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Damage control orthopaedics in polytraumatized patients- current concepts

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ABSTRACT

The principles of fracture management in patients with multiple injuries continue to be of crucial importance. Early treatment of unstable polytraumatized patients with head, chest, abdomen or pelvic injuries, with blood loss followed by immediate fracture fixation (Early Total Care -ETC) may be associated with secondary life threatening posttraumatic systemic inflammatory response syndrome (SIRS). Development of SIRS is typically a function of the type and severity of the initial injury (the "first hit"). Immediate Fracture fixation, using reamed nails or plates, in such unstable patients with multiple injuries is subsequently defined as the "second hit" and may be associated with development of acute respiratory distress syndrome (ARDS) and multiple organ failure (MOF), with relatively high morbidity and mortality.

The other alternative for long bone fracture fixation in unstable polytraumatized patients is based on immediate treatment of life threatening conditions related to the injuries, followed by the initial use of minimally invasive modular external frames for long bone fractures and is called Damage Control Orthopedics (DCO) and is widely accepted. In order to refine the DCO concept and to avoid an overuse of external fixation, the "Safe Definitive Surgery" (SDS) concept has been introduced, which is a dynamic synthesis of both strategies (ETC and DCO). The SDS strategy employs clinical parameters and includes repeated assessment of patients. The following paper is going to summarize historical backgrounds and recent concepts in treatment of polytraumatized patients.

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1. Introduction

Polytraumatic conditions are frequently life-threatening situations that require a special approach. The principles of fracture management in patients with multiple injuries, including head, chest, abdominal or pelvic injuries with blood loss, continue to be of crucial importance. The management of severely injured patient with fractures has changed over the last decades. In the early 70s long bone fractures were mainly stabilized by traction.¹ This concept was associated with numerous complications such as

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pulmonary infections, atrophy of the musculature and thromboembolic complications due to prolonged immobilization.²

Bone and coauthors published a prospective randomized study including 178 multiply injured (ISS > 18) patients and compared the clinical outcome after early (<24 h) and delayed (>48 h) femoral fracture fixation.¹ In this marked publication early total care (ETC) strategy has been associated with less pulmonary complications and reduced length of stay on intensive care unit and hospital. Early fracture fixation resulted in early mobilization, avoided nutritional depletion and long drug therapy and reduced wound infections.^{3,4} Thus, ETC has become a standard approach in polytrauma in the 80s and early 90s. This strategy was further stimulated by advances of osteosynthesis techniques and implants over these decades.

Several authors, however; criticized that early fixation might be







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detrimental for several patient groups.^{5,6} This method of combined surgical procedures may lead to development of an additional, secondary life-threatening inflammatory response reaction, which can cause an excessive inflammatory reaction known as the "secondary hit".^{7–10} ETC in unstable poly-traumatized patients may significantly increase the severity of this systemic inflammatory response (SIRS) and may lead to development of acute respiratory distress syndrome (ARDS) and multiple organ failure (MOF), carrying a relatively high incidence of morbidity and mortality.^{5,11,12}

Later it became clinically evident that definitive stabilization of all fractures in all severely injured patients was inadequate, and the management of major fractures changed to a more selective method called damage control orthopedics (DCO).^{13,14} It has been widely accepted that one should differentiate between those patients who can tolerate prolonged surgical procedures and those for whom this is not advisable.⁸ Nowadays, the "Damage Control Orthopedic" (DCO) strategy is widely accepted in treatment of unstable severely injured patient. The basic principles of DCO include initial stabilization of life-threatening conditions related to the injury with fixation of long bone fractures using modular, minimally invasive external frames and then, only after a few days of metabolic and respiratory recovery, proceeding with the definitive management of the fracture fixation.

This paper describes the basic pathophysiologic aspects of systemic inflammatory response syndrome (SIRS), various clinical conditions and the results of treatment of such patients with multiple injuries as well as the current discussion and treatment options.

2. Pathophysiological conditions of trauma

The Injury Severity Score (ISS) is often used in studies to define polytraumatized patients. Traditionally, the ISS has been calculated by taking the squares of the worst abbreviated injury scale (AIS) score from the three regions with the worst injuries neglecting the physiology of the patients.^{15,16} Considering the above mentioned issue an international expert panel proposed a new "Berlin Definition" of polytrauma.¹⁷ The physiologic parameters used in this definition can be obtained from routine laboratory and physiologic monitoring. The definition implies the following parameters:

- Two injuries that are greater or equal of 3 on the AIS and one or more additional pathological conditions
- Hypotension (systolic blood pressure \leq 90 mmHg)
- Unconsciousness (GCS score ≤ 8)
- Acidosis (base deficit ≤ -6.0 ; Lactate level > 2.5 mmol/l)
- Coagulopathy (PTT \geq 40 s or INR \geq 1.4)
- Age (≥70 years)

Further clincal studies will show whether this uniform definition more closely defines the critically injured patient (polytrauma).

Blunt trauma is usually associated with injuries in the extremities (especially long bone fractures and pelvic fractures) and the trunk (thorax, abdomen, spine). Therefore, the initial assessment of severely injured patient must contain the "**Four Vicious Cycles**" (hemorrhagic shock, coagulopathy, hypothermia, and soft tissue injuries). These cycles are known to induce permeabily changes in vessels and organs and lead to immunological and functional (e.g. liver and lung function) alterations.¹⁸ It has been shown that these parameters appear to be feasible for use in the decision making process in the emergency room. Systolic blood pressure (<90 mmHg), the need for catecholamine therapy and shock index are good clinical marker for hypovolemia (hemorrhagic shock). The critical value for *hypothermia* was described as a body temperature below 33 °C.¹⁹ Hypothermia may be a reason for a heart rhythm disturbance, cardiac arrest or coagulopathy. The dynamic plateler function tests, such as Rotational Thromboelastometry (ROTEM) are used to predict transfusion requirements and mass transfusion. The depletion of plateletes below 90.000/µl on the first posttraumatic day may indicate the developlent of the Disseminated Inravascula Coagulopathy (DIC).^{18–20} Soft tissue injuries are common in blunt trauma patients. The term "Soft Tissue Injuries" includes not only extremity injures or contusions, but also additional associated thoracic-, abdomnial-, and pelvic injuries with an Abbreviated Injury Score (AIS) of 3 and more.²¹ These injuries are known to stimulate the systemic inflammatory response syndrome and alterate the immine function.

Using the parameters of these cascades four classes of patients have been described based on their clinical status: **stable**, **border-line**, **unstable**, **and in extremis**. This classification system may be used to grade the critically injured patients according to their physiology and define the treatment strategy. *Stable* patients and *borderline* patients who improve with resuscitation measures can safely undergo definitive treatment of the major fracture. *Unstable* patients, and those in a critical condition (*in extremis*), should not undergo a prolonged surgical procedure and therefore should be treated initially only by life saving procedures, followed later by the damage control approach (DCO).

The principle of DCO is to avoid worsening of the unstable polytraumatized patient's condition that can result from the "second hit", a phenomenon caused by early major orthopedic procedures. The basic principles of DCO consist of immediate treatment of life-threatening conditions in such patients and primary, minimally invasive external fixation of long bone fractures, followed by metabolic and respiratory stabilization of the patients. After a few additional days of metabolic and respiratory recovery, the definitive fracture management and fixation is performed. Post-traumatic systemic inflammation is considered to be a sterile inflammation that is triggered by released endogenous intracellular components. The exact origin of systemically measured inflammatory markers is still unknown. One may hypothesize there is a systemic spill over of locally released cytokines. Others postulated that Damage Associated Molecular Patterns (DAMPs) such as HMGB-1 are locally released and gain access to the systemic circulation stimulating inflammatory pathways (e.g. Toll-Like Receptor 4 (TLR-4)) and activation of immune cells and endothelial cells.^{21–23}

The development of this hyper-inflammatory reaction is manifested in the activation of the immune system, triggering increased secretion of pro-inflammatory cytokines such as interleukin-6 (IL-6) and IL-8.^{8,10,24} The increase in pro-inflammatory cytokines is evident soon after the injuries occur (6 h) and usually lasts for 24–72 h and is statistically significant for IL-8 and IL-6 as illustrated in Fig. 1.1 and 1.2.²⁴The cytokine response is clinically evident by fever, leukocytosis, hyperventilation and tachycardia. The duration and intensity of this reaction depends on the severity of the trauma.

In patients with severe injuries this increase is significantly higher and (Fig. 1.2) may persist even longer.^{7–9,24} In such patients the "second hit" inflammatory reaction, following ETC procedures, may aggravate the initial acute systemic inflammatory reaction syndrome (SIRS). It may lead to development of acute respiratory



Fig. 1.1. Means (\pm SE) of levels of pro-inflammatory cytokines in injured and control groups immediate after trauma, demonstrating significant rise in level of IL-8 and IL-6 as compared to the other pro-inflammatory cytokines (*p < 0.01) (

After Volpin et al.

[24] Int Orthop. 2014; 38:1303–9).



Fig. 1.2. Means (±SE) of levels of pro-inflammatory cytokines in severe and moderate trauma and in control groups immediate after trauma, showing significant higher levels in severe trauma cases as compared to moderate trauma cases and controls (*P < 0.01) (After Volpin et al. [24] Int Orthop. 2014; 38:1303–9).



Fig. 2. ARDS in a patient with head and abdominal injuries and fractures of both femurs and Lt tibia, 24 h following ETC -initial life saving procedures and then by intramedullary nails of limb fractures (Fig. 2A) vs ARDS of another patient 24 h following DCO- initial life saving procedures and external fixation of his long bone fractures, and only after additional 4–5 days of metabolic and respiratory stabilization, followed by definitive treatment by intramedullary nails of limb fractures (Fig. 2B).

distress syndrome (ARDS- as illustrated in Fig. 2) and multiple organ failure (MOF), which carry relatively high morbidity and mortality.^{24–27} This is very important, as fracture management in unstable patients with multiple injuries continues to be of crucial

importance.^{28–31}

Patients with various orthopedic injuries present a distinct pattern of serum cytokine levels. Significant increased serum levels of pro-inflammatory cytokines IL-6 and IL-8 and low levels of antiinflammatory IL-4 are observed in severely injured patients.^{24,32,33} The higher levels of pro-inflammatory cytokines in injured patients are associated with the reported inflammatory state in reaction to injury. This is very important, as fracture management in patients with multiple injuries, particularly in those with high ISS continues to be of crucial importance.²⁴

The massive secretion of pro-inflammatory cytokines usually induces upregulation of anti-inflammatory cytokines such as IL-4 and regulatory cytokines such as TGF-beta, and IL-10, which together decrease the severity of the inflammatory reaction, as an effort by the body to attenuate the inflammatory activity.^{8,11,24} An imbalance between the early systemic inflammatory response and the later compensatory anti-inflammatory response may be responsible for organ dysfunction and increased susceptibility to infection.^{8,11,24} Large studies analyzing the genetic response demonstrate that in severe blunt trauma, the genomic response is consistent with simultaneously increased expression of genes involved in the systemic inflammatory, innate immune, and compensatory anti-inflammatory responses, as well as in the suppression of genes involved in adaptive immunity.²² Moreover, systemic complications, such as multiple organ failure, differ only in the magnitude and duration of this genomic reprioritization.²²

The causes and effects of changes in the balance of proinflammatory and anti-inflammatory cytokines due to injury should be examined further, including an evaluation of the role of genetic polymorphism in inducing hyper-inflammation. Our preliminary results provide an indication for the involvement of genetic factors, such as polymorphisms in certain genes (e.g. TLR9) that regulate the immune response in accelerated hyperinflammation in response to injury in individuals with severe orthopedic trauma.^{24,32,33} Based on our earlier findings it was suggested that high serum levels of these cytokines can be used as potential reliable biomarkers for predicting the development of systemic inflammatory response syndrome (SIRS) in patients with multiple trauma.²⁴ Secretion of large amounts of pro-inflammatory cytokines and decreased levels of anti-inflammatory cytokines during the acute phase of trauma, mainly in unstable polytraumatized patients, may lead to the development of systemic inflammatory response syndrome (SIRS).

It has been also suggested that the long-term effect of hyperinflammation may be involved in development of acute stress psychological reactions to trauma.^{32–35} Significant increase levels of various cytokines in the synovial fluid of patients with rheumatoid arthritis as well as patients with osteoarthritis, supporting the concept of a pro-inflammatory process in the pathogenesis of osteoarthritis and inflammatory joint diseases and in patients with $^{36-38}$ and in patients aseptic loosening of large joint prostheses. 39

3. Our experience

From 1995 to 2011 there were 196 polytraumatized patients with various body injuries associated with pelvic fractures and/or femoral and/or tibial shaft fractures treated in our hospitals. Patients were grouped according to treatment strategies for stabilization of the femoral shaft fracture as follows: Group A - 99 patients treated with early total care (ETC) and intramedullary nailing (IMN) within 24 h of injury (Fig. 3); Group B- 97 patients treated with temporary external fixation (Fig. 4) as a bridge to IMN (DCO surgery beginning in 2005). The outcomes of their treatment were analyzed retrospectively in this study.

4. Results

The groups were comparable regarding age, gender distribution and mechanism of injury. ISS was slightly higher in group B (DCO) – 32.2 compared to group A (ETC) -28.6. Thoracic, abdominal and head injuries were found in a significantly higher number of patients admitted to the DCO group from 2005 (24.2%) as compared with the ETC group (12,4%). The patients in the DCO group required significantly more fluids (14,2 L) than those in the ETC group (8,2 L) and blood (2,2 vs. 1,3 L, respectively) in the first 24 h. Mean operative time was 40 min for External Fixation and 110 min for IMN. There was a significantly higher incidence of ARDS in ETC group -18.2%, compared with the DCO group -8.6%. The incidence of multiple organ failure (MOF) was significantly higher in the ETC group -12.1% as compared with the DCO group -7.4%. There were three unexpected deaths and two cases of conscious worsening in patients with head injuries in the ETC group. No delayed union and non-union were found.

Various clinical cases of unstable polytraumatized patients, with long bone fractures, are presented in Figs. 5–9, including torn popliteal artery (Fig. 5), pelvic fractures treated initially by Ganz's clamp followed later by ORIF (Fig. 6), combined pelvic fractures with severe perineum injuries (Fig. 7), combined chest and kidney injuries with multiple fractures (Fig. 8) and combined multiple fractures of pelvis' clavicula, wrist and tibial fractures treated according to the principle of Safe Definitive Surgery (SDS) as illustrated in Fig. 9.



Fig. 3. Demonstrating early total care of patient No 1, with head and abdominal injuries, treated by initial intramedullary fixation of fractures of both femurs and Lt tibia, resulting in development of marked ARDS 24 h after operations, as presented in Fig. 2A.



Fig. 4. Demonstrating patient No 2, with head and abdominal injuries and fractures of both femurs and Rt tibia, and Lt forearm fractures. He was treated initially by craniotomy and laparotomy followed by external fixation of his long bone fractures, resulting in development of a very mild ARDS 24 h after external fixation injuries operations. After additional few days of successful metabolic and respiratory recovery the 2nd patient was treated by removal of external fixators followed by intramedullary nails of his lower limbs' fractures and ORIF of the forearm.



Fig. 5a. Demonstrating a 22-year-old male that was injures on RTA. He had chest and abdominal injuries, including hemopneumothorax chest with fracture of ribs of his right died treated by chest drainage, and lacerated tears of the kiver treated by laparotomy. In addition, there were fracture dislocation of the right knee with a tear of the popliteal artery and segmental fracture of the both tibia and left femur, as observed by CT angiography (upper raw). The patient was treated initially by debridement and exploration of the popliteal artery of the right knee and suture of the torn part of it and by trans-knee external fixator of the Rt leg and then by debridement, fasciotomy and external fixation of the Lt tibia (lower raw). The patient was hospitalized in the ICU and was treated by fluids. Fresh frozen plasma, and IV Heparin.



Fig. 5b. 3 days following the popliteal artery repair we noticed beginning of necrosis of the Rt foot and leg. He was treated by few embolectomies of the artery and by IV Heparin, but with no success and we had to perform above knee amputation of his right leg (upper row). Following that he gradually improved. On the 6th day we removed the EF of his left femur and performed closed reduction and IMN of the femur (lower row), but due to his condition during anesthesia we had to leave the external fixator of his left tibia.



Fig. 5c. On the 9th day after injuries he had a further improvement in his condition. He was then been operated and exchange of his EF and closed intramedullary nailing of his left tibia were done. After few weeks an AK prosthesis was implied and he was successfully treated in physiotherapy.

5. Discussion

The findings of this study showed despite higher ISS there is a

significant reduction in the incidence of general systemic complications (ARDS, MOF) in the DCO group in comparison with the ETC group. Modification of the treatment protocol from ETC to DCO was



Fig. 6. Demonstrating a patient with unstable condition following road traffic accident with liver and spleen injuries and "open book" fracture of the pelvis (6.1), treated initially by Gantz's clamp and closure of the pelvis (6.2 and 6.3) and enable to continue the surgical treatment of the abdominal problems. He was treated by open reduction and internal fixation after 2 successful additional weeks of metabolic and respiratory recovery.



Fig. 7. A 62 y old mail was hospitalized 6 h after car incident. On admission he was unstable hemodynamically with severe hemorrhagic shock. He was consensus, pale and had SBP of 50 mmHg, tachycardia (160/minute), initial Hgh 40 gr./l, pH 7.22, lactate 8.2, BE -15, HCO3 - 12.8 and PO2 - 24, indicating severe acidosis. He was treated immediately by DC resuscitation, permission of hypotension and tranexamic acid. He had fractures of the pelvis with severe opening of the symphysis pubis and Rt iliosacral joint dislocation (upper row-red arrows) with a large laceration of his perineum (middle row). After 3 h his SBP increased to 80 mmHg. We started with damage control surgery-close down and single plate fixation of the symphysis pubis, packing of the pelvis and debridement of the wounds of the perineum. All surgeries were done within 45 min. The DC resuscitation continued with hemostatic resuscitation (RBC, fresh frozen plasma, thrombocytes in ratio of 1:1:1). After two days the blood gas analysis (BGA) was: pH 7.42, lactate 3.8, BE- -6.7. After 5 days the BGA was-pH 7.36, lactate 1.5, BE - 0.5. The perineum injury was treated few times with repeated debridement and then by vacuum assisted closure (VAC) of the wounds (middle row). After 7 days we performed posterior ilio-sacral fixation by two plates and screws, through a lateral windows approach (lower row).



Fig. 8a. A 33 Y old male was admitted after a car accident as a driver. At reception he was conscious, contactable, and oriented, but unstable hemodynamically with BP of 80/60, pulse 110 and saturation 100%. On arrival he had massive hematuria. Total body CT demonstrated contusion of both lungs with right hemopneumothorax, (upper arrow) and rupture of his Rt kidney with subcapsular hematoma (lower arrow). There were also multiple fractures of the Rt lower leg, as follows: fracture of the femoral shaft, comminuted supracondylar intraarticular fractures of the distal femur and fracture of the patella (upper row) and comminuted fracture of his Rt ankle (lower row).



Fig. 8b. The patient was intubated on arrival and treated initially urine catheterization and by fluids, blood and antibiotics, followed by closed reduction and trans-bridging external fixation from upper femur to tibia (upper row). Chest CT and radiographs taken two days after the injury, showed significant lung contusions that compromises the lung function mild hemothorax (upper row). The ankle fractures were treated initially by closed reduction and POP slab. 6 days later, following gradual metabolic and respiratory improvement, he was operated upon-the external fixator system was removed followed by closed IMN of the Rt femoral shaft, ORIF by plate and screws of the fracture of the distal femur, and ORIF of the fractured Rt ankle (lower row).

not associated with any increased rate of local complications such as pin-tract infections, delayed unions or non-unions. Primary external fixation does not stimulate any inflammatory reaction. Reaming during intramedullary nailing of long bones is associated with development of the "second hit" phenomenon.⁴⁰ External fixation is a safe procedure for achieving rapid, temporary rigid stabilization in unstable patients with multiple injuries. The average time for external fixation is 35 min with blood loss of 90 cc. as compared with intramedullary nailing of the femur which requires 130 min and results in 400 cc of blood loss.¹⁴ Pape described similar observations of an increase in the incidence of multiple organ dysfunction (MOF) of 46% in patients treated within the first two to four days (ETC) after the initial trauma, in comparison with an incidence of 15.7% in patients with late definitive treatment (DCO after 5–8 days), who had a similar injury severity score.^{40,41} There is a lower rate of complications in the DCO group despite higher ISS in comparison with the ETC group. DCO surgery appears to be a viable alternative for polytraumatized patients with femoral shaft fractures. There is no evidence that early or late definitive fixation of long bone fractures in unstable polytraumatized patients has any beneficial or detrimental effects on survival.

The patients that are suitable to ETC following resuscitation are those who are stable hemodynamic, have stable oxygen saturation and have lactate level of less than 2.5 mmol/l without coagulation disturbances, and have normal body temperatures and normal urinary output of more than 1 cc/kg/hour. The patients who do not respond well to resuscitation should be treated initially with life-saving surgery only and planning should proceed according to their specific condition with definitive treatment only after 5–10 days. At-risk patients requiring ETC include those patients with aortic rupture, chest and abdominal solid organ injuries, coagulopathy, hypoxia and severe intracranial injuries, epidural hematoma, tension pneumothorax, unstable burst cervical or thoracolumbar injuries, dislocation of the knee with damage to the popliteal artery, compartment syndrome and open fractures of limbs.

However, in compound fractures with displacement of the pelvis with symphysiolysis that results in continuous bleeding and unstable hemodynamic condition, it is possible to use simple temporary stabilization with bed sheets or a special brace initially for closure of the pelvis, followed by either Ganz's anti-shock pelvic clamp⁴² that can be applied quickly in the emergency room or by initial external fixation systems in the operating theater (Fig. 6). The definitive open reduction and fixation of pelvic fractures can be done after 1-2 weeks, depending on the patient's metabolic recovery following the polytrauma (Fig. 6.7). Primary external fixation in such patients is a safe procedure. Therefore, the current recommendation for long bone fracture fixation in patients with multiple injuries is to use a modular, minimally-invasive external frame (Figs. 5–7). The basic principles of DCO involve stabilization and control of the injury and then, only after a few days of metabolic and respiratory recovery, definitive management of the fracture fixation.

Over the last decade several publications indicate adverse effects of the damage control strategy.⁴³ Large databases demonstrate high incidence rates (up to 40–50%) of temporal external fixation in multiple injured patients and postulate an uncritical use of damage control orthopedic strategy.⁴³ Authors pointed out that the overzealous use of the external fixation may increases the length of stay in the ICU and hospital, raises the costs and affects

the rates of local infection and non-unions. Moreover, recent studies describe that early definitive treatment in multiply injured patients is associated with advantageous results.^{44–46} Vallier and coauthors published a new protocol for "Early Appropriate Care" (EAC) has been developed.⁴⁷ In severely injured patients with femoral fractures and injuries of pelvis, acetabulum and spine, parameters associated with systemic complications were reevaluated. This study revealed that acidosis (lower pH and slower improvement) was associated with pulmonary complications.⁴⁷ Authors pointed out, that the identification of the hemorrhage and aggressive resuscitation improve the acidosis and reduce the morbidity and mortality. Therefore, early definitive treatment can be performed once the patient has been adequately resuscitated. In the further study by the same study group the Early Appropriate Care (EAC) protocol (using lactate, pH, BE, and adequate resuscitation before surgery) was used to define low-risk and high-risk patients for systemic complications after early (<24 h) and late stabilization (>24 h).⁴⁴ This publication revealed that early treatment in lower-risk group was associated with fewer complications. Among the high-risk group, no differences between early and delayed treatment were found. Authors pointed out that patients with adequate resuscitation can tolerate early definitive treatment.⁴⁴ The same research group have demonstrated in a recent retrospective study that early definitive management (within 24 h of injury) of mechanically unstable fractures of the pelvis, acetabulum, femur and spine resulted in shorter ICU and hospital stays and fewer complications and ARDS, after adjusting for age and associated injury types and severity. Authors suggested to prove these data in a further prospective analysis.⁴⁸

Systematic reviews, however, revealed that lactate level alone is not reliable measure to define status of the patient. Recent discussions indicate that the decision making in the initial phase after trauma cannot be dichotomic (ETC versus DCO), but rather must focus on patient physiology and dynamics. Unreflected use of either approach alone does not respect patient clinical status and might be potentially harmful. Moreover, both concepts do not consider the dynamics of the clinical course (preclinics, operations, complications, etc.). Factors such as rescue time, type and severity of the injury and surgical interventions affect patients physiology. Therefore, a "Safe Definitive Surgery" (SDS) concept has been introduced, which is a dynamic synthesis of both strategies (ETC and DCO).⁴⁹

This concept does not rule out the use of ETC or DCO, but rather put it in perspective of the clinical situation considering the dynamics of the clinical course. Due to repeated reevaluation and assessment of the patients regarding their physiology, dynamic classification and adaptation of the treatment strategy is possible. Thus, advantages of both strategies (DCO or ETC) can be combined, which allow a safe definitive surgery in each situation. Another advantage of this approach is a better adaptation of the surgical strategy to regional differences and preclinical systems. Patients injured in an urban area are subjected earlier to a surgical intervention (e.g. ETC), than patients from sparsely populated regions. The physiological condition can worsen during the operation. The dichotomic approach (ETC versus DCO) do not respect this dynamics. In the other hand, in a territorial states the rescue time might be prolonged. In this scenario, the initial assessment and further clinical evaluation require a special consideration of soft tissues and patients physiology as well (Fig. 9).



Stages of Treatment:

Interventions	Duration in min
Day 0: Chest tube, SI screws, tibia nail, fibula plate, exFix wrist / ICU admission	283
Day 1: Clavicle plating	73
Day 2: Transfer from ICU to ward	
Day 5: Wrist plating	120
Day 14: Discharge rehabilitation	

Fig. 9. Safe Definitive Surgery Concept: Case presentation: 53 years old male patient was hit by a cable car and sustained injuries on upper and lower extremity, unstable thorax and pelvic pain. At the arrival in trauma day the patient was hemodynamically and respiratory stable (RR120/75 mmHg, HR 100 bpm), GCS of 15 points, no signs of coagulopathy and hypothermia. Diagnoses: 1. Fracture clavicle right; 2: serial fracture of the ribs; 3: Lung contusion right; 4: APC II Pelvic ring injury left; 5: lower leg fracture right. 6: fracture of distal radius right).

6. Conclusion

Treatment strategies in severely injured patients have changed over the last decades. Initial assessment includes the dynamic response to resuscitation and evaluation of the "Four Vicious Cycles" (*hemorrhagic shock, hypothermia, coagulopathy and soft tissues*). The main goal is the stabilization of major fractures as early as physiologically safe; "Safe Definitive Surgery" (SDS) concept has been introduced, which is a dynamic synthesis of both strategies -Early Total Care (ETC) and Damage Control Orthopedics (DCO)). This concept does not rule out the use of ETC or DCO, but rather put it in perspective of the clinical situation considering the dynamics of the clinical course. Due to repeated reevaluation and assessment of the patients regarding their physiology, dynamic classification and adaptation of the treatment strategy is possible (Table 1).

Ethical approval

This study was approved by the institutional review boards of our hospitals.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Table 1

Our recommendations.

- Management of polytraumatized patient has changed over the last decades
- Patients with multiple blunt traumas have to be assessed for "four pathophysiologic cascades"

Hemorrhagic Shock/ Acidosis; Hypothermia, Coagulopathy; Soft Tissue Injury

 Physiology of Staged Treatment: It is evaluated by the severity of the Systemic Inflammatory Response Syndrome (SIRS) following the 1st hit and 2nd hit. The patients are classified according to the SIRS as

Stable / Borderline / Unstable / In extremis

- "Safe Definitive Surgery" (SDS) concept has been introduced. It is a dynamic synthesis of both strategies (Early Total Care (ETC) and Damage Control Orthopedics (DCO))
- Staged management in a physiologically stable patients: "Musculoskeletal Temporary Surgery" or "MUST Surgery"

Declaration of competing interest

The authors declare that they have no conflict of interest.

References

- 1. Bone LB, Johnson KD, Weigelt J, Scheinberg R. Early versus delayed stabilization of femoral fractures. A prospective randomized study. J Bone Joint Surg Am. 1989:71(3):336-340.
- 2. D'Alleyrand JC, O'Toole RV. The evolution of damage control orthopedics: current evidence and practical applications of early appropriate care. Orthop Clin N Am. 2013;44(4):499-507.
- 3. Goris RI, Gimbrere IS, van Niekerk IL, Schoots FI, Boov LH, Early osteosynthesis and prophylactic mechanical ventilation in the multitrauma patient. *J Trauma*. 1982:22(11):895-903.
- Riska EB, von Bonsdorff H, Hakkinen S, Jaroma H, Kiviluoto O, Paavilainen T. 4 Primary operative fixation of long bone fractures in patients with multiple injuries. I Trauma, 1977:17(2):111–121.
- 5. Giannoudis PV, Smith RM, Bellamy MC, Morrison JF, Dickson RA, Guillou PJ. Stimulation of the inflammatory system by reamed and unreamed nailing of femoral fractures. An analysis of the second hit. J Bone Joint Surg Br. 1999;81(2): 356-361.
- 6. Rotondo MF, Schwab CW, McGonigal MD, et al. Damage control: an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma*, 1993;35(3):375–382. discussion 82-3.
- 7. Giannoudis PV, Hildebrand F, Pape HC. Inflammatory serum markers in patients with multiple trauma. Can they predict outcome? J Bone Joint Surg Br. 2004;86(3):313-323.
- 8. Roberts CS, Pape HC, Jones AL, Malkani AL, Rodriguez JL, Giannoudis PV. Damage control orthopaedics: evolving concepts in the treatment of patients who have sustained orthopaedic trauma. Instr Course Lect. 2005;54:447-462.
- 9. Pape HC, Rixen D, Morley J, et al. Impact of the method of initial stabilization for femoral shaft fractures in patients with multiple injuries at risk for complications (borderline patients). Ann Surg. 2007;246(3):491-499. discussion 9-501
- 10. Sears BW, Stover MD, Callaci J. Pathoanatomy and clinical correlates of the immunoinflammatory response following orthopaedic trauma. J Am Acad Orthop Surg. 2009;17(4):255-265.
- 11. Lichte P, Kobbe P, Dombroski D, Pape HC. Damage control orthopedics: current evidence. Curr Opin Crit Care. 2012;18(6):647-650.
- 12. Pape HC, Hildebrand F, Pertschy S, et al. Changes in the management of femoral shaft fractures in polytrauma patients: from early total care to damage control orthopedic surgery. J Trauma. 2002;53(3):452-461. discussion 61-2.
- 13. Pape HC, Grimme K, Van Griensven M, et al. Impact of intramedullary instrumentation versus damage control for femoral fractures on immunoinflammatory parameters: prospective randomized analysis by the EPOFF Study Group. J Trauma. 2003;55(1):7-13.
- 14. Scalea TM, Boswell SA, Scott JD, Mitchell KA, Kramer ME, Pollak AN. External fixation as a bridge to intramedullary nailing for patients with multiple injuries and with femur fractures: damage control orthopedics. J Trauma. 2000;48(4): 613-621. discussion 21-3.
- 15. Brenneman FD, Boulanger BR, McLellan BA, Redelmeier DA. Measuring injury severity: time for a change? J Trauma. 1998;44(4):580-582.
- 16. Baker SP, O'Neill B, Haddon Jr W, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma. 1974;14(3):187-196.
- 17. Pape HC, Lefering R, Butcher N, et al. The definition of polytrauma revisited: an international consensus process and proposal of the new 'Berlin definition'. J Trauma Acute Care Surg. 2014;77(5):780-786.
- 18. Pape HC, Giannoudis PV, Krettek C, Trentz O. Timing of fixation of major fractures in blunt polytrauma: role of conventional indicators in clinical decision making. J Orthop Trauma. 2005;19(8):551–562.
- 19. Hildebrand F, van Griensven M, Giannoudis P, et al. Impact of hypothermia on the immunologic response after trauma and elective surgery. Surg Technol Int. 2005;14:41-50.
- 20. Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. Crit Care. 2016;20:100.
- 21. Keel M, Trentz O. Pathophysiology of polytrauma. Injury. 2005;36(6):691-709.
- 22. Xiao W, Mindrinos MN, Seok J, et al. A genomic storm in critically injured humans. J Exp Med. 2011;208(13):2581–2590.
- 23. Huber-Lang M, Lambris JD, Ward PA. Innate immune responses to trauma. Nat Immunol. 2018;19(4):327-341.
- Volpin G, Cohen M, Assaf M, Meir T, Katz R, Pollack S. Cytokine levels (IL-4, IL-6, IL-8 and TGFbeta) as potential biomarkers of systemic inflammatory response in trauma patients. Int Orthop. 2014;38(6):1303-1309.

- 25. Biffl WL, Moore EE, Moore FA, Peterson VM. Interleukin-6 in the injured patient. Marker of injury or mediator of inflammation? Ann Surg. 1996;224(5): 647-664
- 26. Menger MD, Vollmar B. Surgical trauma: hyperinflammation versus immunosuppression? Langenbeck's Arch Surg. 2004;389(6):475-484.
- 27. Kumbhare D, Parkinson W, Dunlop B, et al. Injury measurement properties of serum interleukin-6 following lumbar decompression surgery. J Surg Res. 2009;157(2):161-167.
- 28 Reikeras O Immune depression in musculoskeletal trauma Inflamm Res 2010;59(6):409-414.
- 29. Sarahrudi K. Thomas A. Mousavi M. et al. Elevated transforming growth factorbeta 1 (TGF-beta1) levels in human fracture healing. *Injury*. 2011;42(8): 833-837.
- 30. Sun T, Wang X, Liu Z, Chen X, Zhang J. Plasma concentrations of pro- and antiinflammatory cytokines and outcome prediction in elderly hip fracture patients. Iniury, 2011:42(7):707-713.
- **31.** Lee CC, Marill KA, Carter WA, Crupi RS. A current concept of trauma-induced multiorgan failure. *Ann Emerg Med.* 2001;38(2):170–176.
- 32. Cohen M, Meir T, Klein E, Volpin G, Assaf M, Pollack S. Cytokine levels as potential biomarkers for predicting the development of posttraumatic stress symptoms in casualties of accidents. Int J Psychiatr Med. 2011;42(2):117–131.
- 33. Cohen M, Volpin G, Meir T, et al. Possible association of Toll-like receptor 9 polymorphisms with cytokine levels and posttraumatic symptoms in individuals with various types of orthopaedic trauma: early findings. Injury. 2013;44(11):1625-1629.
- 34. Pervanidou P, Kolaitis G, Charitaki S, et al. Elevated morning serum interleukin (IL)-6 or evening salivary cortisol concentrations predict posttraumatic stress disorder in children and adolescents six months after a motor vehicle accident. Psychoneuroendocrinology. 2007;32(8-10):991–999.
 35. Newport DJ, Nemeroff CB. Neurobiology of posttraumatic stress disorder. Curr
- Opin Neurobiol. 2000;10(2):211-218.
- 36. Hoff P, Buttgereit F, Burmester GR, et al. Osteoarthritis synovial fluid activates pro-inflammatory cytokines in primary human chondrocytes. Int Orthop. 2013:37(1):145-151.
- 37. Rohner E, Matziolis G, Perka C, et al. Inflammatory synovial fluid microenvironment drives primary human chondrocytes to actively take part in inflammatory joint diseases. Immunol Res. 2012;52(3):169-175.
- 38. Matsumoto S, Muller-Ladner U, Gay RE, Nishioka K, Gay S. Ultrastructural demonstration of apoptosis, Fas and Bcl-2 expression of rheumatoid synovial fibroblasts. J Rheumatol. 1996;23(8):1345-1352.
- 39. Hundric-Haspl Z, Pecina M, Haspl M, Tomicic M, Jukic I. Plasma cytokines as markers of aseptic prosthesis loosening. Clin Orthop Relat Res. 2006;453: 299-304.
- 40. Pape HC, Regel G, Dwenger A, et al. Influences of different methods of intramedullary femoral nailing on lung function in patients with multiple trauma. J Trauma. 1993;35(5):709–716.
- 41. Pape HC, van Griensven M, Rice J, et al. Major secondary surgery in blunt trauma patients and perioperative cytokine liberation: determination of the clinical relevance of biochemical markers. J Trauma. 2001;50(6):989-1000.
- 42. Ganz R, Krushell RJ, Jakob RP, Kuffer J. The antishock pelvic clamp. Clin Orthop Relat Res. 1991;(267):71-78.
- 43. Rixen D, Grass G, Sauerland S, et al. Evaluation of criteria for temporary external fixation in risk-adapted damage control orthopedic surgery of femur shaft fractures in multiple trauma patients: "evidence-based medicine" versus "reality" in the trauma registry of the German Trauma Society. J Trauma. 2005;59(6):1375-1394. discussion 94-5.
- 44. Nahm NJ, Como JJ, Wilber JH, Vallier HA. Early appropriate care: definitive stabilization of femoral fractures within 24 hours of injury is safe in most patients with multiple injuries. J Trauma. 2011;71(1):175-185.
- Nahm NJ, Patterson BM, Vallier HA. The impact of injury severity and transfer 45 status on reimbursement for care of femur fractures. J Trauma Acute Care Surg. 2012;73(4):957-965.
- 46. Nahm NJ, Vallier HA. Timing of definitive treatment of femoral shaft fractures in patients with multiple injuries: a systematic review of randomized and nonrandomized trials. J Trauma Acute Care Surg. 2012;73(5):1046-1063.
- 47. Vallier HA, Wang X, Moore TA, Wilber JH, Como JJ. Timing of orthopaedic surgery in multiple trauma patients: development of a protocol for early appropriate care. J Orthop Trauma. 2013;27(10):543-551.
- Vallier HA, Super DM, Moore TA, Wilber JH. Do patients with multiple system injury benefit from early fixation of unstable axial fractures? The effects of timing of surgery on initial hospital course. J Orthop Trauma. 2013;27(7): 405 - 412
- 49. Pape HC, Pfeifer R. Safe definitive orthopaedic surgery (SDS): repeated assessment for tapered application of Early Definitive Care and Damage Control?: an inclusive view of recent advances in polytrauma management. Injury. 2015;46(1):1-3.