Mortality	8 (13.3%)	17 (28.3%)	0.043

Mortality analysis demonstrated superior survival among patients treated using Early Goal-Directed Therapy. Overall mortality was reduced by approximately 15% in comparison to standard care. The findings indicate that

Early Goal-Directed Therapy was associated with improved hemodynamic parameters, enhanced tissue perfusion indicators, shorter intensive care duration, and lower mortality.

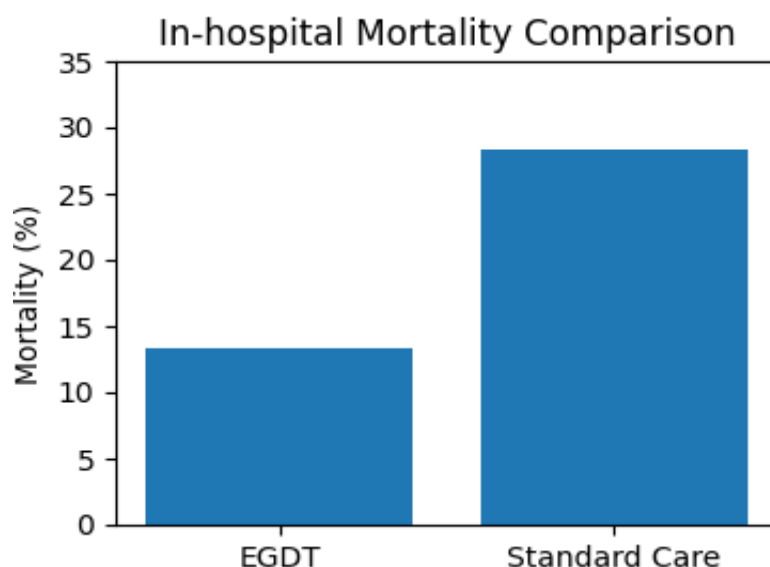


Figure 1. Comparison of In-Hospital Mortality Between Groups

The graphical representation further illustrates reduced mortality rates among patients receiving Early Goal-Directed Therapy compared with those managed through standard sepsis care protocols.

DISCUSSION

The aim of the present study was to determine whether Early Goal-Directed Therapy (EGDT) was more effective than standard care in septic patients and it was concluded that protocolized early resuscitation strategies resulted in better clinical outcomes. The patients who received EGDT showed improved hemodynamic stabilization, increased lactate clearance, reduced length of stay in intensive care unit

(ICU), reduced septic shock progression and reduced in-hospital mortality. The findings underscore the importance of structured management of sepsis, with a particular focus on physiologic optimization, tailored to the individual patient, during the first hours of treatment, as recommended by recent studies in critically ill patients. Recent progress in sepsis care and treatment has highlighted the need to move away from the resuscitation approach to a more personalised, biomarker informed approach to improve survival (1).

The results of decreased mortality in the EGDT group are in line with other studies that have demonstrated the beneficial effect of early protocolized treatment of septic shock. In the

present study, there was a difference between standard care (28.3%) and EGDT (13.3%) that led to clinically significant improvement in survival. Use of early recognition and aggressive hemodynamic optimization was likely a factor in maintaining tissue perfusion and organ dysfunction progression. The same outcomes have been seen in systematic reviews assessing the effectiveness of EGDT, in which a protocol-driven approach has been shown to improve physiologic stability and outcomes of septic shock patients (2).

The most important result of this study was the benefit of EGDT on hemodynamic recovery. The early treatment resulted in a significant improvement of mean arterial pressure, increase in urine output, and decrease in lactate level, indicating a better restoration of tissue perfusion. The increase in serum lactate level is a parameter of resuscitation efficacy, and has been increasingly important over the years as it indicates inadequate oxygen utilization and hypoperfusion. These improvements observed indicate that protocolized fluid therapy and optimization of vasopressors played a major role in achieving physiologic recovery. In comparative studies, it was shown that these hemodynamic parameter improvements occur following EGDT use (3). The present findings also revealed reduced progression to septic shock and reduced number of patients developing renal dysfunction following Early Goal-Directed Therapy. Maintaining organ function is an important therapeutic objective in sepsis because advanced organ failure is a good predictor of death and prolonged hospital stay. Physiologic stabilization early on may minimize inflammatory injury and preserve adequate end-organ perfusion, and minimize secondary complications. The results of investigations that integrated EGDT with careful supportive nursing care also showed clinical recovery and reduced complications in septic patients, highlighting the need for a multi-disciplinary approach to care (4).

The findings of the EGDT group, including a shorter length of stay in the intensive care unit further support the value of early resuscitation strategies. The structured intervention group had fewer ICU days, which meant that they were able to stabilize their clinical condition more quickly and with less burden on healthcare resources. But a number of health systems still struggle with a lack of intensive care, and resource allocation in developing nations can impact patient outcomes. Previous economic analyses of the potential impact of a

shift to EGDT have shown that there is potential for cost-effectiveness gains from increased recovery rates and reduced hospital stay, and that improved approaches to the management of sepsis have wider healthcare value (5). Treatment outcomes in septic patients could be further enhanced with the use of supportive interventions in the setting of hemodynamic optimization. The main purpose of the present study was to evaluate the effectiveness of the resuscitative measures, but supportive care is also of great significance. The prognosis of patients with septic pneumonia with respiratory involvement has been found to be better in studies that have compared the outcomes of nurse-led goal-driven pulmonary rehabilitation interventions. The results suggest that early resuscitation, in addition to supportive care from multiple disciplines, could result in optimal outcomes and reduce the burden of critical illness (6).

Another important factor that affects the outcomes of sepsis is the early administration of antimicrobial medications. The time of antibiotic administration was not a specific focus of the present investigation, but early infection control always be a key component to the successful management of sepsis. Early initiation of antimicrobial therapy and management of hemodynamics seem to go hand in hand to optimize survival. Other post-hoc analyses of antimicrobial timing within EGDT frameworks have demonstrated the need to shorten the delay in treatment during septic shock treatment (7). This variation in response seen in different septic populations is still a factor to take into account when assessing the effectiveness of EGDT. Overall, standardized protocols had significant benefits, however, not for all patients, as found in the present study. Response to treatment may be influenced by patient age, pre-treatment level of illness, comorbidities and infection source. Secondary analyses of large multicenter trials have also found that treatment effects of EGDT vary, further supporting the potential for improved outcomes with individualized patient-centered approaches instead of universal application of the protocol (8).

The physiologic principles of goal-directed therapy are also applicable to perioperative medicine in the care of surgical patients and optimization of surgical care. Hemodynamic monitoring algorithms aimed at optimizing tissue perfusion have been shown to be beneficial in a variety of clinical situations with systemically mediated inflammatory responses

and circulatory instability. Biological rationale for physiologic optimization strategies for critical illness management with goal-directed hemodynamic therapy has been supported by systematic investigations that have compared goal-directed hemodynamic therapy with other approaches, and have demonstrated that postoperative complications are reduced. (9) The use of advanced monitoring devices is continuing to influence the current resuscitation strategies. Pediatric trials of oxygen saturation monitoring during EGDT have emphasized the importance of continuous physiologic monitoring of septic shock management. If monitoring is done correctly, therapy can be adjusted when needed and the accuracy of therapy can be enhanced, particularly in patients with unstable, critically ill status (10). Similarly, systematic reviews comparing intermittent and continuous oxygen saturation monitoring have further emphasized the importance of physiological monitoring that is reliable in the context of structured resuscitations (11).

The concepts of therapy, which are directed towards a goal, have also been shown to be effective in cardiac surgical patients with specific cardiovascular management needs. In a few comparative studies of perioperative hemodynamic optimization, however, the principles of precision-guided physiologic management are applicable to a broader range than in a standard care paradigm for sepsis (12). Standardization of patient management and early intervention are also strongly recommended for the implementation of a structured sepsis bundle in the ED, and have been shown to improve treatment efficiency and patient survival (13). There are also emerging data to support supportive interventions by a nurse as part of a comprehensive sepsis management strategy. Pulmonary rehabilitation (PR) programs with a pulmonary-based intervention approach have shown promising prognostic benefits in septic critical care patients, especially in the elderly and those with the most severe pulmonary infections (14). The same benefits have been described in patients with sepsis from resistant pulmonary pathogens, further supporting the beneficial effects of the multidisciplinary approach to supportive care in addition to hemodynamic optimization (15).

However, fluid management continues to be key in the resuscitation of sepsis. The idea of goal-directed fluid strategies is to deliver adequate organ perfusion without the

complications of fluid overload. Randomized studies of individualized fluid optimization strategies have previously shown the significance of personalized resuscitation strategies that result in better physiologic stability and decrease adverse outcomes (16). Goal-directed fluid therapy has also been demonstrated to have renal benefits in critically ill patients in a meta-analysis (17). Last, new technology, such as ultrasound-guided assessment of fluid status, may further enhance individualized management of sepsis. Comparative studies have been conducted that have compared ultrasound-guided resuscitation with the traditional EGDT protocols, and these studies have shown promise for further refinement of the resuscitation approach. Future concepts for sepsis care and outcomes can be further improved in diverse healthcare settings with advanced monitoring technologies and the successful implementation of the principles of EGDT (18).

CONCLUSION

The present study showed that patients suffering from sepsis who received EGDT had better clinical outcomes than those receiving standard care. Patients receiving protocolized early resuscitation achieved better hemodynamic stabilization, better lactate clearance, fewer vasopressors used, fewer days in the intensive care unit, and less advancement towards septic shock. Additionally, mortality on hospital admission was significantly lower for EGDT-treated patients, highlighting the importance of early physiologic optimization in the treatment of septic patients. The results corroborate the emerging literature in favor of a systematic resuscitation regimen for critically ill septic patients. Early recognition of sepsis and aggressive, targeted therapy seems to be crucial for achieving better tissue perfusion, organ function, and survival outcomes. The principles of Early Goal-Directed Therapy may enhance overall treatment quality and patient recovery, although standard care still be effective in routine clinical practice. Sepsis protocol-based management strategies may play a major role in reducing sepsis-associated morbidity and mortality in tertiary health care institutions. Further, large-scale multicenter studies are recommended in the future to assess the efficacy of individualized approaches and refine evidence-based sepsis treatment protocols for various patient populations.

REFERENCES

- Adrita SA. Recent advances in sepsis management: from early goal-directed therapy to biomarker-driven approaches. *medtigo Journal of Emergency Medicine*. 2024;1(1).
- Acharya P, Virani S, Afreen S, Perthiani A, Sangster E, Lanka N, Malasevskaja I. Efficacy of early goal-directed therapy in septic shock management: a systematic review. *Cureus*. 2024;16(11).
- Elsayed AA, Elhamid Ahmed RA, Beshey BN. Early goal directed therapy versus a protocolized resuscitation care in early management of septic shock. *Egyptian Journal of Anaesthesia*. 2022;38(1):58-63.
- Yuan Z, Yang S, Zhang C, Chen K, Wang M, Hao S, Dong S, Yang Y. Retrospective analysis of the clinical efficacy of early goal-directed therapy combined with meticulous nursing intervention in patients with posttraumatic sepsis. *Journal of Healthcare Engineering*. 2021;2021(1):6706464.
- Higgins AM, Peake SL, Bellomo AR, Ao DJ, Delaney A, Howe BD, Nichol AD, Webb SA, Williams PJ, Harris AH, ARISE Investigators. The cost-effectiveness of early goal-directed therapy: an economic evaluation alongside the ARISE trial. *Critical Care and Resuscitation*. 2021;23(3):329-336.
- Sun J, Han W, Cui N, Li Q, Wang H, Li Z, Luo H, Liu J. Effect of nurse-led goal-directed lung physical therapy on the prognosis of pneumonia in sepsis patients in the ICU: a prospective cohort study. *Journal of Intensive Care Medicine*. 2022;37(2):258-266.
- Bulle EB, Peake SL, Finnis M, Bellomo R, Delaney A, ARISE Investigators, ARISE Working Committee. Time to antimicrobial therapy in septic shock patients treated with an early goal-directed resuscitation protocol: a post-hoc analysis of the ARISE trial. *Emergency Medicine Australasia*. 2021;33(3):409-417.
- Shah FA, Talisa VB, Chang CC, Triantafyllou S, Tang L, Mayr FB, Higgins AM, Peake SL, Mouncey P, Harrison DA, DeMerle KM. Heterogeneity in the effect of early goal-directed therapy for septic shock: a secondary analysis of two multicenter international trials. *Critical Care Medicine*. 2025;53(1):e4-e14.
- Jalalzadeh H, Hulskes RH, Weenink RP, Wolfhagen N, van Dusseldorp I, Schaad RR, Veelo DP, Hollmann MW, Boermeester MA, de Jonge SW. Systematic review and meta-analysis of goal-directed haemodynamic therapy algorithms during surgery for the prevention of surgical site infection. *EClinicalMedicine*. 2024;78.
- Jain P, Rameshkumar R, Satheesh P, Mahadevan S. Early goal-directed therapy with and without intermittent superior vena cava oxygen saturation monitoring in pediatric septic shock: a randomized controlled trial. *Indian Pediatrics*. 2021;58(12):1124-1130.
- Sankar JM, Das RR, Kumar UV. Comparison of intermittent versus continuous superior venal caval oxygen saturation monitoring in early goal directed therapy in septic shock: a systematic review. *Journal of Pediatric Intensive Care*. 2022;11(4):267-274.
- Ramsingh D, Hu H, Yan M, Lauer R, Rabkin D, Gatling J, Florida R, Martinez M, Dorotta I, Razzouk A. Perioperative individualized goal directed therapy for cardiac surgery: a historical-prospective, comparative effectiveness study. *Journal of Clinical Medicine*. 2021;10(3):400.
- Ferrari CL. The impact of early goal directed sepsis bundle sets in the emergency department and the impact of SEP-1 compliance rates.
- Sun J, Cui N, Han W, Li Q, Wang H, Li Z, Cheng W, Luo H, Zhao M. Implementation of nurse-led, goal-directed lung physiotherapy for older patients with sepsis and pneumonia in the ICU. *Frontiers in Medicine*. 2021;8:753620.
- Chen J, Zhou R, Li Z, Li Q, Long Y, Wang H, Cui N. Effect of nurse-led, goal-directed lung physiotherapy on prognosis of patients with sepsis caused by *Acinetobacter baumannii* pulmonary infection. *International Journal of Infectious Diseases*. 2021;103:167-172.
- de Waal EE, Frank M, Scheeren TW, Kaufmann T, de Korte-de Boer D, Cox B, van Kuijk SM, Montenij LM, Buhre W. Perioperative goal-directed therapy in high-risk abdominal surgery: a multicenter randomized controlled superiority trial. *Journal of Clinical Anesthesia*. 2021;75:110506.
- Zhao CC, Ye Y, Li ZQ, Wu XH, Zhao C, Hu ZJ. Effect of goal-directed fluid therapy on renal function in critically ill patients: a systematic review and meta-analysis. *Renal Failure*. 2022;44(1):777-789.

18. Chen ZY, Han X, Liu Y, Wang MJ, Wang BB, Wang L, Jin HX. Critical care ultrasound-guided fluid resuscitation versus early goal-directed therapy in patients with septic shock: a systematic review and meta-analysis.