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Clinical paper

What change in outcomes after cardiac arrest is necessary to change practice? Results of an international survey☆

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ABSTRACT

Background: Efficient trials of interventions for patients with out-of-hospital cardiac arrest (OHCA) should have adequate but not excess power to detect a difference in outcomes. The minimum clinically important difference (MCID) is the threshold value in outcomes observed in a trial at which providers should choose to adopt a treatment. There has been limited assessment of MCID for outcomes after OHCA. Therefore, we conducted an international survey of individuals interested in cardiac resuscitation to define the MCID for a range of outcomes after OHCA.
Methods: A brief survey instrument was developed and modified by consensus. Included were open-ended responses. The survey included an illustrative example of a hypothetical randomized study with distributions of outcomes based on those in a public use datafile from a previous trial. Elicited information included the minimum significant difference required in an outcome to change clinical practice. The population of interest was emergency physicians or other practitioners of acute cardiovascular research.
Results: Usable responses were obtained from 160 respondents (50% of surveyed) in 46 countries (79% of surveyed). MCIDs tended to increase as baseline outcomes increased. For a population of patients with 25% survival to discharge and 20% favorable neurologic status at discharge, the MCID were median 5 (interquartile range [IQR] 3, 10) percent for survival to discharge; median 5 (IQR 2, 10) percent for favorable neurologic status at discharge, median 4 (IQR 2, 9) days of ICU-free survival and median 4 (IQR 2, 8) days of hospital-free survival.
Conclusion: Reported MCIDs for outcomes after OHCA vary according to the outcome considered as well as the baseline rate of achieving it. MCIDs of ICU-free survival or hospital-free survival may be useful to accelerate the rate of evidence-based change in resuscitation care.

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Introduction

There is a large variation in the process and outcome of care for patients with out of hospital cardiac arrest (OHCA).[1–3] Recently, several communities have reported that outcomes after OHCA have improved over time.[4–6] Now, many patients with cardiac arrest can return to a good quality of life if recognized and treated quickly. This variation in and improvement of outcomes emphasizes the need to conduct efficient randomized trials of interventions to accelerate evidence-based changes in resuscitation practices to improve outcomes for patients with OHCA.

Resources for clinical research are limited. Clinical research related to cardiac arrest is underfunded compared to other common clinical conditions.[7] There is heterogeneity in outcomes among randomized trials of interventions for patients with cardiac arrest.[8] The sample size for a trial depends in part on the magnitude of difference in outcomes sought. To optimize use of limited funds, efficient large simple trials of interventions for patients with OHCA should have adequate but not excess power to detect a difference in outcomes. The minimum clinically important difference (MCID) has been defined as the threshold value in outcomes observed in a trial at which patients or providers should choose to adopt a treatment.[9] If a trial reports a significant difference that is larger than the MCID for an outcome, then providers should likely use that intervention to treat patients. But if a trial reports a difference that is smaller than the MCID for an outcome, then rational providers may not use that intervention because the benefits may not be large enough to be important to patients or providers. To date, there has been limited descriptions of MCID for outcomes after OHCA.[10,11] Therefore, we conducted an international survey emergency physicians or other practitioners of acute cardiovascular research to define the MCID for a range of outcomes after OHCA, including novel outcomes for trials in patients with cardiac arrest, such as hospital-free survival and intensive care free survival. A secondary object was to estimate sample sizes of trials necessary to detect MCIDs.

Methods

Survey

A brief survey instrument was developed by several of the authors (GN, GP, FS, FK, MS, SB) and modified by consensus prior to distribution to probe for the minimum clinically important difference for outcomes in trials of interventions in patients with OHCA (see online appendix). Responses were open-ended rather than multiple-choice. The survey was prepared for online completion by using standard electronic data capture software.[12]

Survey questions were preceded by an illustrative example of a hypothetical randomized study to help focus the responses to the questions. MCID were sought for a range of outcomes intended to mimic the distribution of outcomes expected for all patients treated by emergency medical services (EMS) providers; those treated for pulseless electrical activity or asystole; those treated for ventricular fibrillation (VF); and those with VF and spontaneous circulation upon hospital arrival. These outcomes were patterned on those included in the Utstein template for standardized reporting of outcomes after OHCA.[13]

Two additional outcomes were included in the survey. Intensive care morbidity was defined as the number of days alive and permanently out of intensive care (ICU) during the first 30 days post arrest. 'Permanently' was defined as discharged from intensive care without any further readmission. Intensive care includes a ward capable of providing mechanical ventilation but not a ward capable of providing telemetry only. Patients who die before discharge from ICU would be assigned zero days out of intensive care. The day a subject was discharged from the ICU was counted as a full day in the ICU. Similarly, hospital morbidity was defined as the number of days alive and permanently out of hospital up to thirty days post arrest. Again patients who die before discharge will be assigned zero days out of hospital. The distribution of outcomes was estimated from the public use datafile of a previous large randomized trial of interventions in patients with OHCA.[14,15]

Respondents were asked to describe their general characteristics, including age, gender, years since medical school, years in practice and country of residence. No individually identifiable information was collated. The University of Washington Institutional Review Board reviewed this study and determined that it was exempt from human subjects research.

Respondents

The population of interest was emergency physicians or other practitioners of acute cardiovascular research. Individuals invited to participate had previously published at least one peer-reviewed article related to OHCA. These were supplemented as needed by recommendation of peers to achieve at least two responses from each country. Repeat invitations were sent by electronic mail to non-respondents until at least two responses were obtained from any individual country.

Countries

We sought participation from individuals in as many countries as possible with the purpose of representing a diversity of medical practices. After we achieved responses from 50% of individuals, we determined that we had a broad enough set of responses to allow meaningful inferences.

Analysis

Responses were summarized descriptively (R 3.2.1, R Development Core Team available at www.r-project.org; and SAS JMP 11.2.0, SAS Institute, Cary, NC). The median absolute increase in each outcome across the range of baseline rates was used to estimate the number of patients required to detect the MCID in a hypothetical superiority trial. These estimates assumed a single analysis with 90% power, and two-sided alpha = 0.05.

Results

Survey responses

Participation was sought from 321 individuals in 58 countries. Responses were obtained from 161 (50% of sample) individuals in 46 countries (79% of sample) that included India, China, Kenya, Nigeria, and South Africa, many of the European Union countries, as well as North and South American countries including Canada, USA, Mexico, and Brazil (Fig. 1). One response was not usable. The total census population represented by respondents was about 4.5 billion people. Responses were reported overall and then by the subgroup of countries in North America (3 countries; 36 responses) vs. Europe (21 countries; 67 responses) vs. the rest of the world (22 countries; 54 responses).

Table 1 describes the characteristics of the respondents. The majority were male ($n = 129$, 81%). Most of the respondents were physicians ($n = 131$, 82%). Years in practice were mean 15.9 ± 12.3.

Table 2 summarizes the responses to the elicitations of MCID overall and grouped by region. The majority of reported MCIDs were clustered together (i.e. had narrow interquartile range). MCID were not significantly different among North American respondents as compared to those from Europe or the rest of the world.