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Experimental paper

# Closed chest compressions reduce survival in an animal model of haemorrhage-induced traumatic cardiac arrest

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**Abstract**

Closed chest compressions (CCC) are recommended for medical cardiac arrest, but there is little evidence to support their inclusion for traumatic cardiac arrest (TCA).

This laboratory study evaluated CCC following haemorrhage-induced TCA and whether resuscitation with blood improved survival compared to saline. The study was conducted with the authority of UK Animals (Scientific Procedures) Act 1986 (received institutional ethical approval and a Home Office Licence) using 39 terminally anesthetised, instrumented, juvenile Large White pigs. Following baseline measurements, animals underwent captive bolt injury to the right thigh and controlled haemorrhage (30% blood volume). Sixty minutes later there was a further haemorrhage to a MAP of 20 mmHg. The randomised resuscitation protocol was initiated within 5 min: CCC (Group 1); IV whole blood (Group 2); IV 0.9% saline (Group 3); IV whole blood + CCC (Group 4); and IV saline + CCC (Group 5). Fluid was administered as 3 × 10 ml/kg boluses using the Belmont® Rapid Infuser. The LUCAS™ II Chest Compression System delivered CCC. Primary Outcome was attainment of return of spontaneous circulation (ROSC MAP ≥ 50 mmHg) at Study End (fifteen minutes post-resuscitation) and secondary outcomes included haemodynamics.

Mortality (MAP≤10 mmHg) was significantly higher in Group 1 compared to Groups 2 and 3 ($P < 0.0001$). Resuscitation with whole blood was significantly better than saline ($P = 0.0069$), no animals in Group 3 attained ROSC. The addition of chest compressions to fluid resuscitation resulted in a significantly worse outcome with saline resuscitation ($P = 0.0023$) but not with whole blood ($P = 0.4411$). Cardiovascular variables at the end of the Resuscitation Phase and Study End were significantly worse for Group 5 compared to Group 3. Some significant differences were present at the end of the Resuscitation Phase for Group 4 versus Group 2 but these differences were no longer present by Study End.

CCC were associated with increased mortality and compromised haemodynamics compared to intravenous fluid resuscitation. Whole blood resuscitation was better than saline.

**Keywords:** Haemorrhage, Traumatic cardiac arrest, Trauma, Closed chest compressions, Resuscitation, Porcine model, TCA

## Introduction

Closed chest compressions (CCC) are a key component of cardiopulmonary resuscitation protocols in non-traumatic primary cardiac events leading to cardiac arrest. There is evidence suggesting they are as beneficial as combined ventilations and compressions in the pre-hospital environment in non-traumatic cardiac arrest.[1–3] However, the pathophysiology of traumatic cardiac arrest is different, which may necessitate different resuscitation priorities.

The practicalities of performing chest compressions while undertaking intubation, bilateral thoracostomies and securing large

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bore venous access following severe trauma are often difficult but many teams persist in the belief that chest compressions are a vital component of resuscitation for all patients who suffer cardiac arrest.

Resuscitation protocols for traumatic cardiac arrest (TCA) highlight the importance of addressing reversible causes, such as hypoxia treated by definitive airway management, and hypovolaemia treated by fluid resuscitation.[4–6] With such focused treatment, survival rates following TCA are now similar to those from medical causes of cardiac arrest.[7–10]

Intravenous fluid resuscitation is essential for patients in haemorrhagic shock. Massive haemorrhage protocols now facilitate the early availability of blood and blood products, but these are not universally available and crystalloid solutions are often used as the first line resuscitation fluid, particularly in the pre-hospital environment.[11] Currently there is no evidence to support blood over crystalloid solutions in the context of exsanguinating traumatic cardiac arrest.

The aim of this study was to determine whether chest compressions are beneficial following haemorrhage-induced TCA and whether resuscitation with blood improves survival compared to crystalloid.

## Methods

This study utilised a terminally anaesthetised porcine poly-trauma model of tissue injury and severe haemorrhage to induce TCA. Animals were randomised to one of five resuscitation groups. Detailed supplementary methods are available online.

### Ethical statement

The study was carried out with the authority of UK Animals (Scientific Procedures) Act 1986. The work received institutional ethical approval and a UK Home Office licence was granted.

### Experimental procedures

The study was performed in a terminally anaesthetised porcine model of combined tissue injury and severe haemorrhage.

### Instrumentation

Animals were placed supine and following tracheal intubation surgical anaesthesia was maintained with isoflurane and nitrous oxide during instrumentation, after which anaesthesia was converted to intravenous alphaxalone.

### Experimental protocol (Supplementary Fig. 1)

*Baseline*
Three baseline measurements were taken 5 min apart, 30 min after instrumentation.

*Injury phase*
A soft tissue injury was created, with 3 shots to the right thigh using a captive bolt (Cash Special, Accles and Shelvoke, Sutton Coldfield, UK). Two minutes later animals underwent a controlled haemorrhage (30% blood volume) at an exponentially reducing rate as previously described[12] until the mean arterial blood pressure (MAP) was 45 mmHg. Blood was collected into CPD (citrate phosphate dextrose) and stored at room temperature until required for later transfusion.

*Shock phase*
MAP was held at approximately 40 mmHg for the next 60 min either through the removal of blood or the administration of 0.9% saline (200 ml/min).

*TCA phase*
All animals had a further controlled haemorrhage to achieve a MAP of 20 mmHg. Arterial blood and pulse pressures spontaneously deteriorated over the next 5 min, when the decision to initiate resuscitation was given either by a researcher blinded to the randomised protocol or at 5 min after the attainment of the target MAP.

*Resuscitation phase*
Animals underwent 3 cycles of resuscitation according to randomised (Excel) group assignment. Group 1 CCC; Group 2 WB (whole blood); Group 3 (0.9% Saline); Group 4 (WB + CCC); and Group 5 (0.9% Saline + CCC).

Fluid was administered at 10 ml/kg (200 ml/min) and closed chest compressions were performed using the LUCAS™ II Chest Compression System.

Calcium chloride was administered intravenously during resuscitation to maintain arterial ionised calcium at $\geq$1 mM (in line with current UK major trauma centre practice and to reduce confounding factors impacting on mortality).

*Post-resuscitation phase*
Immediately following the third resuscitation cycle animals were categorised according to MAP. Animals in Groups 1, 4 and 5 with a MAP $<$20 mmHg continued with chest compressions whilst animals with a MAP $>$20 mmHg were observed with no additional intervention. Animals in Groups 2 and 3 were observed with no additional intervention.

*Study end*
The study endpoint was 15 min after the completion of the third resuscitation cycle.

### Cardiopulmonary monitoring

End-tidal $CO_2$, ECG monitoring and pulse oximetry commenced following induction of anaesthesia.

Continuous arterial (systemic and pulmonary) and central venous blood pressures were measured using strain gauge manometers and zero pressure for all transducers was set at heart level. The flow-directed balloon-tipped flotation catheter was a used to determine cardiac output by thermodilution as a 6 min rolling average. Blood pressure, heart rate, carotid blood flow and cardiac output were recorded using a computerised data acquisition system (Maclab 8/s, ADInstruments, UK) and associated software (Chart v4.2.3, ADInstruments).

### Blood sample analysis

Paired arterial and mixed venous blood gas measurements were made pre and post-injury; at 15, 30, 45 and 60 min; at TCA; after the third resuscitation cycle; and at Study End.

### Outcomes

The primary outcome of the study was the attainment of ROSC (return of spontaneous circulation), defined as a MAP of ≥50 mmHg, at Study End.

Secondary outcomes included differences in survival and attainment and maintenance of ROSC during the Resuscitation and Post-Resuscitation Phases. Between group comparisons for cardiovascular physiology and blood biochemistry were made at Baseline, TCA, the end of the Resuscitation Phase and at Study End.

### Statistical analysis

A power calculation was performed after 6 animals in each group to determine the final group sizes.

The primary outcome was assessed using Fisher's exact test and a Kruskal–Wallis Z value test followed by a Dunn's test for multiple comparisons (NCSS, LLC, East Kaysville, Utah). A significance level of $P < 0.05$ was used. Physiological data were assessed with a parametric or non-parametric test as appropriate. Results are presented as median and 25 and 75 percentiles (IQR).

## Results

Thirty nine animals were included in the final data analysis.

### Baseline data

Between group comparisons were assessed at Baseline using either one-way ANOVA or Kruskal–Wallis. Although some parameters showed a statistically significant difference (Supplementary Table 1), all were within normal range and differences were of no clinical significance.

At TCA (Supplementary Results Table 2) there was a significant difference in SBP ($P = 0.037$) but this was not clinically significant as the target pressure was MAP.

### Primary outcome

Attainment of ROSC was determined at Study End and the MAP for each group is shown in Fig. 1, with the lowest and highest MAP being Groups 1 and 2 respectively. Resuscitation with fluid (Groups 2 and 3) was significantly better than with CCC (Group 1) ($P = 0.001$); with a significant difference between CCC and WB ($P = 0.004$) and CCC and Saline ($P = 0.004$). Resuscitation with WB was significantly better than saline ($P = 0.001$). There was no significant difference in MAP between groups 2 and 4, resuscitated with WB ($P = 0.343$), but the Saline group (Group 3) had significantly higher MAP than Saline + CCC (Group 5) ($P = 0.014$).

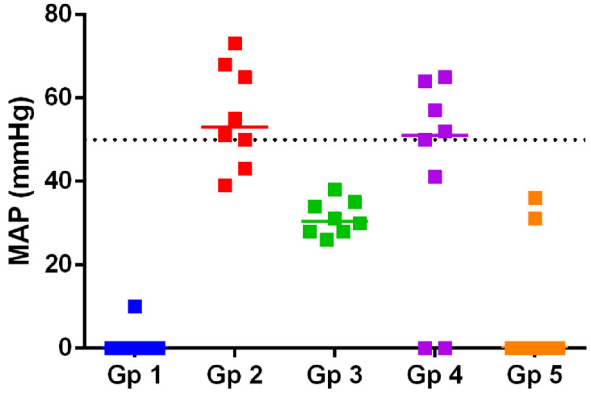


**Fig. 1 – MAP at the Study End, the dashed line equates to ROSC.**

MAP was used to categorise outcome as follows: ROSC (11 animals); DEAD (MAP<10 mmHg and no output, 15 animals); and NO ROSC (alive but MAP between 20 and 50 mmHg, 13 animals).

At Study End all animals in Group 1 were DEAD versus all animals alive in Groups 2 and 3 ($P < 0.0001$), but resuscitation with WB was significantly better than saline (ROSC versus NO ROSC) ($P = 0.0069$).

There was no significant difference in outcome with the addition of closed chest compressions between the groups given whole blood resuscitation (Groups 2 and 4) ($P = 0.4411$), but when the animals were resuscitated with saline (Groups 3 and 5) the addition of chest compressions resulted in a significantly worse outcome ($P = 0.0023$) (Supplementary Fig. 2).

### Secondary outcomes

*The effect of closed chest compressions alone versus fluid only resuscitation*

During the Resuscitation Phase haemodynamic variables improved in the groups given fluid alone (Groups 2 and 3) whereas there was a decline in Group 1 (CCC), which resulted in significant differences in SBP, MAP, DBP, MPAP and MCF at the end of the Resuscitation Phase (Table 1 and Supplementary Fig. 3). The animals resuscitated with saline had significantly lower SBP, MAP, DBP than those resuscitated with WB.

At the end of the Post-Resuscitation Phase (Study End) animals resuscitated with fluid were significantly better than those resuscitated with CCC (Table 2 and Supplementary Fig. 4) with higher SBP, MAP, DBP, CO, and $PaO_2$ and significantly lower $K^+$ concentration. The WB groups, compared to CCC, also had significantly higher MPAP, MCF, $PaCO_2$, BE and calcium ion concentration and lower lactate. Resuscitation with WB was also significantly better than saline with higher SBP, MAP, DBP and $PaCO_2$.

*Effect of the addition of chest compressions to fluid resuscitation*

The combined strategy of fluid and CCC offered no benefit over fluid alone with outcomes significantly worse at the end of the Resuscitation Phase in the combined therapy groups. There was a significant difference in the numbers of animals attaining of ROSC between groups given fluid versus those given fluid + CCC ($P = 0.004$, Groups 2 and 4 and $P = 0.015$ Groups 3 and 5).

The detrimental effect of CCC was most evident in the saline-treated groups (Groups 3 and 5) with significantly worse cardiovascular variables at both the end of the Resuscitation Phase and Study End (Tables 3 and 4 and Supplementary Figs. 5 and 6) for Group 5.

## Discussion

This study, conducted in an animal model of haemorrhage-induced traumatic cardiac arrest, has demonstrated that chest compressions confer no benefit over fluid resuscitation alone, and blood should be the fluid therapy of choice.

**Table 1 – Physiological and arterial blood biochemistry variables at the end of Resuscitation Phase. SBP = Systolic blood pressure: MAP = Mean arterial pressure; DBP = Diastolic blood pressure; MPAP = mean pulmonary artery pressure; CVP = central venous pressure; MCF = mean carotid flow; HCT = haematocrit; BE = base excess. KW = Kruskal-Wallis; OW = one-way ANOVA; NS = non-significant. (CO data not shown as data unreliable at this time point).**

| | Group 1 | Group 2 | Group 3 | |
|---|---|---|---|---|
| SBP (mmHg) | 0.0 (0–12.5) | 92.0[a] (76.5–124.0) | 60.0[a,b] (52.8–69.3) | P = 0.001 (KW) (1v3 0.035; 1v2 < 0.001; 3v2 0.025) |
| MAP (mmHg) | 0.0 (0.0–7.0) | 63.0[a] (53.0–82.8) | 38.5[a,b] (34.0–41.0) | P < 0.001 (KW) (1v3 0.045; 1v2 < 0.0001; 3v2 0.013) |
| DBP (mmHg) | 0.0 (0.0–4.0) | 39.5[a] (34.8–55.0) | 27.0[a,b] (21.8–28.8) | P < 0.001 (KW) (1v3 0.045; 1v2 < 0.0001; 3v2 0.013) |
| MPAP (mmHg) | 7.5 (2.0–15.5) | 29.0[a] (18.3–37.8) | 21.0[a] (17.3–24.8) | P = 0.001 (OW) (1v3 0.017; 1v2 0.001) |
| CVP (mmHg) | 1.0 (−0.9–2.5) | 2.0[a] (1.5–3.0) | 0.5 (0.0– 2.75) | NS (OW) |
| MCF (ml/min) | 0.0 (0– 16.9) | 187[a] (165– 221) | 162 (127– 175) | P < 0.001 (KW) (1v3 NS; 1v2 < 0.001) |
| HCT | 26.8 (23.8–29.0) | 30.8[a] (30.0–32.0) | 17.8[a,b] (17.1–19.8) | P < 0.001 (OW) (1v3 < 0.001; 1v2 0.003; 3v2 < 0.001) |
| pH | 7.51 (7.39–7.54) | 7.13[a] (7.09–7.16) | 7.20[a] (7.14–7.24) | P < 0.001 (OW) (1v3 < 0.001; 1v2 < 0.001) |
| $PaO_2$ (kPa) | 12.9 (9.7– 16.0) | 12.2 (11.5–13.5) | 14.6 (12.7– 15.9) | NS (OW) |
| $PaCO_2$ (kPa) | 1.8 (1.6– 2.5) | 7.10[a] (6.95–7.68) | 5.15[a,b] (4.50– 5.58) | P < 0.001 (KW) (1v3 0.046; 1v2 0.003; 3v2 0.014) |
| Lactate (mM) | 11.9 (9.6– 13.8) | 10.5 (9.5– 12.2) | 9.95 (7.8– 11.3) | NS (OW) |
| BE (mM) | −9.1 (−13.2 to −6.5) | −10.8 (−12.5 to −9.5) | −12.6 (−13.7 to −10.5) | NS (OW) |
| $Ca^{2+}$ (mM) | 1.16 (1.04–1.24) | 1.13 (1.06–1.27) | 1.12 (1.06– 1.16) | NS (OW) |
| $Cl^-$ (mM) | 106 (105– 109) | 105 (103– 107) | 115[a,b] (114–116) | P < 0.001 (KW) (1v3 0.036; 3v2 < 0.001) |
| $K^+$ (mM) | 8.10 (7.20–9.23) | 4.25[a] (4.00– 4.55) | 3.95[a] (3.70– 4.38) | P < 0.001 (OW) (1v3 < 0.001; 1v2 < 0.001) |

[a] significant compared to Group 1.
[b] significant Group 2 versus Group 3.

**Table 2 – Physiological and arterial blood biochemistry variables at the Study End. SBP = Systolic blood pressure: MAP = Mean arterial pressure; DBP = Diastolic blood pressure; MPAP = mean pulmonary artery pressure; CVP = central venous pressure; MCF = mean carotid flow; CO cardiac output (Baxter); HCT = haematocrit; BE = base excess. KW = Kruskal-Wallis; OW = one-way ANOVA; NS = non-significant.**

| | Group 1 | Group 2 | Group 3 | |
|---|---|---|---|---|
| SBP (mmHg) | 0.0 (0–4.3) | 74.0[a] (63.0–100.5) | 47.0[a,b] (41.3–59.0) | P = 0.001 (KW) (1v3 0.004; 1v2 0.004; 2v3 0.001) |
| MAP (mmHg) | 0.0 (0–2.5) | 53.0[a] (44.8–67.3) | 30.5[a,b] (28.0–34.8) | P < 0.001 (KW) (1v3 0.045; 1v2 < 0.001; 2v3 0.013) |
| DBP (mmHg) | 0.0 (0–1.5) | 39.5[a] (30.3–44.0) | 21.5[a,b] (17.8–25.3) | P < 0.001 (KW) (1v3 0.043; 1v2 < 0.001; 2v3 0.015) |
| MPAP (mmHg) | 7.5 (3.0–15.8) | 23.5[a] (16.5–27.5) | 16.0 (13.8–18.5) | P = 0.01 (KW) (1v2 0.007) |
| CVP (mmHg) | 1.5 (0.8–12.4) | 1.0 (−1.0–1.0) | 0.0 (−1.8–1.0) | NS (KW) |
| CO (L/min) | 0.0 (0.0– 0.0) | 3.8[a] (3.3–5.4) | 2.8[a] (2.5–3.4) | P = 0.001 (KW) (1v3 0.049; 1v2 0.001) |
| MCF (ml/min) | 0.0 (0-6.3) | 154[a] (130–179) | 117 (91–141) | P = 0.001 (KW) (1v2 < 0.001) |
| HCT | 26.5 (24.8–29.3) | 30.3 (29.1–33.9) | 21.0[a,b] (19.5–23.5) | P < 0.001 (OW) (1v3 0.004; 2v3 < 0.001) |
| pH | 7.27 (7.16–7.39) | 7.21 (7.19–7.25) | 7.23 (7.21–7.31) | NS (OW) |
| $PaO_2$ (kPa) | 7.95 (5.60–11.2) | 12.7 (11.7–13.6) | 15.3 (13.7–16.4) | P = 0.001 (OW) (1v3 0.001; 1v2 0.047; 2v3 NS) |
| $PaCO_2$ (kPa) | 3.05 (2.10–4.25) | 5.70[a] (5.53–5.90) | 4.00[b] (3.55–4.70) | P < 0.001 (OW) (1v2 < 0.001; 2v3 0.004) |
| Lactate (mM) | 14.7 (13.4–15.0) | 11.3[a] (10.2–12.1) | 12.5 (9.33–13.5) | P = 0.003 (KW) (1v2 0.002) |
| BE (mM) | −14.2 (−17.6 to −12.7) | −9.30[a] (−10.9 to −8.6) | −12.0 (−13.7 to −9.5) | P = 0.006 (OW) (1v2 0.005) |
| $Ca^{2+}$ (mM) | 1.13 (1.00–1.21) | 1.31[a] (1.23–1.38) | 1.19 (1.15–1.25) | P = 0.015 (OW) (1v2 0.013) |
| $Cl^-$ (mM) | 106 (104–107) | 106 (103–108) | 111[a,b] (110–112) | P<0.001 (OW) (1v3 < 0.001; 2v3 < 0.001) |
| $K^+$ (mM) | 9.90 (8.3–12.3) | 3.80[a] (3.63–4.10) | 4.40[a,b] (4.20–5.10) | P < 0.001 (OW) (1v3 0.002; 1v2 0.002; 2v3 0.026) |

[a] significant compared to Group 1.
[b] significant Group 2 versus Group 3.

External cardiac chest compressions were first described in 1960 by Kouwenhoven, and have since become an integral part of resuscitation of the patient in cardiac arrest.[13] However, the applicability and transferability of most studies looking at chest compressions in this context is limited, as most studies exclude patients with a traumatic cardiac arrest. One study using a baboon traumatic cardiac arrest model found that the improvements in haemodynamics seen with chest compressions for normovolaemic cardiac arrest were not reproduced in hypovolaemic arrest.[14] The authors suggested that CCC should not delay correction of the underlying deficit causing TCA, but the study was undertaken in only three animals, perhaps limiting its clinical relevance. A more recent study using a canine model of pulseless electrical activity in TCA found no benefit of chest compressions over fluid therapy alone or fluid combined with chest compressions; in fact the chest compression only group had worse survival, base deficit and ejection fraction.[15] The authors concluded that further research was required to determine whether CPR has a role for the patient in haemorrhagic shock. Our study complements previous work as the injury severity was higher (lower MAP at onset of resuscitation greater degree of shock) as well as including different fluid therapies (crystalloid and blood). The results from all three studies suggest that CCC confers no benefit for haemorrhage-induced TCA.

A recently reported study in pigs evaluated CPR in a model of haemorrhage-induced TCA[16] where animals received CPR +/- aortic

**Table 3 – Physiological and arterial blood biochemistry variables at the end of the Resuscitation Phase. SBP = Systolic blood pressure: MAP = Mean arterial pressure; DBP = Diastolic blood pressure; MPAP = mean pulmonary artery pressure; CVP = central venous pressure; MCF = mean carotid flow; HCT = haematocrit; BE = base excess. MW = Mann-Whitney; t = Student's t-test; NS = non-significant.**

| | Group 2 | Group 4 | | Group 3 | Group 5 | |
|---|---|---|---|---|---|---|
| SBP (mmHg) | 92.0 (76.5– 124.0) | 79.0 (16.8– 96.0) | NS (MW) | 60.0 (52.8– 69.3) | 19.0 (0–70.0) | P = 0.036 (t-T) |
| MAP (mmHg) | 63.0 (53.0– 82.8) | 36.0 (7.3–46.3) | P = 0.003 (t-T) | 38.5 (34.0-41.0) | 14.0 (0-26.5) | P = 0.001 (t-T) |
| DBP (mmHg) | 39.5 (34.8– 55.0) | 20.0 (2.0-33.5) | 0.004 (t-T) | 27.0 (21.8– 28.8) | 8.0 (0–13.0) | P < 0.001 (MW) |
| MPAP (mmHg) | 29.0 (18.3-37.8) | 19.0 (15.0-30.0) | NS (t-T) | 21.0 (17.3-24.8) | 12.0 (7.0-14.0) | P = 0.001 (t-T) |
| CVP (mmHg) | 2.0 (1.5-3.0) | 3.5 (2.3-8.8) | NS (t-T) | 0.5 (0.0- 2.75) | 8.2 (4.0-9.5) | P<0.001 (t-T) |
| MCF (ml/min) | 187 (165– 221) | 129 (23.5-192) | NS (t-T) | 162 (127-175) | 19.2 (0-128) | P = 0.027 (MW) |
| HCT | 30.8 (30.0-32.0) | 27.5 (26.6-30.4) | P = 0.049 (t-T) | 17.8 (17.1– 19.8) | 15.0 (14.3-18.0) | P = 0.034 (t-T) |
| pH | 7.13 (7.09-7.16) | 7.12 (7.06-7.25) | NS (t-T) | 7.20 (7.14– 7.24) | 7.19 (7.13-7.26) | NS (t-T) |
| $PaO_2$ (kPa) | 12.2 (11.5– 13.5) | 10.4 (6.9-11.7) | P = 0.012 (t-T) | 14.6 (12.7– 15.9) | 9.2 (7.5-12.1) | P = 0.001 (t-T) |
| $PaCO_2$ (kPa) | 7.10 (6.95– 7.68) | 6.20 (5.53-7.35) | P = 0.015 (t-T) | 5.15 (4.50-5.58) | 4.65 (3.35-4.80) | NS (t-T) |
| Lactate (mM) | 10.5 (9.5-12.2) | 10.4 (8.1-12.4) | NS (t-T) | 9.95 (7.8- 11.3) | 9.0 (7.9-10.7) | NS (t-T) |
| BE (mM) | −10.8 (−12.5 to −9.5) | −13.3 (−14.5 to −9.1) | NS (t-T) | −12.6 (−13.7 to −10.5) | −14.3 (−16.5 to −10.9) | NS (t-T) |
| $Ca^{2+}$ (mM) | 1.13 (1.06– 1.27) | 1.16 (0.99-1.33) | NS (t-T) | 1.12 (1.06-1.16) | 1.19 (1.00-1.41) | NS (t-T) |
| $Cl^-$ (mM) | 105 (103- 107) | 106 (104-108) | NS (t-T) | 115 (114- 116) | 118 (115-119) | NS (t-T) |
| $K^+$ (mM) | 4.25 (4.00-4.55) | 6.10 (4.98-6.70) | P < 0.001 (t-T) | 3.95 (3.70-4.38) | 5.70 (4.88-6.20) | P = 0.004 (t-T) |

**Table 4 – Physiological and arterial blood biochemistry variables at the Study End. SBP = Systolic blood pressure: MAP = Mean arterial pressure; DBP = Diastolic blood pressure; MPAP = mean pulmonary artery pressure; CVP = central venous pressure; MCF = mean carotid flow; CO cardiac output (Baxter); HCT = haematocrit; BE = base excess. MW = Mann-Whitney; t = Student's t-test; NS = non-significant.**

| | Group 2 | Group 4 | | Group 3 | Group 5 | |
|---|---|---|---|---|---|---|
| SBP (mmHg) | 74.0 (63.0-100.5) | 83.5 (17.0-91.5) | NS (MW) | 47.0 (41.3-59.0) | 0.0 (0-28.0) | P = 0.022 (MW) |
| MAP (mmHg) | 53.0 (44.8-67.3) | 51 (10.3-62.3) | NS (MW) | 30.5 (28.0-34.8) | 0.0 (0.0-15.5) | P = 0.014 (MW) |
| DBP (mmHg) | 39.5 (30.3-44.0) | 34 (7.0-41.3) | NS (t-T) | 21.5 (17.8-25.3) | 0.0 (0.0-10.0) | P = 0.002 (MW) |
| MPAP (mmHg) | 23.5 (16.5-27.5) | 27.0 (26.0-28.0) | NS (t-T) | 16.0 (13.8-18.5) | 5 (1.5-9.0) | P = 0.004 (MW) |
| CVP (mmHg) | 1.0 (−1.0-1.0) | 1.5 (−0.8-4.0) | NS (MW) | 0.0 (−1.8-1.0) | 2 (−0.5-3.8) | NS (t-T) |
| CO (L/min) | 3.8 (3.3-5.4) | 4.0 (2.1-4.4) | NS (t-T) | 2.8 (2.5-3.4) | 0.0 (0.0-3.6) | NS (MW) |
| MCF (ml/min) | 154 (130-179) | 178 (28.3-208) | NS (t-T) | 117 (91-141) | 0.0 (0.0-120) | NS (MW) |
| HCT | 30.3 (29.1-33.9) | 31.0 (29.4-32.0) | NS (MW) | 21.0 (19.5-23.5) | 20.0 (17.3-21.0) | NS (t-T) |
| pH | 7.21 (7.19-7.25) | 7.12 (7.05-7.15) | P = 0.006 (t-T) | 7.23 (7.21-7.31) | 7.04 (6.93-7.17) | P = 0.003 (t-T) |
| $PaO_2$ (kPa) | 12.7 (11.7-13.6) | 11.3 (7.8-12.3) | P = 0.035 (t-T) | 15.3 (13.7-16.4) | 5.1 (3.7-10.1) | P = 0.002 (MW) |
| $PaCO_2$ (kPa) | 5.70 (5.53-5.90) | 6.20 (5.93-6.65) | P = 0.027 (MW) | 4.00 (3.55-4.70) | 6.30 (4.95-8.85) | P = 0.018 (t-T) |
| Lactate (mM) | 11.3 (10.2-12.1) | 13.7 (11.4-14.4) | P = 0.033 (t-T) | 12.5 (9.33-13.5) | 14.0 (12.5-14.9) | NS (MW) |
| BE (mM) | −9.30 (−10.9 to −8.6) | −14.1 (−16.6 to −11.6) | P = 0.012 (t-T) | −12.0 (−13.7 to −9.5) | −15.9 (−18.4 to −14.6) | P = 0.01 (t-T) |
| $Ca^{2+}$ (mM) | 1.31 (1.23-1.38) | 1.38 (1.23-1.49) | NS (t-T) | 1.19 (1.15-1.25) | 1.28 (1.24-1.37) | P = 0.007 (MW) |
| $Cl^-$ (mM) | 106 (103-108) | 106 (105-109) | NS (t-T) | 111 (110-112) | 112 (109-114) | NS (t-T) |
| $K^+$ (mM) | 3.80 (3.63-4.10) | 4.35 (3.58-7.13) | NS (MW) | 4.40 (4.20-5.10) | 8.3 (6.05-12.2) | P = 0.011 (t-T) |

balloon occlusion (ABO). However, this model of TCA is quite different, using a fixed volume haemorrhage (40% blood volume) taken over 20 min followed by induction of ventricular fibrillation (VF) left untreated for 5 min followed by CPR with or without ABO, making any comparison between outcomes with our study impossible.

In our study, CCC had a detrimental effect on cardiovascular parameters, as illustrated in Supplementary Figs. 3–6. CCC (Groups 1, 4 and 5) did increase SBP, MAP, MPAP and MCF but these values fell during the 15second resuscitation pauses, this did not occur in Groups 2 and 3. Additionally CCC caused decreased DBP, which increased during the pauses.

At the end of the resuscitation phase, 7 of the 8 animals in the WB group had attained ROSC compared to only 1 of 8 in WB + CCC (Group 4), but as 5 animals in Group 4 attained partial ROSC, CCC were not re-commenced for the Post-Resuscitation Phase. This resulted in such improvements in haemodynamics that at the Study End there were no significant differences in cardiovascular variables between Groups 2 and 4. Such was the improvement in Group 4 that the difference in numbers of animals attaining ROSC increased and by one minute post-resuscitation there were no longer significant differences between the two groups (P = 0.223), which persisted at 5 and 15 min post-resuscitation (P = 0.714 and 0.441 respectively). However, Group 4 had a significantly higher metabolic acidosis reflecting increased tissue ischaemia, caused by the poor haemodyanamics during the resuscitation phase in this group. It is not known if the significant difference between these 2 groups immediately at the end of the Resuscitation Phase would have persisted if CCC had continued during the Post-Resuscitation Phase, therefore it is not possible to determine whether blood is more important than presence or absence of CCC. The improvements seen in Group 4 Post-Resuscitation were not replicated in Group 5 (Saline + CCC) and systemic and pulmonary pressures remained significantly lower than with saline alone. Five of the nine animals in Group 5 required recommencement of CCC for the Post-Resuscitation Phase and this

combined with the inferior resuscitation fluid (saline versus whole blood) was the likely cause of the poor outcome in this group.

Immediately prior to the onset of resuscitation there were no significant differences between groups, but at the end of the Resuscitation Phase there is evidence of cardiovascular compromise in the groups receiving CCC. We suggest that CCC adversely affected coronary blood flow and that oxygen delivery to the myocardium was compromised in these groups compared to fluid alone. Current fluid resuscitation guidelines for the treatment of hypovolaemic shock recommend the use of blood products if available[17,18] but as blood is not available to all pre-hospital providers, it was important that we evaluated both blood and crystalloid use for TCA.

The current study has several limitations. This was an animal study and long-term recovery was not assessed; however, no animals in the CCC alone group survived to the end of the study, and only 1 out of 6 animals in this group survived the Resuscitation Phase. A recovery model would be required to understand the impact for those animals that attained partial ROSC, as it is not known whether they would have survived and whether they would have a good outcome following definitive resuscitation.

The model represented the clinical scenario of terminal hypovolaemia, but was not true cardiac arrest with no output. The animals were resuscitated with autologous whole blood and thus the impact of delivering component therapy has not been assessed. Finally it was not possible to measure coronary perfusion and determine the effects of CCC on myocardial blood flow.

## Conclusions

The management of patients in traumatic cardiac arrest has progressed over the last decade with the development of treatment algorithms targeting the reversible causes such as hypovolaemia.[4–6] This study supports the rationale that when there is clearly a haemorrhagic pathophysiology, chest compressions should not be performed, and fluid resuscitation with whole blood (or blood component therapy to achieve as close to this as possible) should be initiated.

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## Conflict of interest

All authors are employees of UK Ministry of Defence and as such have no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.04.048.

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