Am J Transl Res 2022;14(5):3278-3285
www.ajtr.org /ISSN:1943-8141/AJTR0141308

Original Article

Promotion of a damage control concept in repairing orthopedic lower limb trauma

Fubin Li, Lecai Gao, Jiangang Zuo, Guanlei Liu

Department of Trauma Surgery, Hebei Province Cangzhou Hospital of Integrated Traditional and Western Medicine, Cangzhou 061001, Hebei, China

Received December 24, 2021; Accepted April 18, 2022; Epub May 15, 2022; Published May 30, 2022

Abstract: Objective: To explore the application value of the concept of damage control orthopaedics (DCO) in clinical treatment of lower limb fractures. Methods: In this retrospective analysis, 157 patients with lower extremity fracture, who received surgery in Cangzhou Hospital of Integrated Traditional Chinese and Western Medicine (Cangzhou Orthopaedic Hospital) during March 2019 and August 2020, were chosen as research subjects. Among them, 73 patients admitted from March to December 2019 were included in the control group, and the other 84 patients admitted from January to August 2020 were included in the observation group. The control group received conventional fracture treatment scheme, and the observation group was treated under the DCO concept. The operation time, postoperative hospital stay, fracture reduction quality, incidence of complications, and bone metabolism and bone healing pre- and post-treatment were compared between the groups. Results: The operation time, time to achieve stable vital signs and hospital stay of the observation group were apparently shorter than those of the control group ($P<0.05$). Visual analog score (VAS) of patients in both groups on postoperative day 3 and 7 were substantially lower than those on postoperative day 1 ($P<0.05$), and VAS scores of patients in the observation group were markedly lower than those in the control group ($P<0.05$). Serum Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in the two groups were significantly reduced on 14th day after surgery compared to those before surgery ($P<0.05$), and the indexes of observation group were lower than those of control group ($P<0.05$). Serum Osteocalcin (BGP), carboxyterminal of type I procollagen (PICP), alkaline phosphatase (ALP), Soluble intercellular adhesion molecule-1 (sICAM-1) and Insulin like growth factor-1 (IGF-1) in the two groups postoperative day 14 were obviously higher than those before operation ($P<0.05$), and the indicators in the observation group were higher than those of the control group ($P<0.05$). The incidence of complications in the control group was significantly higher than that in the observation group ($P<0.05$). Conclusion: The application of the DCO concept in the clinical treatment of lower extremity trauma can effectively promote the rehabilitation of patients with lower extremity trauma, minimize their complications, improve the bone metabolism and bone healing degree, and reduce the degree of pain.

Keywords: Damage control orthopaedics concept, orthopedics, lower extremity trauma, clinical treatment, clinical application

Introduction

Lower extremity fractures are common cases in orthopedic clinics. These injuires are mostly caused by direct or indirect external shock, and usually accompanied by high-energy trauma, bleeding and multiple organ damage [1]. Patients may not only have sensory dysfunction at the site of trauma, but also have massive bleeding and pain (usually including open and closed lower limb fractures, and may even be combined with nerve injury, chest and abdominal injury or craniocerebral injury), and most patients suffer from multiple fractures [2, 3]. Over recent years, due to the lightning speed of traffic development domestically and increasing number of transportation vehicles, the number of patients with orthopedic lower extremity injuries caused by traffic accidents has also been increasing [4]. The condition of patients with orthopedic trauma to the lower extremity can progress rapidly. Hemorrhagic shock can cause serious damage to the physiological balance and metabolic function of patients, and the consequent serious complications such as hyperthermia, acidosis, and coagulopathy may threaten the life and safety of patients [5, 6]. The mechanism of coagulation disorder is complex. Researchers believe that the primary cause of coagulation disorder is the sharp drop of body temperature caused by massive bleeding. Hypothermia will hinder the platelet function of patients and lead to blood coagulation. The pathological mechanism of metabolic acidosis lies in the disorder of cell metabolism and the increase of anaerobic metabolism caused by prolonged low blood flow perfusion. Pyruvate is transformed into lactic acid in cytoplasm, and the blood lactic acid level increases rapidly, which leads to acidosis [7-10]. For the above cases, quick and effective first-aid measures should be taken during treatment, including disinfection and hemostasis, and the changes of respiratory signs, acid-base and humoral imbalance of patients should be closely observed [11, 12]. If the lower extremity fracture is not properly treated in time, it is easy to produce systemic inflammatory response syndrome, which sorely threatening the life safety of patients. However, it is difficult to meet the treatment needs of orthopedic patients with lower extremity fractures only by applying conventional treatment procedures. Therefore, it is particularly important to seek a more effective and reliable first-aid rule for orthopedic trauma of lower extremities [13].

Damage Control Orthopaedics (DCO) treatment refers to the phased treatment of fractures to reduce the body injury caused by complete treatment in the early clinical stage, so as to reduce further injury to patients and improve the clinical treatment and recovery efficacy [14]. Although the traditional early comprehensive treatment of lower limb trauma has a certain therapeutic effect, there are risks-immediate ultimate orthopaedic surgery for critically injured patients may lead to disability. With the development of medical concepts, DCO theory has been gradually applied to the clinical treatment of lower limb trauma in orthopedics. Before the implementation of the definitive surgical plan, different treatment methods should be selected for different patients, and the current overall instability and severity of accompanying injury should be weighed, so as to improve patient tolerance and lay a foundation for subsequent treatment [15]. DCO technology, as a newly developed medical treatment measure in recent years, gradually exert a crucial clinical value in the treatment of orthopedic diseases, and has achieved good curative effect. At present, there are still puzzles in the understanding and application of DCO among clinical medical staff in China. This study provides objective evaluation, basis and application methods in clinical treatment of lower extremity trauma based on damage control theory, and it develops a personalized treatment plan for each patient, which is of great significance to reduce adverse reactions and promote the recovery of patients' limb function.

Data and methods

Clinical data

This study is a retrospective analysis. A total of 157 patients with lower extremity fracture, who received surgery in Cangzhou Hospital of Integrated Traditional Chinese and Western Medicine (Cangzhou Orthopaedic Hospital) during March 2019 to August 2020, were chosen as the research subjects. The patients included 29 with tibial plateau fractures, 23 with middle and distal tibia and fibula fractures, 13 with lower femoral and femoral ankle fractures, and 92 with multiple fractures. The patients were assigned into control group (n=73) and observation group (n=84) considering their admission time. The research was conducted with the approval of Ethics Committee of the hospital (2019011002).

Inclusive criteria

(1) Patients with an age of 18-60 years old; (2) Patients with lower extremity trauma and indicated for operation, including open fracture and multiple trauma; (3) Patients who were surgically treated; (4) Patient or family member who voluntarily signed the informed consent form; (5) Patients with complete postoperative follow-up results; and (6) Patients without operation-related contraindications.

Exclusive criteria

(1) Patients with autoimmune diseases, malignant tumor or mental disorders; (2) Patients who underwent a single simultaneous operation for lower extremity fractures and fractures at other sites; (3) Patients with pathologic fracture due to tumor or infection; or (4) Patients who were unwilling to participate in postoperative follow-up or lost to follow-up.

Methods

The control group was treated with conventional wound treatment methods, including removal of necrotic tissue, and surgical treatment for

Table 1. Comparison of baseline data between the two groups

Baseline data	Observation group (n=84)	Control group (n=73)	t/χ^2	*P*
Gender				
Male	56	28	0.379	0.538
Female	52	21		
Age (yd, $\overline{x}$±s)	49.24±9.38	49.02±10.52	0.139	0.890
BMI (kg/m^2 $\overline{x}$±s)	24.15±3.54	24.38±2.90	0.441	0.660
Type of trauma				
Open fracture	33	32	0.333	0.564
Multiple trauma	51	41		
Hypertension (n, %)	21 (25.00)	18 (24.66)	0.256	0.613
Diabetes (n, %)	17 (20.24)	12 (16.44)	0.375	0.541

Note: Gender, trauma, hypertension and diabetes were compared by χ^2; and the age and BMI were compared by student t-test.

fracture as soon as possible. In general, the first aid ideas for the control group were mainly based on anatomical restoration. The observation group was treated with the DCO concept and was treated in stages prior to definitive fracture surgery. (1) Firstly, the bleeding was stopped, and the open fracture trauma was cleaned in time. Blood volume compensation was given immediately for the patients who developed hemorrhagic shock. Patients with extremely severe limb damage were treated with decisive amputation. (2) The ISS score was used to accurately assess the actual injury of the patient. The patients with a score ≥ 20 points were sent to ICU for emergency treatment; the patients with a score <20 points were sent to the intensive care unit of orthopedics for first aid. Meanwhile, patient's metabolic acidosis, coagulation disorders, and low temperature symptoms were corrected to ensure smooth ventilation. (3) Patients' vital signs were observed in real time to determine best treatment scheme of fracture surgery.

Observation of indicators

Primary indictors: (1) Operation time, time to achieve stable vital signs and overall hospital stay were compared between the two groups.

(2) The pain degree and swelling degree of the two groups were compared on 1 d, 3 d and 7 d after surgery. The pain degree was measured by VAS, with a score ranging from 0 to 10 points. The higher score indicated more severe of pain.

(3) The incidence of complications was compared between the two groups.

Secondary indicators: (1) The changes in serum inflammatory factors, bone metabolism and bone healing indexes before surgery and 14 days after surgery were compared between the two groups. Five ml of peripheral blood was extracted from the patients and the serum was separated. The bone metabolism indexes (osteocalcin (BGP), type I procollagen carboxy-terminal propeptide (PICP) and serum alkaline phosphatase (ALP)), the bone healing indexes (soluble intercellular adhesion molecule-1 (sicAM-1) and insulin-like growth factor-1 (IGF-1)), and the inflammatory cytokines (interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)) were compared between the two groups. All the above indicators were detected by ELISA kit, which was purchased from Shanghai Yaji Biotechnology Co., LTD.

(2) The living quality of the two groups was compared 14 days after surgery, which was evaluated by SF-36 Scale. The scale contained eight dimensions, including psychological states, emotional role, physical states, physical role, pain degree, social functioning, vitality and general health. Each dimension was scored on a scale of 0 to 100 points, with a higher score indicating a better quality of life.

Statistical analysis

SPSS 25.0 was used for statistical analysis. The measurement data were represented by ($\overline{x}$±s). The inter-group comparison was conducted using independent samples t-test, and the intra-group comparison was conducted using paired t-test. Percentage (%) was used to express enumeration data, and χ^2 test was used for comparison. P<0.05 was considered with statistically significant difference.

Results

Comparison of baseline data

The baseline data of the two groups were statistically insignificant and as such the two groups were comparable (P>0.05) (**Table 1**).

Table 2. Comparison of operation time, time to achieve stable vital signs and total hospital stay between the two groups ($\bar{x}$±s)

Group	Number of cases	Operation time (min)	Time to achieve stable vital signs (min)	Total hospital stay (d)
Observation group	84	86.34±15.42	3.10±1.21	22.39±5.46
Control group	73	97.30±17.52	4.52±1.65	27.65±6.12
t	-	4.169	6.200	5.691
P	-	0.000	0.000	0.000

Note: The operation time, stable time of vital signs and hospital stay of the two groups were compared by student t-test.

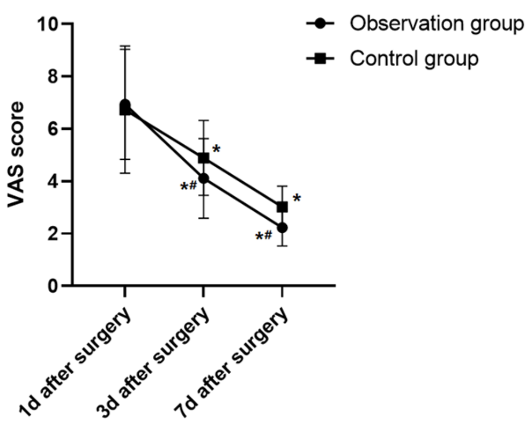

Figure 1. Comparison of postoperative VAS scores between the two groups (points, $\bar{x}$±s). Note: Compared with the same group on the 1st day after operation, paired t-test was used, (*P<0.05); Independent sample T test was used for comparison with control group (#P<0.05). VAS, visual analog score.

Comparison of operation time, time to achieve stable vital signs and total hospital stay

The operation time, time to achieve stable vital signs and hospital stay in the observation group were remarkably shorter than those in the control group (all P<0.05) (**Table 2**).

Comparison of postoperative pain

The two groups showed no significant difference in VAS score 1 d after surgery (P>0.05). The VAS scores of two groups on postoperative 3 d and 7 d substantially decreased compared with those on 1d after surgery (P<0.05), and the observation group had remarkably lower scores than the control group (P<0.05) (**Figure 1**).

Comparison of inflammatory factor levels before and after surgery

The two groups had no statistical differences in preoperative serum IL-6 and TNF-α levels (all P>0.05). The serum IL-6 and TNF-α levels decreased significantly on the 14^{th} day after surgery compared to that before surgery in both groups (all P<0.05), and the observation group had significantly lower levels than the control group (all P<0.05) (**Table 3**).

Comparison of bone metabolism indicators before and after surgery

The two groups had no statistical differences in preoperative serum BGP, PICP and ALP levels (all P>0.05). The levels of BGP, PICP, ALP, sICAM-1 and IGF-1 in the two groups on postoperative day 14 were obviously higher than those before operation (all P<0.05), and the observation group had significantly higher levels than the control group (all P<0.05) (**Table 4**).

Comparison of bone healing indicators before and after operation

The two groups had no significant difference in serum sicAM-1 and IGF-1 levels prior to surgery (all P>0.05). The levels of serum sICAM-1 and IGF-1 in the two groups increased remarkably on postoperative day 14 compared to those before surgery (P<0.05), and the observation group had notably higher levels than the control group (all P<0.05) (**Table 5**).

Comparison of living quality between the two groups

The psychological state, physical state, pain degree, vitality and overall health score in SF-36 scale of patients in the observation group were remarkably higher than those in the control group (P<0.05), as shown in **Table 6.**

Comparison of the incidence of complications

The complication rate was 2.38% in the observation group, which was statistically lower than 12.33% in the control group (P<0.05) (**Table 7**).

Table 3. Comparison of serum inflammatory factor levels between the two groups before and after surgery ($\overline{x}\pm s$)

Group	Number of cases	IL-6 (ng/L)		TNF-α (ng/ml)	
		Before surgery	14 d after surgery	Before surgery	14 d after surgery
Observation group	84	279.38±63.94	133.93±47.39*	2.75±0.42	1.59±0.35*
Control group	73	286.49±78.02	173.03±51.21*	2.81±0.47	1.83±0.49*
t	-	0.627	4.967	0.845	3.564
P	-	0.531	0.000	0.400	0.001

Note: Compared with the same group before operation, paired t test was used (*P<0.05).

Table 4. Comparison of bone metabolism indicators between the two groups before and after surgery ($\overline{x}\pm s$)

Group	Number of cases	BGP (μg/L)		PICP (μg/L)		ALP (μg/L)	
		Before surgery	14 d after surgery	Before surgery	14 d after surgery	Before surgery	14 d after surgery
Observation group	84	4.37±0.63	5.98±0.93*	112.73±28.39	146.48±36.40*	79.26±15.64	134.59±24.53*
Control group	73	4.48±0.71	5.23±0.79*	114.02±29.03	121.04±30.44*	83.42±19.02	108.23±27.65*
t	-	1.029	5.401	0.281	4.709	1.503	6.330
P	-	0.305	0.000	0.779	0.000	0.135	0.000

Note: Compared with the same group before operation, paired t test was used (*P<0.05). BGP, osteocalcin; PICP, procollagen type I carboxy-terminal propeptide; ALP, alkaline phosphatase.

Table 5. Comparison of bone healing indexes between the two groups before and after surgery ($\overline{x}\pm s$)

Group	Number of cases	sICAM-1 (μg/L)		IGF-1 (μg/L)	
		Before surgery	14 d after surgery	Before surgery	14 d after surgery
Observation group	84	102.24±21.30	153.92±35.30*	191.85±65.60	298.56±73.84*
Control group	73	107.02±23.89	120.35±34.27*	185.64±60.22	251.23±64.52*
T	-	1.325	6.024	0.615	4.246
P	-	0.187	0.000	0.540	0.000

Note: Compared with the same group before operation, paired t test was used (*P<0.05). sICAM-1, soluble intercellular adhesion molecule-1; IGF-1, insulin like growth factor-1.

Table 6. Comparison of quality of life between the two groups (points, $\overline{x}\pm s$)

Living quality	Observation group (n=84)	Control group (n=73)	t	*P*
Psychological states	75.48±6.50	70.29±4.58	5.701	0.000
Emotional role	69.83±5.64	70.95±6.52	1.154	0.250
Physical states	57.92±4.09	54.39±5.94	4.382	0.000
Body role	64.38±7.89	63.27±8.33	0.857	0.393
Pain degree	69.05±9.37	62.38±7.04	4.981	0.000
Social Functioning	58.96±10.24	56.48±12.01	1.397	0.165
Vitality	62.17±9.32	57.42±7.44	3.493	0.001
General health	67.58±4.99	61.21±5.84	7.370	0.000

Note: the comparison of the two groups of indicators in the table adopts student t-test.

Discussion

The conventional treatment of lower limb trauma is trauma removal, disinfection and hemostasis. Although the above measures have a certain effect on preventing wound infection, the effect on controlling the patient's disease progression is still not ideal. Damage control provides timely emergency treatment for the patients, which can bpromote the patient's best treatment opportunity, so that the medical staff can have more sufficient time to determine a scientific, reasonable and effective treatment plan, and create favorable conditions for subsequent surgical treatment [16]. Finally, the changes in patients' vital signs should be closely monitored, thus improving the treatment safety [17].

The results of this study showed that the operation time, time to achieve stable vital signs and hospital stay in the observation group were significantly shorter than those in the control group, and the complication rate was appar-

Table 7. Comparison of the incidence of complications between the two groups [n (%)]

Group	Number of cases	Shock	Multiple organ dysfunction syndrome	Total
Observation group	84	1 (1.19)	1 (1.19)	2 (2.38)
Control group	73	5 (6.85)	4 (5.48)	9 (12.33)
χ^2	-	-	-	5.923
P	-	-	-	0.015

Note: the incidence of complications was compared by χ^2 test.

ently lower than that in control group, which is consistent with a previous report [18]. Treatment under the DCO concept can help to control the patient's condition, reduce complications and create favorite conditions for surgical treatment, thus shortening the hospitalization time of patients and promoting their recovery.

Bone metabolism and bone healing are involved in the healing process of patients with limb fractures. The literature has shown that metabolism indicators, BGP, PICP and ALP, are positively correlated with the activity and function of bone cells in the body [19-21]. In addition, sICAM-1 and IGF-1 can be increased after treatment [22, 23]. This study observed the changes in bone metabolism and bone healing indicators before and after surgery in the two groups. The results revealed that the increase of postoperative bone metabolism indexes (BGP, PICP, ALP) and bone healing indexes (sICAM-1, IGF-1) in the observation group were obviously higher than those in control group. This indicates that effective control of the patient's condition through the DCO concept and phased surgical treatment is more conducive to promoting the postoperative healing of patients. The levels of inflammatory factors in patients with lower limb fracture can be rapidly elevated. Inflammatory factors not only reflect the degree of body injury, but also trigger an inflammatory cascade that leads to multiple organ dysfunction [24]. Our results also showed that the postoperative IL-6 and TNF-α in the observation group were notably lower than those in control group, and the postoperative pain in the observation group was lighter than that in control group. This shows that applying the DCO concept to manage the patient's condition and perform surgery under effective control of the conditions are conductive to postoperative disease recovery and the remission of the body's inflammatory response and pain alleviation. According to previous reports [25], effective treatment can greatly promote the repair of patients' trauma, which is of great value to their postoperative rehabilitation, which agrees with the results of this study.

Inevitably, there are still some drawbacks in this study. The sample size included in this study is relatively small, which is a limitation of this study. In the later research, the sample size will be further expanded, and the treatment and operation process of injury control concept will be standardized, so as to provide a more scientific basis for its extensive clinical application.

Applying the DCO concept to clinical treatment of lower extremity trauma can effectively promote the recovery of lower extremity trauma, reduce complications, improve bone metabolism and bone healing degree, and reduce pain of the patients.

Acknowledgements

This work was supported by Cangzhou Science and Technology Bureau Project (No. 2041060-45).

Disclosure of conflict of interest

None.

Address correspondence to: Lecai Gao, Department of Trauma Surgery, Hebei Province Cangzhou Hospital of Integrated Traditional and Western Medicine, 31 Huanghe West Road, Yunhe District, Cangzhou 061001, Hebei, China. Tel: +86-0317-2078139; E-mail: glecai@163.com

References

[1] Held M, Engelmann E, Dunn R, Ahmad SS, Laubscher M, Keel MJB, Maqungo S and Hoppe S. Gunshot induced injuries in orthopaedic trauma research. A bibliometric analysis of the most influential literature. Orthop Traumatol Surg Res 2017; 103: 801-807.

[2] Klima S, Cornwall J, Kieser D and Hammer N. The utility and benefit of a newly established

postgraduate training course in surgical exposures for orthopedic and trauma surgery. Arch Orthop Trauma Surg 2019; 139: 1673-1680.
[3] Snavely JE, Service BC, Miller D, Langford JR and Koval KJ. Needlestick and sharps injuries in orthopedic surgery residents and fellows. Infect Control Hosp Epidemiol 2019; 40: 1253-1257.
[4] Gelaw AY, Gabbe BJ, Simpson PM and Ekegren CL. Pre-injury health status of major trauma patients with orthopaedic injuries. Injury 2020; 51: 243-251.
[5] Weidert S, Andress S, Suero E, Becker C, Hartel M, Behle M and Willy C. 3D printing in orthopedic and trauma surgery education and training: possibilities and fields of application. Unfallchirurg 2019; 122: 444-451.
[6] Morgan C, Ahluwalia AK, Aframian A, Li L and Sun SNM. The impact of the novel coronavirus on trauma and orthopaedics in the UK. Br J Hosp Med (Lond) 2020; 81: 1-6.
[7] Rascoe AS, Kavanagh MD, Breslin MA, Hu E and Vallier HA. Transcutaneous hemoglobin screening in an adult orthopaedic trauma population. J Orthop Trauma 2020; 34: e165-e169.
[8] Lycke C, Bork H, Feindt B, Spiegl UJA, Josten C, Fakler JKM and Roth A. Evaluation of the fall risk of orthopedic trauma surgery patients by establishing a fall risk score and a procedure instruction in clinical routine. Z Orthop Unfall 2019; 157: 440-444.
[9] Sullivan SD, Lehman A, Nathan NK, Thomson CA and Howard BV. Age of menopause and fracture risk in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination: results from the Women's Health Initiative Clinical Trials. Menopause 2017; 24: 371-378.
[10] Yoon YC, Oh CW and Oh JK. Significance of orthopedic trauma specialists in trauma centers in Korea. Arch Orthop Trauma Surg 2019; 139: 1379-1384.
[11] Kim JW, Lee Y, Seo J, Park JH, Seo YM, Kim SS and Shon HC. Clinical experience with three-dimensional printing techniques in orthopedic trauma. J Orthop Sci 2018; 23: 383-388.
[12] Leighton R, Watson JT, Giannoudis P, Papakostidis C, Harrison A and Steen RG. Healing of fracture nonunions treated with low-intensity pulsed ultrasound (LIPUS): a systematic review and meta-analysis. Injury 2017; 48: 1339-1347.
[13] Jarman MP, Weaver MJ, Haider AH, Salim A and Harris MB. The national burden of orthopedic Injury: cross-sectional estimates for trauma system planning and optimization. J Surg Res 2020; 249: 197-204.
[14] Mulders MA, Bentohami A, Beerekamp MS, Vallinga J, Goslings JC and Schep NW. Demographics, fracture patterns and treatment strategies following wrist trauma. Acta Orthop Belg 2019; 85: 234-239.
[15] Słowik R, Wałaszek M, Zieńczuk W, Różańska A, Wójkowska-Mach J, Kołpa M, Wolak Z and Kawik Ł. Analysis of the incidence of surgical site infections after open reposition of long bone fractures and closed fracture settings in a 7-year follow-up in an orthopedic and trauma ward in southern Poland. Przegl Epidemiol 2020; 74: 336-345.
[16] Normore R, Greene H, DeLong A and Furey A. The orthopedic trauma symposium: improving care of orthopedic injuries in Haiti. Can J Surg 2017; 60: 228-235.
[17] Yang BW and Waters PM. Implementation of an orthopedic trauma program to safely promote resident autonomy. J Grad Med Educ 2019; 11: 207-213.
[18] Wei N, Zhou Y, Chang W, Zhang Y and Chen W. Displaced intra-articular calcaneal fractures: classification and treatment. Orthopedics 2017; 40: e921-e929.
[19] Langerhuizen DWG, Janssen SJ, Mallee WH, van den Bekerom MPJ, Ring D, Kerkhoffs GMMJ, Jaarsma RL and Doornberg JN. What are the applications and limitations of artificial intelligence for fracture detection and classification in orthopaedic trauma imaging? A systematic review. Clin Orthop Relat Res 2019; 477: 2482-2491.
[20] Pervez M, Kitagawa RS and Chang TR. Definition of traumatic brain injury, neurosurgery, trauma orthopedics, neuroimaging, psychology, and psychiatry in mild traumatic brain injury. Neuroimaging Clin N Am 2018; 28: 1-13.
[21] Kampe K, Kohler M, Albrecht D, Becker C, Hautzinger M, Lindemann U and Pfeiffer K. Hip and pelvic fracture patients with fear of falling: development and description of the "Step by Step" treatment protocol. Clin Rehabil 2017; 31: 571-581.
[22] Anthony CA, Volkmar AJ, Shah AS, Willey M, Karam M and Marsh JL. Communication with orthopedic trauma patients via an automated mobile phone messaging robot. Telemed J E Health 2018; 24: 504-509.
[23] Pesch S, Hanschen M, Greve F, Zyskowski M, Seidl F, Kirchhoff C, Biberthaler P and Huber-Wagner S. Treatment of fracture-related infection of the lower extremity with antibiotic-eluting ceramic bone substitutes: case series of 35 patients and literature review. Infection 2020; 48: 333-344.
[24] Cimbanassi S, O'Toole R, Maegele M, Henry S, Scalea TM, Bove F, Mezzadri U, Capitani D, Sala F, Kanakaris N, Coccolini F, Ansaloni L, Sgardello S, Bindi F, Renzi F, Sammartano F, Masse A, Rampoldi A, Puoti M, Berlusconi M,

Moretti B, Rueger J, Arnez Z, Del Bene M, Chieregato A, Menarini M, Gordini G, De Blasio E, Cudoni S, Dionigi P, Fabbri A, Scandroglio I and Chiara O. Orthopedic injuries in patients with multiple injuries: results of the 11th trauma update international consensus conference Milan, December 11, 2017. J Trauma Acute Care Surg 2020; 88: e53-e76.

[25] Fousekis K, Billis E, Matzaroglou C, Mylonas K, Koutsojannis C and Tsepis E. Elastic bandaging for orthopedic- and sports-injury prevention and rehabilitation: a systematic review. J Sport Rehabil 2017; 26: 269-278.