Ethical Considerations for Conducting a Randomized Controlled Trial in Transport

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Abstract

Although recent studies support the rapid transfer of patients experiencing time-sensitive emergencies, limited data exist to support the use of air transport for nonurgent patient transfers. The nature of medical transport and the heterogeneity of patients who are transferred present unique challenges in designing and conducting clinical research trials that could contribute to the evidence-based decision making for patient care and transport. The current regulatory framework presents several barriers to conducting such research in the medical transport setting. We present a hypothetic study that randomizes patients to either ground or air transport as an exemplar. We discuss informed consent, risk, and the impracticality of conducting community consultations in a medical transport setting. Finally, recommendations for potential changes to current regulations are presented. These are directed at facilitating the conduct of emergency research through a system of oversight that integrates characteristics of quality improvement and health services research.

Introduction

Developing an evidence base for the science of medical transport will require an extensive amount of research focused on patients who are acutely ill or injured and require transfer. The barriers to and difficulties of conducting research with critically ill or injured patients have been extensively explored in the literature.[1-3] However, to date, little progress has been made in facilitating research and modifying regulatory environments to enable the ethical conduct of research in this vulnerable population.[4] Notwithstanding the challenges, we are obligated to the public to continually improve practice and conduct the required research to allow us to inform patients, surrogates, and other clinicians regarding whether, when, how, and why critical care transport services should be provided.[5] The purpose of this paper is to explore the current barriers to conducting research in the transport setting.

Some of the most vulnerable patients are those who are ill or injured and require medical care that is not available at their current location. Definitive intervention requires moving these patients by ambulance, helicopter, or fixed wing aircraft to the most appropriate center for further medical care, yet the effect of the transfer itself on patients both during and after transfer remains poorly understood. Recent studies support the transport of patients who are experiencing time-sensitive emergencies such as trauma[6] and myocardial infarction.[7,8] For these patients, use of the shortest transfer time to definitive care, which frequently is air transport, is noncontroversial. Alternatively, several studies have reported worse outcomes for critical care patients who undergo interfacility transport in situations in which intervention is not time sensitive.[9,10] A primary question that remains unresolved involves how to optimally move nonurgent patients.

The current regulatory environment severely limits the feasibility of conducting research in critically ill or injured patients primarily because of the requirement for informed consent. Waiving the requirement for informed consent using the emergency research waiver requires that community consultations be conducted. This presents several hurdles that may prove challenging for research conducted in a medical transport setting. Additionally, health care delivery is evolving into a learning health care system (that blurs the distinction between comprehensive data collection required to support today's electronic medical records and quality reporting systems), with activities that would have been previously labeled as research.[11] The conventional criteria that differentiate clinical practice from research is considered by some as no longer applicable.[11]

In this article, we explore the barriers to conducting emergency research under the current regulatory framework using a hypothetic study that proposes to randomize patients to either ground or air transport as an exemplar. We specifically focus on informed consent, risk, and the impracticality of community consultations. We propose several recommendations for possible changes to the current regulations to enable the conduct of emergency research while maintaining our moral obligation to uphold patient safety and respect their rights.

Background

Approximately 400,000 patients are transferred by helicopter, with another 150,000 transferred by fixed wing aircraft each year in the United States.[12] In addition, there are 264 registered ground critical care ambulances that also transport patients[12]; however, the annual number of completed ground patient transfers in the United States on an annual basis is not currently available. The primary justification for using air transport is to reduce the out-of-hospital time that patients experience, especially for patients being transferred between intensive care units (ICUs). The importance of out-of-hospital time stems from the assumption that while patients are in the transport environment, they are at increased risk for physiologic compromise because of the stressors of transport, limited resources available for care, the potential for equipment failure, and limited capability of the providers to respond if physiologic decompensation occurs. To date, this assumption has not been confirmed; there have been no reports of increased complication rates or increased mortality during ground transport when compared with air.

There are multiple factors that contribute to high use of elective (ie, not time sensitive) helicopter transfers.

Emergency rooms may request that a complicated patient be transferred out as quickly as possible in order to relieve busy departments of the resource-intensive patient. Another factor is the consideration of distance. Transport protocols often use trip distance as a deciding factor, with longer trips increasing the likelihood of helicopter use regardless of the patient's condition or needs, reflecting the assumption that faster is better.

The high rate of air transport may suggest that the prevailing approach is to err on the side of caution and request helicopter transport under the assumption that it is superior to ground transport both in the care provided and the outcomes achieved. To date, we noted only 1 review of a large series of transfers that found a 2% increase in the likelihood of a critical event for every 10 minutes of an urgent medical transfer when cared for by varying levels of paramedics.[13] Another study suggests that the distance of transport may present greater risk for minor adverse events.[14] In their discussion of health care regionalization, Singh and MacDonald[15] note that the actual health impact and risk of transferring critically ill patients to a higher level of care within a regionalized health system are not precisely known.

With the exception of time-sensitive diagnoses, there is currently no evidence to support that nonurgent patient transfers conducted by critical care transport teams, especially those staffed with advanced providers (eg, nurse practitioner and physician), experience similar risk. Recent evidence suggests that even time-sensitive patients being transported for surgical intervention over long distances experience an improved physiologic state both during and after transfer with improved clinical outcomes when transferred by advanced practice critical care transport teams to high-volume quaternary hospitals.[16] The lack of compelling evidence creates the conditions for clinical equipoise regarding the efficacy of helicopter versus ground transport for nonurgent interfacility transfers.

Example Study

Several methodologic approaches could be used to answer the question of differences in morbidity and mortality for patients who are transferred by helicopter versus ground. The choice of method depends on several factors, including the feasibility of conducting the study. One option would be to design a rigorous prospective observational study that creates matched cohorts of like patients and compares them based on the mode of transport. Robust statistical analyses using propensity scoring and matching with sensitivity analysis can provide similar results to the gold standard results of a randomized clinical trial.[17,18] The primary benefits of conducting an observational study include the correspondence with real-world conditions, negating a primary criticism of clinical trials that have strict inclusion and exclusion criteria limiting the generalizability of study findings. However, observational designs are vulnerable to selection biases and the possibility that unobserved covariates could have an effect on the outcome under study.

The threat of selection bias is a primary concern in answering the specific research question of interest here. Selection bias, reflected in providers' and systems' decisions for mode of transport, presents a major barrier that can be controlled via the randomization of mode of transport. Even though an observational study design could be used to investigate differences in outcomes, the heterogeneity of patients, referral processes, and provider preferences could confound study conclusions and require very large samples to obtain sufficient subjects for matching. Therefore, for the purposes of this article, we explore the feasibility of conducting a randomized clinical trial.

In this hypothetic trial, the study population would include patients who are referred for transfer, who have a nonurgent diagnosis, and who would, under standard care, be equally likely to be transported by ground as by air. A common example of a patient who would fall into this category would be a patient with respiratory failure who was intubated and stabilized in a small hospital emergency department or ICU and is being transferred to a larger tertiary care hospital. Enrolling patients like this into a randomized trial will be the example case for discussion.

Informed Consent

The primary issue in conducting research in emergency and critical care settings is the requirement to obtain informed consent. Although progress has been achieved with the addition of the emergency research waiver of consent amendment in 1996,[19] major regulatory barriers still remain both in the United States and Europe,[20] where limited emergency research is conducted at the present time.

The challenges of obtaining informed consent for patient enrollment have been discussed[3,4,21-25] and are applicable to the conduct of this trial. There are several considerations to explore for this trial related to obtaining informed consent. The primary practical or logistic consideration concerns the inability to prospectively identify subjects who are referred for transfer and who are usually at outside hospital locations. The only possible method of obtaining consent for enrollment would be to call the patient or surrogate before dispatching the mode of transport to retrieve the patient. Although possible in some instances, the telephone call option would rarely be feasible because many patients in these situations lack decisional capacity, and surrogate decision makers are often not available at the time of the referral call. An alternative option would be to obtain informed consent from the patient or surrogate once a transport team arrives at the referring facility. However, postarrival consenting is not a reasonable option because if a patient or surrogate refuses participation, another transport team and alternative mode of transport may have to be dispatched depending on the first mode that is assigned. This would entail increased cost and inappropriate allocation of resources.

Another possibility would be the application of the emergency research consent waiver (ERCW). Under current regulations, the ERCW under section 46.101(i) of 45 CFR 46[26]