Injury, Int. J. Care Injured 44 (2013) 217–220

Contents lists available at SciVerse ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Early fracture stabilisation in the presence of subclinical hypoperfusion

Ben Grey [a,b,*], Reitze N. Rodseth [c,d], David J.J. Muckart [e,f]

[a] Edendale Hospital, Pietermaritzburg, South Africa
[b] Department of Orthopaedics, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, South Africa
[c] Perioperative Research Unit, Department of Anaesthetics, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, South Africa
[d] Department of Anaesthetics, Inkosi Albert Luthuli Central Hospital, Durban, South Africa
[e] Level 1 Trauma Unit and Trauma Intensive Care, Inkosi Albert Luthuli Central Hospital, Durban, South Africa
[f] Department of Surgery, University of KwaZulu-Natal, South Africa

ARTICLE INFO

Article history:
Accepted 30 August 2012

Keywords:
Early fracture fixation
Polytrauma
Subclinical hypoperfusion
Occult hypoperfusion

ABSTRACT

Introduction: In polytrauma patients with an injury severity score (ISS) > 16, early long bone and pelvic fracture fixation within 24 h after injury has been shown to be beneficial. In contrast, surgery in the presence of subclinical hypoperfusion (SCH), defined as normal vital signs with a serum lactate ≥ 2.5 mmol/L may be detrimental. This study aimed to investigate the effect of fracture fixation in polytrauma patients with SCH.

Methods: We undertook a database review extracting 88 polytrauma patients with a new injury severity score (NISS) > 16 with significant long bone or pelvic fractures (extremity NISS ≥ 9) who underwent surgical fracture stabilisation within 48 h of injury. In the group of patients with normal vital signs (mean arterial pressure ≥ 60 mmHg and heart rate ≤ 110 beats/min) we compared outcomes between those with a normal preoperative lactate (<2.5 mmol/L) and those with a raised lactate (≥2.5 mmol/L).

Results: Of the 36 patients with normal preoperative vital signs, 17 had normal lactates (control group) and 19 abnormal lactates (SCH group). There were no significant differences in the method of fixation or theatre time between the groups. The SCH group required more inotropic support in the first 24 h post surgery ($p = 0.02$) and had higher sequential organ failure assessment (SOFA) scores on day 3 ($p = 0.003$). Although not reaching mathematical significance those with SCH required on average 10 days longer on mechanical ventilation.

Conclusion: Early fracture fixation in patients with SCH as defined by normal vital signs and a lactate ≥ 2.5 mmol/L is associated with significant postoperative morbidity. Consideration should be given to delaying surgery in this cohort.

Introduction

Early fixation of long bone and pelvic fractures is recommended in stable polytrauma patients.[1,2] In those with an injury severity score (ISS) > 18, early fixation of long bone and pelvic fractures within 24 h of injury reduces the incidence of fat embolism syndrome, acute respiratory distress syndrome (ARDS) and complications associated with prolonged immobilisation.[3–8] In patients with significant head, chest, or abdominal injuries however, a staged approach to definitive fracture fixation has been shown to be beneficial.[9–12]

A recent large retrospective cohort study showed that in polytrauma patients (ISS > 15) delaying internal femoral fixation beyond 12 h decreased mortality by 50%.[12] Patients with severe abdominal trauma benefited the most from this approach. The authors speculated that the adverse outcomes seen with intramedullary femoral fixation during the first 12 h may have been due to the presence of "occult" hypoperfusion caused by inadequate resuscitation.

Subclinical hypoperfusion (SCH) is defined as the normalisation of vital signs in response to resuscitation but with the persistence of a serum lactate > 2.5 mmol/L.[13] A prospective study of haemodynamically stable polytrauma patients (ISS ≥ 20) found that persistent occult hypoperfusion for more than 24 h resulted in a statistically significant increase in mortality, multisystem organ failure and respiratory complications when compared to patients who corrected their lactate levels within 24 h.[13]

It is thus possible that undertaking surgery during this period of physiologic vulnerability may negatively affect patient outcomes. This study aimed to investigate the effect of fracture fixation in polytrauma patients with SCH.

* Corresponding author at: Department of Orthopaedics, Nelson R. Mandela School of Medicine, Private Bag 7, Congella 4013, South Africa. Tel.: +27 31 2604293.
E-mail address: bcgrey@gmail.com (B. Grey).

0020–1383/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.injury.2012.08.062

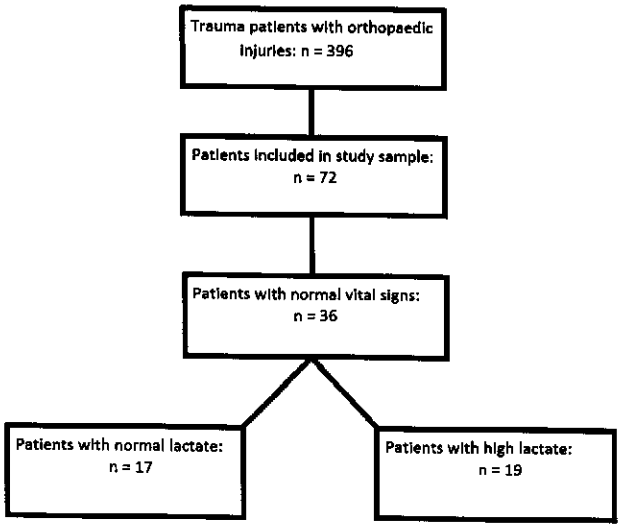

Fig. 1. Identification of eligible polytrauma patients with NISS > 16 and significant pelvic or long bone fractures who underwent surgical fracture stabilisation within 48 h of injury. NISS, new injury severity score.

Methods

A database review was performed at the Level 1 Trauma Unit at Inkosi Albert Luthuli Central Hospital (IALCH), Durban, South Africa. Ethics approval was obtained from the Biomedical Research Ethics Committee, University of KwaZulu-Natal (BE 207/09). All polytrauma patients treated in the unit since its opening in March 2007 until October 2010 were reviewed. Data were extracted using the hospital data management system Medicom and the Trauma Unit Database.

Injury severity was graded with the new injury severity score (NISS).[14] Polytrauma patients were defined as those with a NISS > 16, with severe injury defined as a NISS ≥ 9 in any compartment. Within this group we selected patients with significant pelvic or long bone fractures (extremity NISS ≥ 9) who underwent surgical fracture stabilisation within 48 h of injury. We excluded children younger than 13 years, patients who underwent their initial surgery at another hospital and those who did not undergo surgical fracture stabilisation.

Patients with normal vital signs defined as a mean arterial pressure (MAP) ≥ 60 mmHg and heart rate (HR) ≤ 110 beats/min were separated into a control group (lactate < 2.5 mmol/L) and a SCH group (lactate ≥ 2.5 mmol/L). Patients were then stratified into three risk groups based on their NISS (<30, 30–44, >44). The number of patients requiring inotropic support within the first 24 h following surgery was chosen as the primary study endpoint. Ventilation time, sequential organ failure assessment (SOFA) scores on days 3 and 7 and mortality were used as secondary endpoints.

Statistical analysis

Standard descriptive statistics were used to describe patient characteristics, including means and standard deviations for continuous variables. All data analyses were performed using SPSS 15.0 for Windows (SPSS, Chicago, IL), using a χ^2 test for categorical data, and Student's *t*-test, one-way ANOVA and the Wilcoxon test where appropriate. Statistical significance was defined as two-sided *p*-value < 0.05.

Results

During the study period 396 trauma patients with orthopaedic injuries were treated at this facility of whom 88 were eligible for inclusion.

Forty patients (45.4%) underwent surgical fracture fixation within 12 h and 69 (78.4%) within 24 h of injury. Of the 30 patients transferred directly from scene 24 (80%) underwent fixation in <12 h and a total of 28 (93.3%) within 24 h.

A preoperative lactate was not available in 16 cases. Of the remaining 72 patients, 36 presented preoperatively with normal vital signs, 17 in the control group (lactate < 2.5 mmol/L) and 19 in the SCH group (lactate ≥ 2.5 mmol/L) (Fig. 1).

The characteristics of the patients included in the study are shown in Table 1. There were statistically significantly more males and a higher average lactate in the SCH group. Table 2 shows the modes of fracture stabilisation in the group.

Table 3 shows the postoperative outcomes of the two groups. Patients in the SCH group required more inotropes in the first 24 h ($p = 0.02$), had higher SOFA scores on day 3 ($p = 0.003$) and had a non-significant increase in SOFA scores on day 7 ($p = 0.06$). There was also a trend towards longer ventilation time in this group, but this was not statistically significant (13.38 vs. 2.65 days, $p = 0.11$).

Discussion

In patients with multiple injuries, the treatment of life-threatening injuries is prioritised. Unstable pelvis and long bone fractures are initially immobilised with non-operative means and surgical fracture stabilisation occurs after resuscitation and management of significant head, chest or abdominal injuries.

Trauma scoring systems have been developed to assist in the assessment of injury and to predict patient outcomes. Both the

Table 1
Characteristics of polytrauma patients with normal vital signs ($n = 36$) undergoing fracture fixation within 48 h of injury.

	Normal lactate ($n = 17$)	Subclinical hypoperfusion ($n = 19$)	*p*-Value
Age (SD)	34.2 (14.37)	37.3 (15.37)	0.54
Male sex (%)	8 (47.1)	17 (89.5)	0.01[a]
Mean NISS (SD)	28 (9.55)	32.1 (8.42)	0.18
Chest NISS (SD)	8.9 (10.2)	8.8 (10.57)	0.98
Abdomen NISS (SD)	2.7 (5.82)	4.6 (9.68)	0.48
Head and neck NISS (SD)	2.4 (5.56)	7.2 (9.19)	0.06
Average time to OT	15.71 (11.6)	14.58 (9.06)	0.75
Compound fracture (%)	11 (64.7)	12 (52.2)	1
NISS < 30, $n = 23$ (%)	13(76.4)	10 (52.6)	0.18
NISS 30–44, $n = 11$ (%)	3 (17.6)	8 (42.1)	0.16
NISS > 45, $n = 2$ (%)	1 (5.9)	1 (5.3)	1
Average lactate (SD)	1.6 (0.41)	4.5 (1.52)	<0.001[a]

SD: standard deviation; OT: operating theatre; NISS: new injury severity score.
[a] Statistically significant.

Table 2
Mode of surgical fracture stabilisation.

Fixation method	Normal lactate ($n=17$)	Subclinical hypoperfusion ($n=19$)	p-Value
Intramedullary nailing	10	8	0.50
External fixation	5	10	0.19
Other	2	1	0.59

injury severity score (ISS) and the NISS are anatomically based scores useful in research, but are less helpful in triage and decision making in the acute setting.[14,15]

The haemodynamic state of the polytrauma patient is one of the major factors affecting the orthopaedic management of major fractures. For haemodynamically stable patients, early definitive fracture fixation, also known as "Early Total Care" has been shown to improve outcome.[1] A prospective randomised study by Bone et al.[5] showed that the timing of fracture fixation did not adversely affect outcome in patients with isolated femur fractures (ISS < 18). In their study none of these patients developed acute respiratory distress syndrome (ARDS), fat embolism syndrome (FES) or needed postoperative ventilation. In patients with multiple injuries (ISS > 18) early femoral fracture fixation decreased the incidence of FES, ARDS, pneumonia and time in ICU. The haemodynamic state of patients at the time of femoral fracture fixation was not reported.

A large statewide hospital discharge database review examined patients with femur fractures.[16] They found that early femoral fracture fixation in polytrauma patients (ISS ≥ 15) decreased mortality significantly when compared to non-operative management (3.8% vs. 24% mortality, $p < 0.001$). Fixation during day 1 showed a trend to higher mortality (3.8%) when compared to fixation during days 2–4 (1.8%) and after day 4 (1.5%), but this was not statistically significant.

Certain studies have identified injury patterns which predict a worse outcome when fracture fixation is undertaken early. Patients with severe head, chest or abdominal injuries have been shown to benefit from a staged approach to long bone fracture fixation. In patients with severe chest trauma (AIS ≥ 2), early femoral nailing (<24 h) was associated with an increased incidence of ARDS (33% vs. 7.7%) and mortality (21% vs. 4%) when compared to fixation after 24 h.[9] In patients with severe closed head injuries (Glasgow Coma Scale (GCS) < 9), femoral fixation within 2 h of admission was associated with an eight-fold increase in the risk of intra-operative hypotension, while femoral fixation within 24 h doubled the risk of intra-operative hypotension.[11] Similarly Morshed et al. showed that delayed femoral fixation >12 h in polytrauma patients (ISS ≥ 15) reduced mortality by up to 50% and patients with severe abdominal trauma (AIS ≥ 3) benefited the most from this staged approach.[12] The authors speculated whether occult hypoperfusion was responsible for the higher mortality when fracture fixation was performed during the first 12 h, but this was not substantiated.

Occult hypoperfusion implies that although vital signs have normalised following resuscitation, a state of cellular hypoxia still exists, as evidenced by a persistent raised lactate. This phenomenon is well described by Barbee et al.[17] who emphasise that at the end of resuscitation when the haemodynamic parameters and oxygen deficit as gauged by oxygen delivery may appear normal, there remains a substantial oxygen debt which needs to be repaid with further resuscitation. We feel that the term subclinical hypoperfusion is a more appropriate term. The term "occult" implies that which cannot be seen, while in truth the problem is that the hypoperfusion is not clinically noticeable, but is easily detected by the measurement of lactate. Lactate is formed during anaerobic metabolism and hyperlactatemia after injury is most likely due to inadequate tissue perfusion. The initial lactate level as well as the duration of hyperlactatemia has been shown to correlate well with mortality and the incidence of multiple organ failure in trauma victims.[18,19] A pilot study examined the incidence of subclinical hypoperfusion in 62 trauma patients. When using base excess 11% of patients were identified as having SCH, with a significant association between hospital length of stay and SCH as detected by base excess elevation. The use of the cardiac index (16%), shock index (6%) and rate over pressure evaluation (3%) did not show a significant association with length of stay.[20] Persistent subclinical hypoperfusion for longer than 24 h is associated with a higher infection rate, more respiratory complications, higher incidence of multiple organ dysfunction and an increased mortality rate.[13,21]

Undertaking fracture fixation during this period of physiological vulnerability may worsen cellular hypoxia and cellular injury and therefore negatively impact patient outcome. Our findings are in agreement with those of Crowl et al. who in a series of 47 stable patients with femur fractures undergoing early (<24 h) intramedullary fixation, identified 20 patients with subclinical hypoperfusion. These patients had a higher incidence of post-operative complications when compared to similar patients with a serum lactate < 2.5 mmol/L (50% vs. 20%, $p < 0.01$).[22] The spectrum of post-operative outcomes included respiratory, cardiac, haematological, neurological, gastro-intestinal, musculoskeletal and infectious complications. The time period between surgical intervention and complication was however not specified, therefore factors other than surgery could have influenced outcome.

Our study suffers from limitations inherent to all retrospective reviews. Patient group size was limited by incomplete data and total patient numbers were small. Of the 72 polytrauma patients undergoing early fracture fixation only half were haemodynamically stable at the time of surgery and 53% of these stable patients had SCH. Our incidence of SCH is similar to the study by Crowl et al. who identified SCH in 42% of their stable patients going for femoral fracture fixation.

Table 3
A comparison of patient outcomes between those with subclinical hypoperfusion and those with a normal lactate following fracture fixation within 48 h of injury.

	Normal lactate ($n=17$)	Subclinical hypoperfusion ($n=19$)	p-Value
Preoperative inotropes (%)	0	1 (5.3)	1
Post op 24 h inotropes used (%)	1 (5.9)	8 (42.1)	0.02*
Length of ventilation days (SD)	2.65 (7.18)	13.38 (24.23)	0.11
SOFA day 3 (SD)	2.38 (2.06)	5.32 (3.33)	0.003*
SOFA day 7 (SD)	1.86 (1.57)	3.79 (2.86)	0.06
Died	0	1 (5.3)	1
Duration of surgery minutes (SD)	219.41 (83.44)	248 (101.75)	0.36

SD: standard deviation; SOFA: sequential organ failure assessment.
* Statistically significant.

A variety of long bone and pelvic fractures as well as fracture patterns were grouped together to ensure adequate group sizes, but all the patients had significant long bone or unstable pelvic ring fractures and there were similar numbers of open fractures in each group. There was no statistical difference in the number of pelvic fractures between the two groups.

Although most studies have focused mainly on the timing of intramedullary long bone fixation, we included patients who had external fixation of unstable pelvic ring or long bone fractures, as well as other methods of internal fixation of long bone fractures. Fixation methods did not differ significantly between the two groups. No internal fixation of pelvic fractures was done in the first 48 h and there was no statistically significant difference in the number of unstable pelvic ring fractures requiring external fixation between the two groups. Furthermore there was no significant difference in operative time.

On this basis our data indicate that the major factor dictating postoperative morbidity is the presence of SCH at the time of surgery and operative intervention should be postponed until tissue hypoxia has been corrected. Organ dysfunction deteriorates significantly and although the difference in duration of mechanical ventilation was not mathematically significant a five-fold increase in ventilatory time is clinically relevant.

Conclusion

Early fracture fixation in haemodynamically stable polytrauma patients with subclinical hypoperfusion, as identified by an elevated serum lactate level, is associated with an increased need for inotropic support, a higher incidence of multiple organ dysfunction as measured by the SOFA score, and the need for prolonged mechanical ventilation.

Conflict of interest

We declare that we have no conflicts of interest.

References

1. Pape HC, Hildebrand F, Pertschy S, Zelle B, Garapati R, Grimme K, *et al.* Changes in the management of femoral shaft fractures in polytrauma patients: from early total care to damage control orthopedic surgery. *Journal of Trauma* 2002;53(3):452–61. discussion 461–62.
2. Giannoudis PV, Pape HC. Damage control orthopaedics in unstable pelvic ring injuries. *Injury* 2004;35(7):671–7.
3. Riska EB, Myllynen P. Fat embolism in patients with multiple injuries. *Journal of Trauma* 1982;22(11):891–4.
4. Johnson KD, Cadambi A, Seibert GB. Incidence of adult respiratory distress syndrome in patients with multiple musculoskeletal injuries: effect of early operative stabilization of fractures. *Journal of Trauma* 1985;25(5):375–84.
5. Bone LB, Johnson KD, Weigelt J, Scheinberg R. Early versus delayed stabilization of femoral fractures. A prospective randomized study. *Journal of Bone and Joint Surgery* 1989;71(3):336–40.
6. Seibel R, LaDuca J, Hassett JM, Babikian G, Mills B, Border DO, *et al.* Blunt multiple trauma (ISS 36), femur traction, and the pulmonary failure-septic state. *Annals of Surgery* 1985;202(3):283–95.
7. Latenser BA, Gentilello LM, Tarver AA, Thalgott JS, Batdorf JW. Improved outcome with early fixation of skeletally unstable pelvic fractures. *Journal of Trauma* 1991;31(1):28–31.
8. Vallier HA, Cureton BA, Ekstein C, Oldenburg FP, Wilber JH. Early definitive stabilization of unstable pelvis and acetabulum fractures reduces morbidity. *Journal of Trauma* 2010;69(3):677–84.
9. Pape HC, Auf'm'Kolk M, Paffrath T, Regel G, Sturm JA, Tscherne H. Primary intramedullary femur fixation in multiple trauma patients with associated lung contusion – a cause of posttraumatic ARDS? *Journal of Trauma* 1993;34(4):540–7. discussion 547–48.
10. Jaicks RR, Cohn SM, Moller BA. Early fracture fixation may be deleterious after head injury. *Journal of Trauma* 1997;42(1):1–5. discussion 5–6.
11. Townsend RN, Lheureau T, Protech J, Riemer B, Simon D. Timing fracture repair in patients with severe brain injury (Glasgow Coma Scale score < 9). *Journal of Trauma* 1998;44(6):977–82. discussion 982–83.
12. Morshed S, Miclau 3rd T, Bembom O, Cohen M, Knudson MM, Colford Jr JM. Delayed internal fixation of femoral shaft fracture reduces mortality among patients with multisystem trauma. *Journal of Bone and Joint Surgery* 2009;91(1):3–13.
13. Blow O, Magliore L, Claridge JA, Butler K, Young JS. The golden hour and the silver day: detection and correction of occult hypoperfusion within 24 hours improves outcome from major trauma. *Journal of Trauma* 1999;47(5):964–9.
14. Osler T, Baker SP, Long W. A modification of the injury severity score that both improves accuracy and simplifies scoring. *Journal of Trauma* 1997;43(6):922–5. discussion 925–26.
15. 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. *Journal of Trauma* 1974;14(3):187–96.
16. Fakhry SM, Rutledge R, Dahners LE, Kessler D. Incidence, management, and outcome of femoral shaft fracture: a statewide population-based analysis of 2805 adult patients in a rural state. *Journal of Trauma* 1994;37(2):255–60. discussion 260–61.
17. Barbee RW, Reynolds PS, Ward KR. Assessing shock resuscitation strategies by oxygen debt repayment. *Shock* 2010;33(2):113–22.
18. Abramson D, Scalea TM, Hitchcock R, Trooskin SZ, Henry SM, Greenspan J. Lactate clearance and survival following injury. *Journal of Trauma* 1993;35(4):584–8. discussion 588–89.
19. Manikis P, Jankowski S, Zhang H, Kahn RJ, Vincent JL. Correlation of serial blood lactate levels to organ failure and mortality after trauma. *American Journal of Emergency Medicine* 1995;13(6):619–22.
20. Thom O, Taylor DM, Wolfe RE, Myles P, Krum H, Wolfe R. Pilot study of the prevalence, outcomes and detection of occult hypoperfusion in trauma patients. *Emergency Medicine Journal* 2010;27(6):470–2.
21. Claridge JA, Crabtree TD, Pelletier SJ, Butler K, Sawyer RG, Young JS. Persistent occult hypoperfusion is associated with a significant increase in infection rate and mortality in major trauma patients. *Journal of Trauma* 2000;48(1):8–14. discussion 14–5.
22. Crowl AC, Young JS, Kahler DM, Claridge JA, Chrzanowski DS, Pomphrey M. Occult hypoperfusion is associated with increased morbidity in patients undergoing early femur fracture fixation. *Journal of Trauma* 2000;48(2):260–7.