Does Advanced Life Support Provide Benefits to Patients?: A Literature Review

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Abbreviations:
ALS = advanced life support
BLS = basic life support
BLS-D = BLS-Defibrillation
CPR = cardiopulmonary resuscitation
EMS = emergency medical services
EMT-I = emergency medical technician-intermediate
EMT-P = emergency medical technician-paramedic
OPALS = Ontario Prehospital Advanced Life Support

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Abstract

Introduction: Emergency medical services have invested substantial resources to establish advanced life support (ALS) programs. However, it is unclear whether ALS care provides better outcomes to patients compared to basic life support (BLS) care.

Objective: To evaluate the current evidence regarding the benefits of ALS.

Methods: Electronic medical databases were searched to identify articles that directly compared ALS versus BLS care. A total of 455 articles were found. Articles were excluded for the following reasons: (1) the article was not written in English; (2) BLS response was not compared to an ALS response; (3) a physician or nurse was included as part of the ALS response; (4) it was an aeromedical response; or (5) defibrillation was included in the ALS, but not the BLS, scope of care. Twenty-one articles met the inclusion criteria for this literature review.

Results: Results were divided into four categories: (1) trauma; (2) cardiac arrest; (3) myocardial infarction; and (4) altered mental status.

Trauma: The majority of articles showed that ALS provided no benefits over BLS in urban trauma patients. In fact, most studies showed higher mortality rates for trauma patients receiving ALS care. Further research is needed to evaluate the benefits of ALS for rural trauma patients, and whether ALS care improves outcomes in subgroups of urban trauma patients.

Cardiac Arrest: Cardiac arrest studies show that early CPR plus early defibrillation provide the greatest improvement in survival. However, most cardiac arrest research includes defibrillation as an ALS skill which has now moved into the BLS scope of care. The 2004 multi-center OPALS study provided good evidence that ALS does not improve cardiac arrest survival over early defibrillation. Further research is needed to address whether any ALS interventions improve cardiac arrest outcome.

Myocardial Infarction: Only one study directly compared the outcome of BLS and ALS care on myocardial infarction. The study found no difference in outcomes between BLS and ALS care in an urban setting.

Advanced Life Support: Only one study directly compared the outcome of BLS and ALS care on patients with altered mental status. The study found that the same number of patients had improved to "alert" on arrival at the emergency department, but there was a decreased length of emergency department stay for patients treated by ALS for hypoglycemia.

Limitations: This review article does not take into account the benefits of ALS interventions, such as thrombolytics, dextrose, or nitroglycerin, since no studies directly compared these interventions to BLS care. Furthermore, only one study in this literature review was a large, multi-center trial.

Conclusions: ALS shows little, if any, benefits for urban trauma patients. Cardiac arrest studies show that ALS does not provide additional benefits over BLS-defibrillation care, but more research is needed in this area. In two small studies, ALS care did not provide benefits over BLS care for patients with myocardial infarctions or altered mental status. Larger-scale studies are needed to evaluate which specific ALS interventions improve patient outcomes.

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Introduction

In 1998, Bissell *et al* published an extensive literature review evaluating the efficacy of advanced life support (ALS). The authors explored whether ALS provides superior benefits to patients than does basic life support (BLS).[1] Bissell found that the preponderance of evidence available at that time pointed towards the benefits of ALS care, while acknowledging that an ALS ambulance service requires greater equipment and personnel expenses than does a BLS service.

Since 1998, paradigm shifts in both emergency care and large, multi-center trials have provided additional evidence regarding the efficacy of ALS. For example, defibrillation has shifted from ALS to BLS care, and the Ontario Prehospital Advanced Life Support (OPALS) group conducted a multi-center trial in prehospital ALS.[2]

This goal of this paper is to update the 1998 paper and further evaluate the evidence from the medical literature regarding the question: Does ALS care provide better outcome for emergency medical services (EMS) patients than does BLS care?

Definitions

Advanced Life Support (ALS) care is defined as care provided by Emergency Medical Technicians-Intermediates (EMT-Is) or EMT-Paramedics (EMT-Ps) as defined in the National Highway Traffic Safety Administration's National Standard Curriculum for EMT-Is and EMT-Ps.[3–4] Advanced life support care includes administering medications, cardioversion, and endotracheal intubation. Advanced life support providers have nine to 10 times the amount of training of BLS providers.

Methods

The online medical research databases available through the Tulane University School of Medicine and the University of Maryland-Baltimore County library were searched. These databases included OVID, PubMed, MD Consult, and Lexis-Nexus. The databases were searched using a combination of the following terms: "emergency medical services", "advanced life support", and "basic life support". Only articles published after 1984 were included.

Four-hundred fifty-five unique articles were found. To be included in the study, the article must have compared a BLS ambulance response to an ALS level response. For example, a study that compared standard ALS care with a new ALS intervention would not have been included in the review.

Articles were excluded for the following reasons: (1) the article was not written in English; (2) BLS response was not compared to an ALS response; (3) a physician or nurse was included as part of the ALS response; (4) it was an aeromedical response; or (5) defibrillation was included in the ALS, and not in the BLS scope of practice.

The 21 articles that met the inclusion criteria for this literature review are listed in Table 1. The study type and the main findings of each article are included.

Results

The articles are presented using the following clinical categories: (1) Trauma; (2) Cardiac Arrest; (3) Myocardial Infarction; and (4) Altered Mental Status.

Trauma

Early research regarding ALS care for trauma patients showed some benefit to patients who received ALS care. Jacobs *et al* compared ALS and BLS care for trauma patients by comparing trauma scores in the field and on arrival at the emergency department.[5] They found that patients who received ALS care showed statistically significant improvement in trauma scores when compared to patients who received BLS care ($p = 0.01$). No mortality statistics were provided.

Potter *et al* found that patients who received ALS care had a lower mortality rate in the first 24 hours than did patients who received BLS care (36% vs. 73%, $p < 0.05$).[6] ALS care significantly reduced the incidence of pulmonary failure in trauma patients. However, ALS care did not decrease overall mortality compared to BLS care. In addition, patients who received ALS treatment showed no reduction in hospital length of stay, intensive care unit stay, or disability after head injury.

Murphy *et al* showed mixed results about the benefits of ALS care for trauma patients.[7] The provision of ALS care was associated with improved trauma scores. Also, ALS care improved survival rates for patients with blunt trauma, but decreased survival for victims of penetrating trauma.

A cohort study by Sampalis *et al* found that ALS provided no benefits over BLS in a sample of 360 trauma patients.[8] Cayten *et al* also showed no difference in survival rates between trauma patients who received BLS care vs. ALS care.[9] Among patients involved in motor vehicle crashes, patients who received ALS care showed greater improvement in trauma scores and blood pressures than did patients who received BLS care. Again, there was no difference in mortality rates between the two levels of care. In 2000, Eckstein *et al* retrospectively reviewed 496 patients with serious traumatic injuries.[10] The authors compared ALS and BLS care by examining two variables: (1) ventilation via endotracheal tube versus bag-valve-mask ventilation; and (2) administration of intravenous fluids. Although the authors found no increased scene time for ALS patients, the survival rate was nearly six times higher for patients who received ventilation via bag-valve-mask rather than intubation ($p < 0.005$). There was a slightly higher survival rate among patients who received intravenous fluids, but the difference was not statistically significant ($p = 0.09$).

The most comprehensive meta-analysis comparing BLS vs. ALS care in trauma patients was done by Liberman *et al*.[11] The authors compiled the statistics from 49 articles that compared BLS care to ALS care in trauma. They found that the odds ratio for dying was 2.59 times higher for trauma patients receiving ALS compared with patients receiving BLS. This ratio was adjusted for injury severity.

Lead Author	Year	Study Type	Findings
Jacobs LM	1984	Retrospective chart review	ALS improves trauma scores and long-term survival in trauma patients
Potter D	1988	Retrospective chart review	ALS improves short tem, but not long-term survival
Murphy JG	1993	Retrospective chart review	ALS confers better outcomes in victims of blunt trauma, but not penetrating trauma
Sampalis JS	1993	Prospective cohort	ALS provided no benefit over BLS
Cayten CG	1993	Prospective observational	ALS showed no benefit in trauma patients with transport times <35 minutes
Eckstein M	2000	Retrospective chart review	ALS does not improve survival rates in major trauma victims
Liberman M	2000	Meta-analysis	ALS shows no benefit over BLS in trauma patients
Liberman M	2003	Prospective cohort	ALS shows no benefit in trauma patients in areas with Level-1 trauma patients
Svenson JE	1996	Epidemiological	ALS improves survival among pediatric trauma victims
Rutledge R	1994	Epidemiological	ALS improves survival for rural trauma victims
Reines HD	1988	Epidemiological	ALS improves survival for rural trauma victims
Messick WJ	1992	Epidemiological	ALS is associated with decreased trauma deaths
Rutledge R	1992	Epidemiological	ALS is associated with decreased trauma deaths
Alexander RH	1984	Epidemiological	ALS is associated with decreased trauma deaths
Eisen JS	1998	Prospective cohort	ALS provided no benefit over BLS in for all complaints in an urban setting
Rainer TH	1997	Prospective observational	ALS skills provide no advantage over defibrillation
Adams J	1996	Prospective observational	Intubation showed no advantages over bag-valve-mask in cardiac arrest
Pitetti R	1997	Retrospective chart review	ALS provided no benefit over BLS in pediatric cardiac arrest
Nichol G	1999	Meta-analysis	Cardiac arrest survival is improved by bystander CPR, early defibrillation, and ALS; cannot differentiate benefits of defibrillation versus ALS
Stiell IG	2004	Multicenter clinical trial	ACLS provides no advantage over rapid defibrillation
Shuster M	1995	Prospective chart review	ALS provides no benefit to cardiac patients in an urban setting
Adams J	1996	Retrospective chart review	ALS provided no benefit over BLS to patients with altered levels of consciousness except for hypoglycemic patients

Table 1—Overview of articles and findings (ACLS = advanced cardiac life support; ALS = advanced life support; BLS = basic life support; CPR = cardiopulmonary resuscitation)

In 2003, Liberman *et al* found that in urban areas with Level-I trauma centers, there was no benefit to ALS care.[12] Patients who received ALS care had a mortality rate of 29% and patients receiving BLS care had a mortality rate of 18%.

Several epidemiological studies have looked at ALS care on a broad scale.[13–18] These studies all found that ALS care increased survival in rural areas and in children. However, the presence of ALS care was closely tied to the presence of a hospital or trauma center. Thus, it is difficult to determine whether increased survival resulted from ALS or from definitive medical care.

In summary, there is poor evidence that ALS care improves outcomes of trauma victims in urban areas. In fact, in urban areas, ALS care seems to worsen outcomes for trauma patients. The increased risk of mortality for these patients has been shown in both retrospective case reviews and prospective observational studies. Although no randomized, controlled trials have looked at ALS care for urban trauma patients, a comprehensive meta-analysis showed the odds of dying for patients who received ALS care were more than double those who receive BLS care.

However, there is no clear definition of an "urban trauma patient". In studies that showed a worse outcome for trauma patients receiving ALS care, patients were transported to a Level-I trauma center. Most had transport times of <15 minutes. No studies evaluated the efficacy of ALS care when the patient was not transported to a trauma center. One study has suggested that ALS benefits trauma patients with transport times of >35 minutes, but this has not been evaluated in other studies.[19] Other studies have evaluated the on-scene times for BLS vs. ALS, but not the overall scene time. Several epidemiological studies do suggest that ALS care benefits trauma patients in rural areas, but these studies are fraught with confounders. For example, in rural areas, it was unclear whether the benefits of ALS care arose from ALS or from having a hospital in the county where the accident or injury occurred.

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Further research into the efficacy of ALS in trauma patients should focus on defining a transport time beyond which ALS care may be beneficial. Research also should examine outcomes comparing patients transported to trauma centers vs. non-trauma centers. In addition, ALS care may benefit certain subgroups of patients, such as those with head injuries or traumatically obstructed airways.

Non-Trauma Patients

General

Eisen *et al* reviewed the call reports of 1,397 patients with seven different chief complaints including chest pain, altered mental status, and shortness of breath.[20] The authors compared the outcomes of the patients who received BLS care versus the cohort that received ALS care. They concluded that there was no difference between the ALS-treated and BLS-treated groups in emergency department length of stay, admission rates, or hospital length of stay.

Cardiac arrest

Outcomes of victims of cardiac arrest are one of the most examined indicators in EMS systems. Bissell *et al* published an extensive review of the efficacy of ALS in several areas of EMS care including cardiac arrest, trauma, and seizures.[21] The authors reviewed literature between 1966 and 1995. However, this analysis is difficult to apply today in light of present EMS care. Most of the articles cited by Bissell conclude that ALS has the greatest impact on out-of-hospital cardiac arrest survival. However, in the articles written before 1995, defibrillation was considered an ALS skill. Currently, defibrillation with automated external defibrillators (AEDs) is practiced by EMT-Basics and even laypersons. Therefore, ALS care must be considered separately and as treatment beyond defibrillation to determine the impact of ALS on cardiac arrest survival.

A study by Rainer *et al* found that witnessed cardiac arrests, early bystander cardiopulmonary resuscitation (CPR), shockable rhythms, and defibrillation were associated with better outcomes for victims of cardiac arrest.[21] In this study, ALS procedures such as intubation conferred no advantage over CPR and defibrillation alone. The survival rates between ALS units and BLS-defibrillation (BLS-D) units showed similar results.

Similar findings were reported by Adams *et al*.[22] The authors reviewed the records of 8,651 victims of cardiac arrests to determine the survival rates of patients who were intubated versus those patients who received ventilation via bag-valve-mask only. The survival rate was 2.5 times greater for patients who were not intubated.

A retrospective analysis of pediatric cardiac arrest also questioned the effectiveness of ALS care.[23] The study of 189 pediatric cardiac arrest victims used the endpoint of survival to hospital discharge. There was no difference in the survival rates of children who had received ALS treatment compared with those who received BLS treatment. This finding may be expected, given the severe pathology typical of pediatric cardiac arrest patients.

A more definitive answer regarding the role of ALS in out-of-hospital cardiac arrest was published by the OPALS group in 2004.[2] The OPALS group first established a rapid defibrillation program in 17 cities in which a defibrillator reached a patient in <8 minutes in >90% of the responses. After 12 months, the OPALS group added an ALS program to the rapid defibrillation programs. After adding the ALS program to the communities, there was statistical improvement in the rates of return of spontaneous circulation and admission to the hospital. However, there was no increase in the rate of hospital discharges or improved neurological outcome.

The available data comparing the benefits of ALS care to BLS care in treating out-of-hospital cardiac arrest suggest that ALS provides no advantage over early defibrillation and CPR. It is known that CPR plus early defibrillation, rather than CPR alone, significantly increases the survival of cardiac arrest victims.[24] The OPALS study provided additional evidence that prehospital ALS does not benefit patients in cardiac arrest beyond early defibrillation and CPR. Further research should focus on determining whether any specific ALS interventions improve cardiac arrest outcomes (e.g., medications or intubation). If follow-up studies to OPALS research reach the same conclusion, rapid defibrillation programs, rather than ALS care, will be the essential component in improving out-of-hospital cardiac arrest.

Myocardial infarction

Shuster *et al* prospectively studied 3,000 patients with acute cardiac illness that were treated by either BLS crews or ALS crews.[25] They found no difference in length of hospital stay or mortality. The authors concluded that ALS care provided no benefit to patients in an urban setting with average transport times of <10 minutes.

Altered mental status

Adams *et al* researched whether ALS care influenced the outcome of patients with altered mental status.[26] The authors studied a cohort of patients with altered mental status transported by a BLS ambulance and a cohort transported by an ALS ambulance. The authors found that the same percentage of patients in each group had improved to "alert" on arrival at the hospital. The principle diagnoses of the patients were seizure, hypoglycemia, and stroke. There was no difference in the number of patients admitted to the hospital or the mortality between the ALS and BLS cohorts. However, treatment of hypoglycemic patients by ALS units significantly decreased the time that patients spent in the emergency department (p <0.005).

Limitations

This review does not take into account the benefits of other ALS interventions over BLS care. For example, the FAST-MAG found that prehospital administration of magnesium to stroke victims reduces morbidity.[27] Paramedics can safely administer thrombolytics before arriving at the hospital.[28,29] In addition, this review does not take into account standard ALS treatments such as dextrose, nalaxone, and nitroglycerin.

Of the papers reviewed, only one was a randomized, controlled trial. Most of the studies either were retrospective chart reviews or prospective cohort studies, which only can establish association, not causation. Several of the other papers were epidemiological studies that examined a large number of variables.

Conclusions

The benefits of ALS care vary with the illness or injury being treated, as well as some other variables, such as transport time and the severity of the pathology. In trauma patients, there is poor evidence that ALS care improves survival in patients with short transport times to Level-I trauma centers as well as for patients with penetrating trauma. However, there is no clear definition of what constitutes a "short" transport time. Further research should focus on defining response times for which ALS will be beneficial and specific types of injuries or levels of injury severity for which ALS may decrease mortality.

In cardiac arrest victims, there are few studies that compare BLS-D level care to ALS care. The largest study on the benefits of ALS in cardiac arrest, published by the OPALS group, concluded that rapid defibrillation greatly improved cardiac arrest survival and that ALS provided no benefits over rapid defibrillation. Further research should seek to replicate the conclusions of the OPALS group as well as determine whether any specific ALS interventions might improve cardiac arrest survival.

Only weak evidence exists regarding the benefits of ALS care in other medical illnesses. There have been very few studies that have directly compared ALS and BLS care, so no conclusions can be drawn for these patients. This review did not consider the benefits of ALS interventions such as administration of glucose or nalaxone because there were no studies that compared these interventions to BLS care.

Evidence-based treatments is an increasingly important trend in medicine and EMS is no exception. No longer can treatments be validated by anecdote or tradition. Benefits must be proven in well-conducted scientific studies. Since the literature review published by Bissell *et al* in 1988, important strides have been made in EMS research, while at the same time, the character of what is included in ALS and BLS interventions has changed. The OPALS group has conducted one of the few, large, multi-center, clinical trials involving EMS. Similar types of randomized controlled trials will be needed to accurately evaluate the role of ALS in improving morbidity and/or mortality under specific conditions and with controlled levels of pathology severity.

As often is the case with medical research, the findings presented here demonstrate the complexity of establishing causal relationships in medicine and indicate a need for more targeted research to answer specific policy questions. As more research determines relative benefits of basic and advanced life support, EMS systems may need to shift paradigms in order to most effectively meet the needs of their patients.

References

1. Bissell RA, Eslinger DG, Zimmeraman L: The efficacy of advanced life support: A review of the literature. *Prehosp Disast Med* 1997;13(1):77–87.
2. Stiell IG, Well GA, Field B, *et al*: Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med* 2004;351:647–656.
3. National Highway and Transportation Safety Administration: *Emergency Medical Technician-Intermediate: National Standard Curriculum*. Washington, DC: U.S. Government Printing Office, 1999.
4. National Highway and Transportation Safety Administration: *Emergency Medical Technician-Paramedic: National Standard Curriculum*. Washington, DC: U.S. Government Printing Office, 1998.
5. Jacobs LM, Sinclair A, Beiser A, D'Agostino RB: Prehospital advanced life support: Benefits in trauma. *Journal of Trauma-Injury Infection & Critical Care* 1984;24(1):8–13.
6. Potter D, Goldstein G, Fung SC, Selig M: A controlled trial of prehospital advanced life support in trauma. *Ann Emerg Med* 1988;17(6):582–588.
7. Murphy JG, Cayten CG, Stahl WM, Glasser M: Dual response runs in prehospital trauma care. *Journal of Trauma-Injury Infection & Critical Care* 1993;35(3):356–362.
8. Sampalis JS, Lavoie A, Williams JI, Mulder DS, Kalina M: Impact of on-site care, prehospital time, and level of in-hospital care on survival in severely injured patients. *Journal of Trauma-Injury Infection & Critical Care* 1993;34(2):252–261.
9. Cayten CG, Murphy JG, Stahl WM: Basic life support versus advanced life support for injured patients with an injury severity score of 10 or more. *Journal of Trauma-Injury Infection & Critical Care* 1993;35(3):460–466.
10. Eckstein M, Chan L, Schneir A, Palmer R: Effect of prehospital advanced life support on outcomes of major trauma patients. *Journal of Trauma-Injury Infection & Critical Care* 2000;48(4):643–648.
11. Liberman M, Mulder D, Sampalis J: Advanced or basic life support for trauma: Meta-analysis and critical review of the literature. *J Trauma* 2000; 49(4):584–599.
12. Liberman M, Mulder D, Lavoie A, *et al*: Multicenter Canadian study of prehospital trauma care. *Ann Surg* 2003;237(2):153–160.
13. Svenson JE, Spurlock C, Nypaver M: Factors associated with the higher traumatic death rate among rural children. *Ann Emerg Med* 1996;27(5): 625–632.
14. Rutledge R, Smith CY, Azizkhank RG: A population-based multivariate analysis of the association of county demographic and medical system factors with per capita pediatric trauma death rates in North Carolina. *Ann Surg* 1994;219(2):205–210.
15. Reines HD, Bartlett RL, Chudy NE, *et al*: Is advanced life support appropriate for victims of motor vehicle accidents: The South Carolina Highway Trauma Project. *Journal of Trauma-Injury Infection & Critical Care* 1998;28(5):563–570.
16. Messick WJ, Rutledge R, Meyer AA: The association of advanced life support training and decreased per capita trauma death rates: An analysis of 12,417 trauma deaths. *Journal of Trauma-Injury Infection & Critical Care* 1992;33(6):850–855.
17. Rutledge R, Messick J, Baker CC, *et al*: Multivariate population-based analysis of the association of county trauma centers with per capita county trauma death rates. *Journal of Trauma-Injury Infection & Critical Care* 1992; 33(1):29–37.
18. Alexander RH, Pons PT, Krischer J, Hunt P: The effect of advanced life support and sophisticated hospital systems on motor vehicle mortality. *Journal of Trauma-Injury Infection & Critical Care* 1984;24(6):486–490.
19. Cayten CG, Murphy JG, Stahl WM: Basic life support versus advanced life support for injured patients with an injury severity score of 10 or more. *Journal of Trauma-Injury Infection & Critical Care* 1993;35(3):460.
20. Eisen JS, Dubinsky I: Advanced life support vs. basic life support field care: An outcome study. *Acad Emerg Med* 1998;5(6):592–598.
21. Rainer TH, Marshall R, Cusack S: Paramedics, technicians, and survival from out-of-hospital cardiac arrest. *J Accid Emerg Med* 1997;14(5):278–282.
22. Adams JN, Sirel J, Marsden K, Cobbe SM: Heartstart Scotland: The use of paramedic skills in out-of-hospital resuscitation. *Heart* 1997;78(4):399–402.
23. Pitetti R, Glustein JZ, Bhende MS: Prehospital care and outcome of pediatric out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2002;6(3):283–290.

24. American Heart Association: *BLS for Healthcare Providers*. Dallas: American Heart Association, 2001, pp 90–121.
25. Shuster M, Keller J, Shannon H: Effects of prehospital care on outcome in patients with cardiac illness. *Ann Emerg Med* 1995;26(2):138–145.
26. Adams J, Aldag G, Wolford R: Does the level of prehospital care influence the outcome of patients with altered levels of consciousness? *Prehosp Disast Med* 1996;11(2):101–104.
27. Saver JL, Kidwell C, Eckstein M, Starkman S, for the FAST-MAG Pilot Trial Investigators: Prehospital neuroprotective therapy for acute stroke: Results of the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) pilot trial. *Stroke* 2004;35(5):e106–e108.
28. Morrow DA, Antman EM, Sayah A, *et al*: Evaluation of the time saved by prehospital initiation of reteplase for ST-elevation myocardial infarction: Results of the Early Retavase-Thrombolysis in Myocardial Infarction (ER-TIMI) trial. *J Am Coll Cardiol* 2002;40(1):71–73.
29. Pedley DK, Bissett K, Connolly EM, *et al*: Prospective observational cohort study of time saved by prehospital thrombolysis for ST elevation myocardial infarction delivered by paramedics. *BMJ* 2003;327(7405):22–26.