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Damage control orthopedics and decreased in-hospital mortality: A nationwide study

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ABSTRACT

Introduction: While various strategies of fracture fixation in trauma victims have been discussed, the effect of damage control orthopedics (DCO) on significant clinical outcome is inconclusive. We examined the mortality of patients managed with DCO, comparing those without DCO, using a nationwide trauma database.

Patients and Methods: We retrospectively identified patients with extremity injury, defined as patients with an Abbreviated Injury Scale (AIS) of ≥2 in an upper or lower extremity, in the database that included more than 200 major hospitals from 2004 to 2016. We included those who were age ≥15 years and underwent ORIF. Patients with missing survival data or invalid vital signs at hospital arrival were excluded. Patient data were divided into DCO or non-DCO groups, and propensity scores were developed to estimate the probability of being assigned to the DCO group, using multivariate logistic regression analyses adjusted for known survival predictors, such as age, vital signs at arrival, Abbreviated Injury Scale in extremity, ISS, presence of vascular injury, surgical procedure before fracture treatment, and transfusion requirement. The primary outcome, in-hospital mortality, was compared between the two groups after propensity score matching. Survival analyses were performed, and hazard ratio was adjusted according to age, systolic blood pressure on arrival, and Injury Severity Score.

Results: Of the 19,319 patients included in this study, 4407 (22.8%) underwent DCO. After the propensity score matching, 3858 pairs were selected. In-hospital mortality was significantly lower among patients in the DCO than those in the non-DCO groups (40 [1.0%] vs. 66 [1.7%]; odds ratio = 0.60; 95% confidence interval [CI] = 0.41–0.89; $P = 0.01$). Survival analyses showed that DCO was independently associated with decreased mortality in patients with extremity injury (adjusted hazard ratio = 0.30; 95% CI = 0.20–0.46; $P < 0.01$).

Conclusions: DCO was associated with decreased in-hospital mortality in patients with major fractures. Further clinical study on DCO by selecting patient population should be considered eventually to develop an appropriate strategy for major fractures.

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Introduction

The timing of internal fixation for major fractures affects the duration of recumbency and inflammatory cascade in trauma victims, which could generate additional morbidities depending on physiologic patient status [1]. While various investigators have challenged the optimal strategy of fracture fixation, some management schemes have been suggested in the last decades, such as early total care (ETC) [2–4], damage control orthopedics (DCO) [5,6], and early appropriate care (EAC) [7–9].

These strategies have been studied with two major concepts: early fracture fixation to minimize pulmonary or infectious complications during prolonged immobilization, and minimal stabilization followed by definitive fixation to avoid additional physiologic insults during initial resuscitation [10–12]. Although most physicians have accepted that physiologically unstable patients with severe injuries must be managed with staged treatment as DCO, considerable debate exists regarding criteria to identify patients who would tolerate early internal fixation as ETC [10,13,14]. Furthermore, while the idea of safe definitive surgery ideally in the first 24 h after aggressive resuscitation has emerged as EAC, and several studies reported potential benefits in selected patients, the clearance process for major orthopedic surgery remains inconclusive [8,9,15–17].

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Studies demonstrating improved significant clinical outcomes, such as mortality in patients managed with staged treatment, are also generally lacking, which might impede development of widely acceptable protocols. After DCO was first described in cases with femoral shaft fractures in 2000 [5], several benefits of staged management in DCO have been reported to have a protective effect on inflammatory response, pulmonary/hepatic dysfunction, and incidence of acute respiratory distress syndrome (ARDS) [6,18,19]. However, while a multicentre study in Europe identified the incidence of ALI was significantly lower in polytrauma patients undergoing DCO, mortality rates were not different between patients managed with or without DCO [20]. A recent RCT, which was terminated because of unexpected low patient recruitment, also revealed comparable sepsis-related organ failure assessment scores between DCO and early definitive treatment groups, concluding no advantage of DCO [21].

Accordingly, in an effort to eventually develop an appropriate strategy involving early definitive care and staged treatment, we sought to determine the efficacy of DCO in patients with major fractures. We examined the mortality of patients treated with DCO compared with those treated only with internal fixation in a nationwide database using propensity score matching analysis, which is one of the most reliable methods for reducing the effects of confounding factors in a retrospective study. We hypothesized that DCO is independently associated with decreased in-hospital mortality in trauma victims, applied in conjunction with other standard trauma resuscitations.

Patients and methods

Study design and setting

We conducted a retrospective cohort study using data from the Japan Trauma Data Bank (JTDB). The JTDB was established as a Japanese nationwide trauma registry in 2003 and has been maintained by the Japanese Association for the Surgery of Trauma and the Japanese Association for Acute Medicine, with more than 200 participating major hospitals, including tertiary care centres. Data were collected prospectively and entered into the online data collection portal by treating physicians or volunteer registrars designated by each hospital. All collaborating hospitals obtained individual local institutional review board approval for the Conduct of Human Research before the study was started.

Study population

We retrospectively reviewed data recorded in the JTDB and identified patients with major extremity fractures, defined as patients with an Abbreviated Injury Scale (AIS) of $\geq$2 in an upper or lower extremity and who arrived at each participating center between 2004 and 2016. Inclusion criteria were patients aged $\geq$15 years who underwent ORIF. Patients with missing or unknown survival data were excluded as were patients with invalid data on vital signs upon hospital arrival.

Data collection and definitions

Available data included age, sex, mechanism of injury, prehospital vital signs, vital signs upon arrival, any surgical procedures or angiography, transfusion within 24 h after arrival, AIS score, ISS, postoperative complications, length of hospital stay, and survival status during discharge. DCO was defined as staged treatment with external fixation or skeletal traction followed by internal fixation. Conflicting and/or ambiguous data elements were coded as missing data.

Outcome measures

The primary outcome was in-hospital mortality, recorded as death before discharge to home or other healthcare facilities in the database. Secondary outcomes were 28-day mortality and postoperative complication (pulmonary complications, including ARDS and pulmonary edema; cardiac complications, including fatal arrhythmia, acute coronary syndrome, cardiac arrest, and acute kidney injury; and surgical site complications, including refracture, pseudarthrosis, and osteomyelitis).

Statistical analysis

The patients were divided into DCO and non-DCO groups. The DCO group consisted of patients managed with DCO, whereas the non-DCO group consisted of those who were treated only with internal fixation.

Because several cofounders can affect survival after injury, such as age, vital signs at hospital arrival, AIS score in the upper/lower extremity, and ISS, propensity score matching was performed to compare the primary outcome between both groups and to assess secondary outcomes [22]. A multivariate logistic regression was used to find propensity scores to predict the probability of being assigned to the DCO compared with the non-DCO groups. Relevant covariates were identified from known survival predictors in trauma victims with major fractures and entered into the propensity model to ensure high-fidelity propensity scores [1,4,7–10,16,17,23–25]. Patients with missing covariates were excluded from propensity score calculation. The precision of discrimination by propensity scores was analyzed with the c-statistic. Propensity score matching extracted one-to-one matched pairs of patients, where a nearest-neighbor matching algorithm with a caliper width of 0.2 of the standard deviation of the logit-transformed propensity score was applied [22,26]. The group comparability after matching was assessed with distribution of prespecified falsification endpoints that are expected to be unrelated to selecting treatment strategy as DCO [27].

Intergroup comparison of primary and secondary outcomes after propensity score matching was performed using linear regression analysis. Then, sensitivity analyses were performed to validate the primary results. To confirm if the results were not dependent on the method of matching, inverse probability weighting and logistic regression analysis were performed (using the propensity score as covariate in logistic regression analysis) for the in-hospital mortality.

In addition to comparing in-hospital mortality between the DCO and non-DCO groups, Kaplan–Meier plots of survival curves up to 180 days after injury for each group were drawn. Hazard ratio (HR) for overall hospitalization was calculated and adjusted with age, systolic blood pressure on hospital arrival, and ISS using a proportional hazards model.

Several subgroup analyses were also performed to evaluate the heterogeneity of patients with major extremity fractures. Given that hemodynamically unstable patients have been suggested to obtain significant benefit from DCO, one selected subgroup included patients who arrived at hospital with hypotension, defined as systolic blood pressure $<$90 mmHg. Another subgroup consisted of patients with severe traumatic brain injury, defined as AIS of $\geq$4 in the head, considering that an additional brain insult during extensive fracture surgery has been concerned in previous studies [1,6,10,13]. Primary and secondary outcomes were compared between the DCO and non-DCO groups in the selected patients using univariate analyses.

Descriptive statistics were presented as means $\pm$ standard deviation, median (interquartile range), or number (%). Results were compared using unpaired *t*-tests, Mann–Whitney *U* tests,

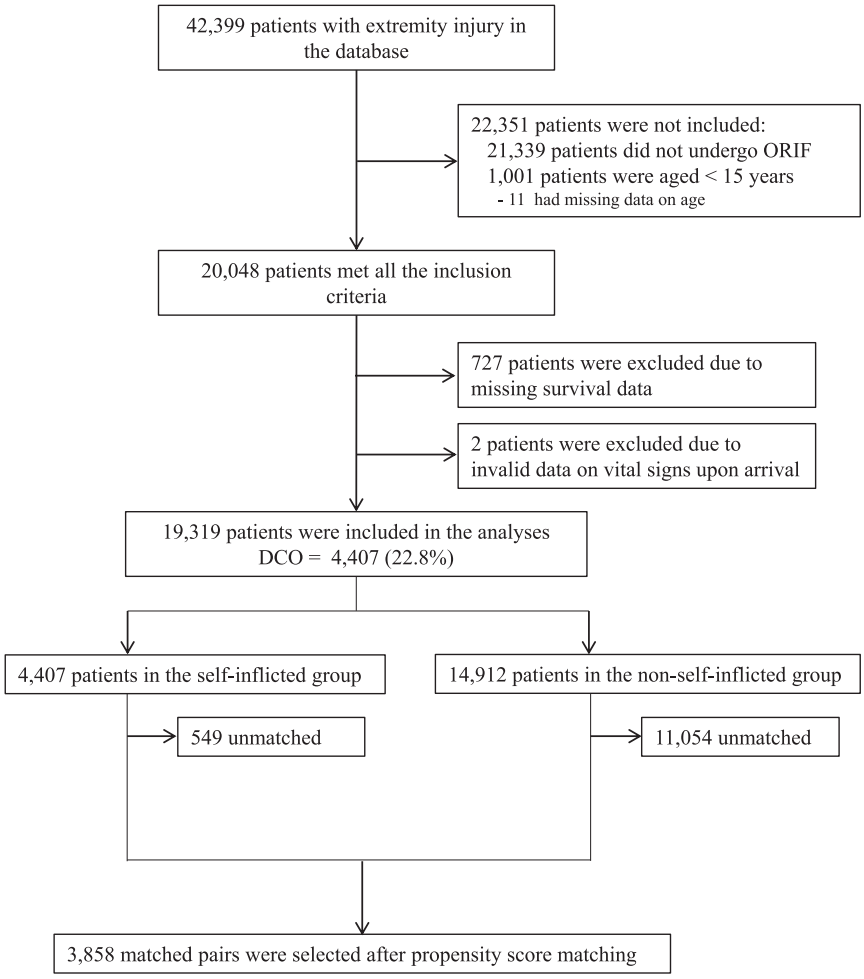

Fig. 1. Patient flowchart. Of the 42,339 patients with extremity injury, 19,319 were included in the analyses and 3858 pairs were identified in the propensity score matching. DCO, damage control orthopedics.

chi-square tests, or Fisher's exact tests, as appropriate. For the testing of all hypotheses, a two-sided α threshold of 0.05 was considered statistically significant. All statistical analyses were conducted using the IBM SPSS Statistics, version 24.0 (IBM, Armonk, NY, USA) and Microsoft Excel (Microsoft, Redmond, WA, USA).

Results

After the screening process, a total of 42,399 patients with major extremity fractures who presented to collaborating hospitals during the study period were identified. Among them, 21,060 patients underwent internal fixation, whereas 1001 were aged <15 years. Although 20,048 patients satisfied all inclusion criteria, 727 were excluded due to missing or unknown survival data and two due to invalid data on vital signs at hospital arrival. The patient flow diagram is summarized in Fig. 1.

Of the 19,319 patients eligible for this study, 4407 (22.8%) were treated with DCO and 14,912 (77.2%) were not. Patient characteristics are summarized in Table 1. Patients in the DCO group were significantly younger, had a significantly lower Glasgow Coma Scale (GCS) score at arrival (64 ± 24 vs. 66 ± 22 years and 14.4 ± 1.7 vs. 14.6 ± 1.4, respectively), and had a higher ISS (13.0 ± 9.6 vs. 11.1 ± 7.1) than those in the non-DCO group. Furthermore, more patients in the DCO group had a vascular injury in the extremity (40 [0.9%] vs. 64 [0.4%]), had transfusion within 24 h after arrival (640 [14.7%] vs. 1189 [8.1%]), and underwent craniotomy, thoracotomy, or laparotomy before fracture surgery (53 [1.2%] vs. 90 [0.6%]) than those in the non-DCO group. The mechanism of injury (blunt vs. penetrating) was statistically comparable between the two groups.

Considering these nonnegligible biased distributions in the known survival predictors of patients with extremity injury, propensity score matching was performed. The final propensity model predicting allocation to the DCO group included covariates such as age, sex, vital signs at arrival (GCS and systolic blood pressure), AIS in the upper/lower extremity, ISS, vascular injury in the extremity, surgical procedure before fracture treatment, intraabdominal angiography, and transfusion within 24 h after hospital arrival. This model was validated to have high discrimination for the probability of being assigned to the self-inflicted group (c-statistic = 0.681).

Among the 4407 patients in the DCO group, 3858 matched with those in the non-DCO group. The patient characteristics after matching are summarized in Table 1. The standardized difference of covariates before and after matching is shown in Supplementary Table S1. Group comparability after matching was confirmed with a well-balanced distribution of mechanism of injury, which was prespecified as falsification endpoints [27]. Propensity score matching analysis revealed that in-hospital mortality was significantly lower in the DCO than in the non-DCO groups (40 [1.0%] vs. 66 [1.7%]; odds ratio [OR] = 0.60; 95% confidence interval [CI] = 0.41–0.89; $P = 0.01$; Table 2). The Kaplan–Meier plots of survival curves up to 180 days after injury for both groups are shown in Fig. 2.

Table 1
Characteristics of patients with extremity injury.

	Before matching			After matching	
	DCO	non-DCO	*P* value	DCO	non-DCO
Case	4407	14,912		3858	3858
Age, years, median (IQR)	71 (39)	73 (32)	<0.001	71 (39)	59 (40)
missing data	0 (0.0%)	0(0.0%)			
Sex, male, *n* (%)	2105(47.8%)	6440(43.2%)	<0.001	1850(48.0%)	1779 (46.1%)
missing data	3(0.1%)	2(0.0%)			
GCS on arrival, median (IQR)	15(0)	15(0)	0.020	15(0)	15(0)
missing data	340(7.7%)	2415(16.2%)			
Systolic BP on arrival, mmHg, median (IQR)	138(40)	139(38)	0.001	139(40)	131(30)
missing data	61(1.4%)	370(2.5%)			
AIS of upper extremity, median (IQR)	0(0)	0(2)	<0.001	0(0)	0(0)
missing data	0(0.0%)	0(0.0%)			
AIS of lower extremity, median (IQR)	3(0)	3(1)	<0.001	3(0)	3(0)
missing data	0(0.0%)	0(0.0%)			
ISS, median (IQR)	9(4)	9(1)	<0.001	9(4)	9(0)
missing data	1(0.0%)	5(0.0%)			
Vascular injury in extremity, *n* (%)	40(0.9%)	64(0.4%)	<0.001	24(0.6%)	31(0.8%)
missing data	0(0.0%)	0(0.0%)			
Transfusion within 24 h, *n* (%)	640(14.7%)	1189(8.1%)	<0.001	507(13.1%)	354(9.2%)
missing data	51(1.2%)	230(1.5%)			
Other surgery before fixation, *n* (%)	53(1.2%)	90(0.6%)	<0.001	35(0.9%)	54(1.4%)
missing data	1(0.0%)	5(0.0%)			
Angiography for intraabdominal organs, *n* (%)	68(1.5%)	55(0.4%)	<0.001	34(0.9%)	23(0.6%)
missing data	0(0.0%)	0(0.0%)			
Mechanism of Injury, penetrating, *n* (%)	20(0.5%)	102(0.7%)	0.090	14(0.4%)	18(0.5%)
missing data	59(1.3%)	209(1.4%)		52(1.3%)	53(1.4%)

DCO, damage control orthopedics; GCS, Glasgow Coma Scale; BP, blood pressure; AIS, abbreviated injury scale.

Table 2
Impact of DCO on in-hospital mortality and secondary outcomes.

	DCO	non-DCO	*P* value	OR	95% CI
In-hospital mortality, *n* (%)	40(1.0%)	66(1.7%)	0.011	0.60	0.41–0.89
Mortality at 28 days, *n* (%)	35(0.9%)	61(1.6%)	0.008	0.60	0.38–0.87
Pulmonary complication, *n* (%)	17(0.4%)	20(0.5%)	0.621	0.85	0.44–1.62
Cardiac complication, *n* (%)	15(0.4%)	20(0.5%)	0.397	0.75	0.38–1.47
Surgical site complication, *n* (%)	11(0.3%)	11(0.3%)	1.000	1.00	0.43–2.31

DCO, damage control orthopedics.

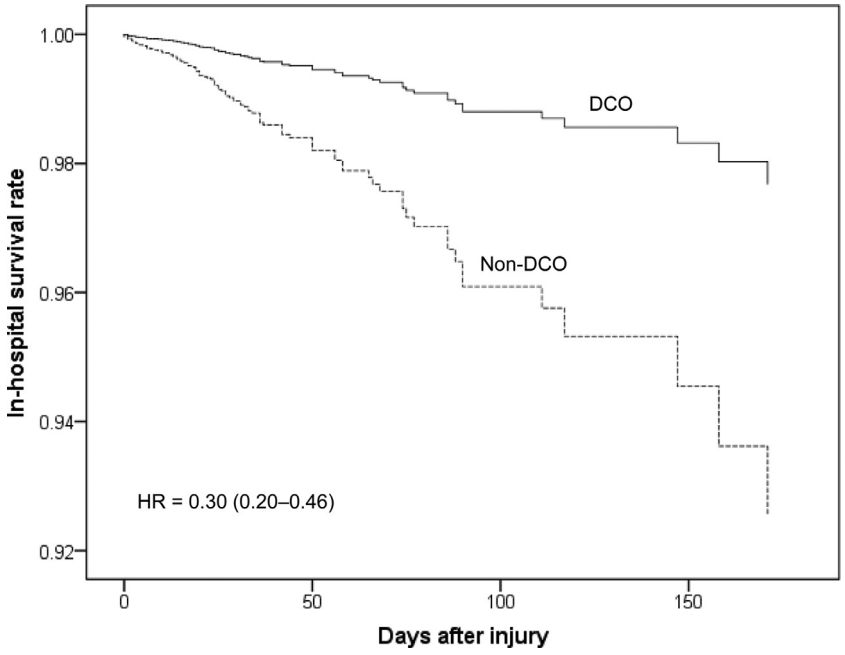

Fig. 2. Kaplan–Meier survival curves of patients treated with or without DCO. The significantly lower in-hospital mortality was observed in the DCO compared with the non-DCO groups (HR = 0.30; 95% CI = 0.20–0.46; $P < 0.01$). CI, confidence interval.

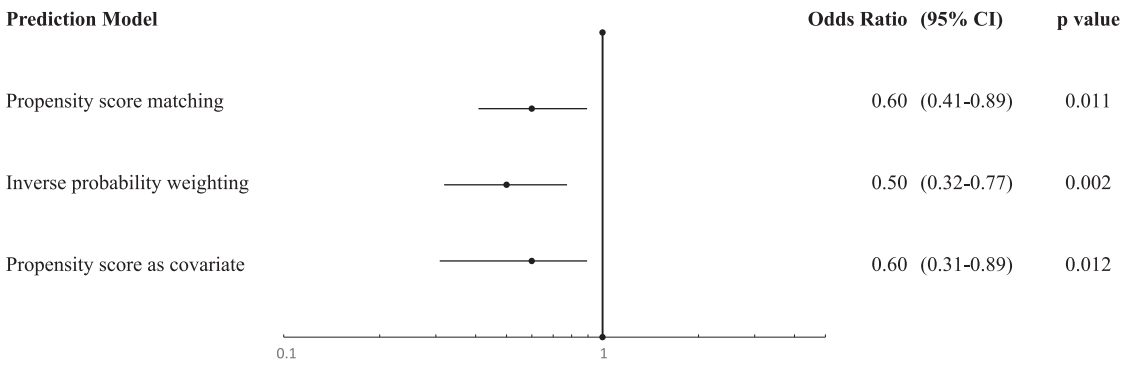

Fig. 3. Effect of DCO management on in-hospital mortality. DCO strategy was independently associated with lower in-hospital mortality (OR = 0.60; 95% CI = 0.41–0.89; $P = 0.01$) in propensity score-matched analysis, which was conducted as a primary analysis. To confirm that the results were not dependent on the matching method, inverse probability weighting and logistic regression analyses were performed (using the propensity score as the covariate in logistic regression analysis).

Table 3
Impact of DCO in subgroup analyses.

	DCO	non-DCO	*P* value	OR	95% CI
Hypotension upon arrival, *n*	168	132			
In-hospital mortality, *n* (%)	5(3.0%)	5(3.8%)	0.753	0.78	0.22–2.78
Mortality at 28 days, *n* (%)	5(3.0%)	4(3.0%)	1.000	0.98	0.26–3.73
Pulmonary complication, *n* (%)	1(0.6%)	2(1.5%)	0.584	0.39	0.04–4.34
Cardiac complication, *n* (%)	0(0.0%)	3(2.3%)	0.084	N/A	N/A
Surgical site complication, *n* (%)	0(0.0%)	2(1.5%)	0.193	N/A	N/A
Severe head injury, *n*	138	130			
In-hospital mortality, *n* (%)	3(2.2%)	4(3.1%)	0.716	0.70	0.15–3.18
Mortality at 28 days, *n* (%)	2(1.4%)	3(2.3%)	0.676	0.62	0.10–3.79
Pulmonary complication, *n* (%)	1(0.7%)	0(0.0%)	1.000	N/A	N/A
Cardiac complication, *n* (%)	1(0.7%)	1(0.8%)	1.000	0.94	0.06–15.21
Surgical site complication, *n* (%)	1(0.7%)	1(0.8%)	1.000	1.24	0.06–15.21

DCO, damage control orthopedics.

Survival analyses showed that DCO was independently associated with decreased mortality in patients with extremity injury (HR = 0.30; 95% CI = 0.20–0.46; $P < 0.01$).

Inverse probability weighting analysis confirmed that DCO was significantly associated with lower in-hospital mortality (OR = 0.50; 95% CI = 0.32–0.77; $P < 0.01$; Fig. 3), and logistic regression with propensity score as a covariate validated that the association between DCO and mortality was not dependent on the matching method used (OR = 0.60; 95% CI = 0.31–0.89; $P = 0.01$).

Secondary outcomes, including 28-day mortality and postoperative complications, are shown in Table 2. Lower mortality at 28 days after injury was identified in the DCO compared with the non-DCO groups (35 [0.9%] vs. 61 [1.6%]; OR = 0.60; 95% CI = 0.38–0.87; $P < 0.01$; Table 2), whereas incidence of postoperative complications did not significantly differ between the groups.

Subgroup analyses were performed to evaluate the heterogeneity of patients with extremity injury treated with DCO. Comparable mortality and postoperative complication rates were found in patients who arrived at hospital with hypotension (in-hospital mortality = 5 [3.0%] in the DCO group vs. 5 [3.8%] in the non-DCO group; $P = 0.75$; Table 3). Among the patients with severe traumatic brain injury, mortality and postoperative complications were also comparable between the two groups.

Discussion

We used propensity score matching to show that DCO was independently associated with decreased in-hospital mortality in patients with extremity injury (OR for in-hospital mortality = 0.60; 95% CI = 0.41–0.89). Notably, the relationship was consistent based on several sensitivity analyses, indicating that the results were not dependent on the method of matching or statistical approach (inverse probability weighting analysis, OR = 0.50; 95% CI = 0.32–0.77 and multivariate logistic regression, OR = 0.60; 95% CI = 0.31–0.89). Furthermore, a significantly low HR for death from DCO was detected after adjustment of covariates, including age, systolic blood pressure on hospital arrival, and ISS.

While discussion has been ongoing regarding the overall effectiveness and optimal indications for DCO, some studies have suggested that severely injured patients would benefit most from DCO [1,6,18,28–30]. A retrospective study of 191 patients treated with DCO for femoral shaft fracture due to instability of the clinical condition revealed that the incidence of multiple organ failure decreased significantly with DCO management compared with ETC [6]. Another prospective study including 409 patients with ISS >15 identified that those who underwent DCO had a significantly shorter operation time and lower blood loss [28]. A retrospective study of inflammatory response to fracture fixation in 174 patients with ISS of ≥20 also found that the DCO group had smaller postoperative systemic inflammatory response syndrome scores [29].

Despite its widespread application in polytrauma patients, limited data exist regarding crucial clinical outcomes, such as reduction of mortality [20,21,30]. A trauma registry analysis of 462 multiple-injured patients comparing DCO and ETC reported no significant differences in mortality and pulmonary complications [30]. Similar results were revealed in a RCT of polytrauma patients, in which sustained inflammatory response with high concentration of serum interleukin was found in patients treated with early definitive fixation [20]. Another RCT on femoral shaft fracture included 34 patients with a probability of survival of 40–80% and identified a longer intensive care unit stay in patients treated with DCO [21].

Several reasons should be considered for the inconclusive findings in mortality or vital outcomes of previous studies. First, although clinical outcomes of polytrauma patients are significantly

affected by initial haemorrhagic control or resuscitative procedures during resuscitation, regardless of strategy of fracture fixation [25,31], it has not been adjusted nor examined in control groups in the past studies. Second, given that the impact of DCO on mortality would not be high [21], inadequate or small sample size might have affected statistical power to elucidate the clinical benefits of DCO. Third, trauma centres with available protocols considering different strategies, such as ETC, DCO, and EAC, would lack equipoise between different management and control groups at such centres and might possess nonnegligible selection biases.

We conducted this study to elucidate the inconclusive results of previous studies by adjusting significant survival predictors, using a nationwide database in Japan that included more than 200 participating major hospitals, including tertiary care centres. Required surgical procedure before fracture fixation and other clinical variables that would affect favorable outcome were adjusted in this study, and the robustness of the association between management with DCO and decreased in-hospital mortality was validated.

Our results must be interpreted in the context of the study design. We analyzed data of the JTDB, in which neither the indication for DCO nor exact location of fracture was recorded. The result might have been modified if the reason that some patients did not undergo DCO treatment was an unmeasured strong outcome predictor, such as inappropriate experience with DCO by the orthopedic surgeon, unavailability of instruments for external fixation, or missed diagnosis of vital injuries other than fracture. However, given that we included measurable outcome predictors, such as AIS scores and ISS that have been validated for differentiating severity of injury, to the propensity model, our result probably would still show the relationship between DCO strategy and favorable clinical outcomes.

Another limitation of our study is the fact that the imbalance between the DCO and non-DCO groups remained in a few variables after propensity score matching [22], including age and systolic blood pressure on hospital arrival. Although biased distribution might have affected the results, survival analysis, in which HR was adjusted with age, systolic blood pressure on hospital arrival, and ISS, obtained the association between DCO and decreased in-hospital mortality in patients with extremity injury. Notably, the inverse probability weighting analysis and logistic regression with propensity score as a covariate validated the robustness of the results, without using matching procedures.

Furthermore, because we included all patients who underwent internal fixation for major fractures (AIS of ≥ 2) to maximize sample size to detect even a slight difference in mortality, injury severities of our current study population were different from those of previous studies on DCO. Although limited in scope, given that the propensity score matching process selected severe enough patients from the non-DCO group, who had been injured equally as patients treated with DCO, we believe our results might be adopted in patients with severe injuries in different regions or countries. It should be emphasized that subgroup analyses on patients who arrived with hypotension and those who had severe traumatic brain injury detected low ORs with DCO for incidence of mortality or postoperative complications without statistical significance.

Finally, since this is a retrospective study, results are not conclusive. Although we revealed reduced in-hospital mortality in the DCO versus the non-DCO groups, residual cofounding and unmeasured survival predictors would exist as impediments to confirm the efficacy of DCO strategy. Additional clinical investigations, including a RCT, are needed to validate our results.

Conclusions

DCO was associated with decreased in-hospital mortality in patients with extremity injury. Further clinical study on DCO by selecting patient population should be considered eventually to develop an appropriate strategy for major fractures.

Data statement

The data related to this study were used under licence from the Japanese Association for Trauma Surgery and the Japanese Association for Acute Medicine, and restrictions apply to the public availability of these data. Data are, however, available from the authors upon reasonable request and with permission of the Japanese Association for Trauma Surgery and the Japanese Association for Acute Medicine

Declaration of Competing Interest

The authors declare no conflicts of interest.

Sources of funding

The authors have no sources of funding.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2019.09.028.

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