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Clinical paper

Post-admission outcomes of participants in the PARAMEDIC trial: A cluster randomised trial of mechanical or manual chest compressions☆

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ABSTRACT

Background: The PARAMEDIC cluster randomised trial evaluated the LUCAS mechanical chest compression device, and did not find evidence that use of mechanical chest compression led to an improvement in survival at 30 days. This paper reports patient outcomes from admission to hospital to 12 months after randomisation.
Methods: Information about hospital length of stay and intensive care management was obtained through linkage with Hospital Episode Statistics and the Intensive Care National Audit and Research Centre. Patients surviving to hospital discharge were approached to complete questionnaires (SF-12v2, EQ-5D, MMSE, HADS and PTSD-CL) at 90 days and 12 months. The study is registered with Current Controlled Trials, number ISRCTN08233942.
Results: 377 patients in the LUCAS arm and 658 patients in the manual chest compression were admitted to hospital. Hospital and intensive care length of stay were similar. Long term follow-up assessments were limited by poor response rates (53.7% at 3 months and 55.6% at 12 months). Follow-up rates were lower in those with worse neurological function. Among respondents, long term health related quality of life outcomes and emotional well-being was similar between groups. Cognitive function, measured by MMSE, was marginally lower in the LUCAS arm mean 26.9 (SD 3.7) compared to control mean 28.0 (SD 2.3), adjusted mean difference −1.5 (95% CI −2.6 to −0.4).
Conclusion: There were no clinically important differences identified in outcomes at long term follow-up between those allocated to the mechanical chest compression compared to those receiving manual chest compression.

Background

High quality chest compressions are associated with improved outcomes from cardiac arrest [1–3]. However, maintaining high quality chest compressions is physically challenging [4] so the concept of a mechanical chest compression device, which automates the process of chest compressions, is attractive [5]. The out of hospital, randomised assessment of a mechanical chest compression device (PARAMEDIC) trial was a cluster randomised open-label clinical effectiveness trial which compared mechanical chest compressions, delivered by the LUCAS-2 device (Physiocontrol, Lund) to manual chest compressions (control) delivered by National Health Service ambulance personnel. The initial findings of the trial have been previously reported [6,7]. The study did not find an advantage to LUCAS chest compressions for the rate of return of spontaneous

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circulation, (LUCAS 32% vs control 31%, adjusted OR (adjusted odds ratio(aOR)) 1.0 (95% confidence interval 0.9–1.1)), survived event (LUCAS 23% vs control 23%, aOR 1.0 (0.8–1.1)) or 30-day survival, (LUCAS 6% vs control 7%, aOR 0.9 (0.6–1.2)). However slightly more patients in the LUCAS arm had an unfavourable neurological outcome compared to those receiving manual chest compressions (5% vs 6% respectively, aOR 0.7 (0.5–1.0)).

Most previous randomised controlled trials in out of hospital cardiac arrest have focused on short term outcomes (return of spontaneous circulation, survival to discharge) [8]. Gross neurological function is usually measured with tools such as Cerebral Performance Score (CPC) and modified Rankin Scale (mRS). However, these tools may be insensitive to some of the more subtle, yet important longer term neurocognitive and functional impairments experienced by survivors of cardiac arrest [9–11]. The spectrum of impairment of health related quality of life following cardiac arrest includes memory and cognitive dysfunction, affective disorders and post-traumatic stress disorder (PTSD) [10,12].

This paper extends the findings from the original trial by reporting on longer term outcomes amongst those who survived beyond hospital discharge. In addition, through linkage with national administrative data, hospital and intensive care unit length of stay, mode of death and organ donation rates after death are presented.

Data and methods

The PARAMEDIC trial examined the effectiveness of LUCAS-2, a mechanical cardiopulmonary resuscitation (CPR) device, in 4471 out-of-hospital cardiac arrest patients compared to standard manual CPR. The study was designed as a cluster randomised trial, whereby the ambulance vehicles were randomised to carry the LUCAS CPR device (intervention) or not (control). Full details of study design are presented in the trial protocol, which has been published previously [13]. In brief, adults who sustained out of hospital cardiac arrest, where resuscitation was attempted by ambulance personnel and were attended by a trial vehicle were eligible for inclusion. Those with cardiac arrest caused by trauma or with known or clinically apparent pregnancy were excluded. The primary outcome (30-day survival) and some of the secondary outcomes (survived event, survival to discharge, neurological status and survival at 3 and 12 months) have been previously reported [6]. This study reports the pre-defined secondary outcomes of health-related quality of life, cognitive function, anxiety and depression, post-traumatic stress, hospital and intensive care length of stay. These outcomes are also presented in the in-depth trial report published as a Heath Technology Assessment Monograph [7]. Post-hoc additional analyses included reporting intensive care and hospital free days, mode of death and organ donation rates after death.

Linkage with Health & Social Care Information Centre (HSCIC) and the Intensive Care National Audit Research Centre (ICNARC)

The UK Health & Social Care Information Centre (HSCIC) and Intensive Care National Audit & Research Centre (ICNARC), were contacted for the hospital data of patients who survived long enough to be admitted to hospital. This analysis was based on the combination of the original trial, and linked HSCIC and ICNARC data. Approvals were obtained from the Coventry and Warwickshire Research Ethics Committee, HSCIC Data Access Advisory Group (DAAG) and ICNARC.

The trial recruitment was run between April 15, 2010, and June 10, 2013. Patient flow was shown in the CONSORT diagram (Fig. 1). Of the 4471 randomised patients, 2695 (951 or 35.3% in LUCAS) were not known to be deceased at emergency department. No patient recruited after March 2013 were linked to HSCIC because the 2013–14 data were not available before our linkage application. Therefore, 2398 (843 or 35.2% in LUCAS) were considered eligible for linkage.

Information on hospital length of stay was provided by Hospital Episodes Statistics (HES) admitted and A&E datasets. Approximately 40–50% of patients admitted to hospital after cardiac arrest are admitted to intensive care [14]. ICNARC provided data for intensive care duration, survival, temperature management, organ donation and withholding of treatment information.

HES admitted patient care data were used to calculate hospital length of stay and survival to hospital discharge, with supplementary discharge and death data collected in the trial. Hospital length of stay was defined as days between cardiac arrest and discharge from or death in hospital. ICU length of stay was defined as days between ICU admission and discharge from or death in ICU. Patients who did not achieve sustained ROSC at hospital handover were assumed to have a hospital stay of zero days. Intensive care-free days was defined as the number of days that a patient was alive and not requiring intensive care during the first 30 days after the cardiac arrest. Hospital-free survival days was defined as the number of days alive post-hospital discharge during the first 30 days after the cardiac arrest. Re-admission to hospital or ICU was not counted.

Follow-up questionnaires

Patients who were alive and consented to long-term follow-up were contacted by letter at the relevant follow-up point. Non-responders were sent a 2nd letter followed by a telephone call before being declared lost to follow-up. Participants were asked to self-complete several patient-reported outcome measures including two generic measures of health-related quality of life (HRQoL) – Short-Form 12-item Health Survey version 2 (SF-12v2) [15] and the single item EuroQoL-Visual Analogue Scale (EQ-VAS) [16] – and domain-specific measures of emotional well-being – Hospital Anxiety and Depression Scale (HADS), Mini-Mental State Examination (MMSE) [17] and the PTSD Civilian Checklist (PTSD-CL) [18]. Questionnaires were returned by post to the trial co-ordinating centre at Warwick Clinical Trials Unit.

Analysis

Patients' outcomes were compared by treatment arm, using fixed-effect logistic and linear regression models to obtain unadjusted and adjusted odds ratios (OR) or mean difference and 95% confidence intervals (CI). The pre-specified covariates used in the adjusted models were age, sex, response time (time interval from 999 call to arrival of the trial vehicle), bystander CPR, and initial rhythm. We attempted adjusting for the clustering design using multilevel logistic models (using the GLIMMIX procedure with logit link function based on the binomial distribution). Because of the extremely low survival rates in each cluster (vehicle), the multilevel models could not be fitted with the vehicle random effect since this effect was not estimable. For this reason, we assumed that the intra-cluster correlation coefficient was negligible (0.001) and ordinary logistic regressions were fitted. Analyses used complete cases only, with no imputation. Intention to treat approach was used for all analyses, which were conducted in SAS v9.3 and v9.4 (Cary, NC, USA).

Results

The trial ran between April 15, 2010, and June 10, 2013 (which included 12 months' follow-up). During this time 4471 patients were enrolled of which 1652 were allocated to receive LUCAS and 2819 manual chest compression of which 1099 and 1868 were