

Complications relating to enteral and parenteral nutrition in trauma patients: a retrospective study at a level one trauma centre in South Africa

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Abstract

Objectives: The aim of the study was to compare the incidence of complications in patients receiving enteral and parenteral nutrition (PN), and review how the early initiation of enteral feeding and early achievement of caloric goal would affect the incidence of complications.

Design: The design was a retrospective audit of an ethics-approved prospective trauma registry and electronic medical record.

Setting: The setting was a level one trauma centre intensive care unit.

Subjects: One thousand and two consecutively treated patients were selected from 1 096 in the database.

Outcome measures: Demographic data, nutrition, route of administration, time of initiation and complications in the form of sepsis, pneumonia and feed intolerance, were determined.

Results: Patients receiving total PN (TPN) during their length of stay had a hazard ratio of 9.11 for the development of sepsis, compared to patients who were solely fed via the enteral route (p -value < 0.001). The patients who reached their nutritional goal late showed a hazard ratio of 2.67 for the development of sepsis, compared to patients who reached the goal early (p -value < 0.001). Patients with late initiation of feeding also had a greater risk of developing sepsis, with a hazard ratio of 2.41, compared to patients with early initiation (p -value < 0.001). Patients achieving the nutritional goal late had a 17.9% increased risk of developing pneumonia (p -value < 0.001).

Conclusion: This study confirms previous findings that the use of TPN is a strong predictor of the development of sepsis, compared to enteral nutrition. Causality linkage should be made with caution owing to the study design.

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Introduction

Trauma remains a worldwide leading cause of unnatural death, and a major cause of permanent disability, mainly affecting those aged 1-44 years. Trauma results in profound economic consequences, owing to the productive life-years lost.^{1,2} The almost 13/1 000 of the population injured in KwaZulu-Natal per year is among the highest injury rates in the world. The healthcare system in South Africa is also unique as advanced healthcare facilities coexist with resource-constrained institutions.³

Trauma systems and trauma centres have demonstrated effectiveness, providing care with significantly lower mortality and fewer complications.¹

There was a recent paradigm shift with regard to nutrition in the critically ill with the objective of preserving lean body mass, often referred to as nutritional therapy.^{4,5} Critically ill trauma patients

endure a catabolic phase during the acute post-injury period, with hyperglycaemia and insulin resistance, among others, even if the patient was not previously diabetic.⁶⁻¹⁰ Critically ill patients lose approximately 5-10% skeletal muscle mass per week during their initial stay in the intensive care unit (ICU). Nutritional support is an essential component for improved outcome.^{8,11,12}

Early enteral nutrition has been defined by the European Society for Clinical Nutrition and Metabolism (ESPEN) as feeding initiated within the first 24-48 hours of admission to the ICU,⁸ and in meta-analyses has been shown to reduce mortality in trauma¹³ and the development of multiple organ failure by attenuating the systemic inflammatory response. A classic study on trauma patients showed that early enteral nutrition results in a significantly lower incidence of intra-abdominal abscesses and pneumonia than that recorded in patients given hypocaloric parenteral nutrition (PN).¹⁴ Subgroup analysis showed that trauma patients had the most significant

reduction in complications when compared with high-risk surgical patients.¹³ At least 50–65% of the patient's caloric goal has to be delivered in order to attenuate the systemic inflammatory response and to prevent pathophysiological changes in the gut.^{15–17}

On the other hand, PN, commonly provided via a central venous catheter,^{3,6} is used mainly in patients suffering from prolonged gastrointestinal dysfunction such as a discontinuous gut, high-output enterocutaneous fistulae, intolerance to enteral feeding⁸ and in cases when an escalating dose of inotropic support is required, although this last aspect is controversial and early enteral nutrition after initial stabilisation may well be possible.^{18,19}

Intolerance, aspiration (believed to be a common cause of pneumonia in the ICU setting), diarrhoea, bowel ischaemia (not a common cause) and the risk of underfeeding are common complications relating to enteral nutrition. Intolerance can present as abdominal distension, increased nasogastric output or changes in the stools.^{4,20–24}

Mechanical ventilation is a defined risk factor for the development of pneumonia, referred to as ventilator-associated pneumonia (VAP). Patients who develop pneumonia after 72 hours of invasive mechanical ventilation are defined as having acquired VAP, and approximately 10–30% of the mechanically ventilated patient population develops VAP, with a mortality rate of 30–40%.^{25,26}

Enteral feeding is contraindicated in patients who are in shock, or in patients requiring high-dose inotropic support, especially while the dose is still being titrated to effect.²⁷ This is because of reduced splanchnic blood flow in these patients, leading to the development of non-occlusive bowel and gut necrosis, caused by ischaemia.⁸ Fortunately, this occurs in less than 1% of hypotensive critically ill patients. Underfeeding, common in critically ill patients, has been shown to correlate with an increase in complications, particularly infections, and is even common in enterally fed patients.^{1,7}

PN complications include those directly relating to the route of administration, such as complications associated with venous access; mechanical complications, i.e. iatrogenic pneumothorax and infectious complications; and metabolic complications relating to PN, including hepatobiliary complications, i.e. cholestasis. Insulin therapy in patients receiving PN may prevent cholestasis.⁹

ESPEN suggests the early start of supplementary PN on day 2–3, while the American Society for Parenteral and Enteral Nutrition (ASPEN) recommends holding supplementary PN until day 8 if the patient is not overtly malnourished.⁶ Trying all of the options to achieve EN prior to starting PN is suggested in the 2014 Canadian guidelines.²⁸

Thus, the aims of the study were to compare the incidence of complications in trauma patients who had an early versus those with a later EN start, to compare patients who reached their feeding goal early versus those who reached it late, and to assess the difference in the incidence of complications between patients fed EN solely versus those who received PN at some point during their stay at the trauma ICU.

Method

The trauma service at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal, opened in March 2007 to treat patients with life-threatening major injuries. The service is a “closed unit”, managed by critical care-certified trauma surgeons, who care directly for all admissions from door to discharge.¹ Allied health services, specialities and subspecialities are available in house. Patients are managed until their discharge to a regional base hospital or until death. University of KwaZulu-Natal Biomedical Research Ethics Committee approval of the prospective database (BE207-09) covers the registry and the electronic patient record system of the hospital for research purposes.

The Injury Severity Score (ISS) is a standardised method originally designed to quantify the injuries and potentially predict the outcome for injuries caused by blunt trauma, and predicts mortality by assessing anatomical injuries as per the Abbreviated Injury Scale (AIS), by summing the square of the three highest regional AIS scores. The score ranges from 1–75, with scores of < 9 defined as mild trauma, scores from 10–15 being intermediate, and scores > 15 as severe trauma.^{29–31} The AIS is determined per organ in a standard fashion. While it is not a perfect system, it is the one used in this unit owing to the multiple-system trauma population served.

Nutritional support is coordinated by the team in discussion with the dedicated ward dietitian. Continuous enteral feeding was commenced as per the feeding protocol with an assessment of tolerance using clinical and biochemical markers, but without routine gastric residual measurement. Escalation of the feed rate was per unit protocol, advanced every 2–4 hours if tolerated, with the aim of achieving the goal feed within 48 hours. Enteral nutrition was withheld above the inotrope dose of 13.4 µg/minute. Adrenalin is the primary inotrope of use in the unit.

With minimal exceptions, patients were admitted after acute trauma and were otherwise nutritionally “normal” prior to injury. The patients were placed on a standardised intravenous insulin infusion protocol, adjusted hourly as per the softer serum glucose range of 4.5–8.3 mmol/l. Feeding was commenced within the first 24 hours wherever possible, and at least within 48 hours when enteral nutrition feeding was planned. PN was not used early (before day 5). Neither was supplemental PN used in the enteral nutrition group. However, crossover enteral feeding was used when weaning patients off PN feeds. The standard PN regimen included soy bean oil, medium-chain triglycerides, olive oil and fish oil (SMOF). The feed requirements were calculated using the modified Schofield equation.

This single-centre retrospective audit included patients admitted from the opening of the trauma unit on 26 March 2007 until 31 December 2011. Inclusion criteria included survival more than 24 hours post admission, and patients who were fed (even where the length of stay was less than 24 hours), and who survived.

Data were exported to a Microsoft® Excel® spreadsheet. Tables I and II detail the definitions used in the present study and the variables utilised. Statistical analyses were performed using Statistica®. Mean,

Table I: Definitions used in the present study

Author	Patient information	Definitions
Genton, Romand and Pichard ⁸	Early-start enteral nutrition	Within 24-48 hours post admission to the intensive care unit
Krenitsky ¹⁰	Early-goal enteral nutrition	Within 96 hours of feeding initiation
Hardcastle, Samuels and Muckart ³	High ISS	An ISS score above 15
Hardcastle, Samuels and Muckart ³	Low ISS	An ISS score of 1-15

ISS: Injury Severity Score

Table II: The data points collected in the present study

Variables collected	
	Age and sex
	Mechanism of injury
	Abbreviated Injury Scale and Injury Severity Score
	Outcome (alive versus dead)
	Length of stay (intensive care unit)
	Recorded complications
	Nutrition care plan
	Time of initiation and goal feed achievement
	Termination reason

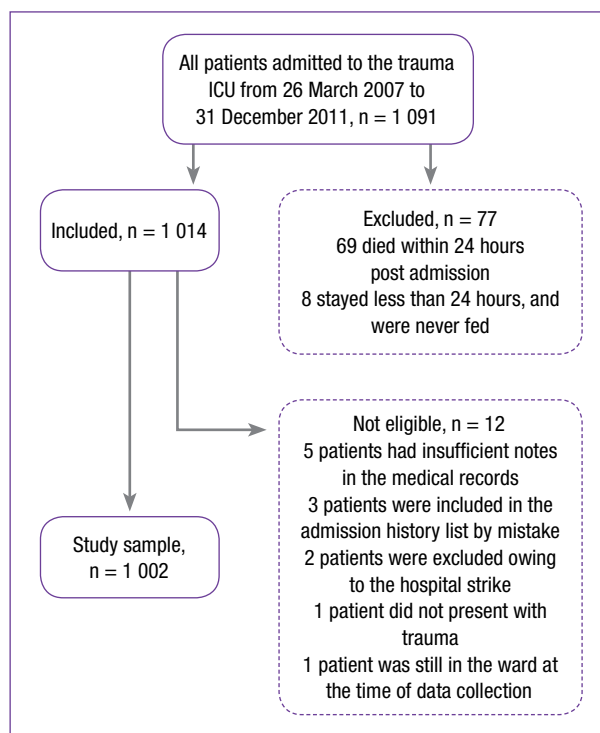
median, standard deviation (SD) and range were used for descriptive purposes, using Student’s t-test, the Fischer chi-square test, logistic regression and the omnibus test of model coefficients. A p-value < 0.05 was considered to be significant for all statistical analyses.

Times were recorded for every 24 hours of stay within one hour of accuracy, starting from the time of admission. The cause of the discontinuation was recorded for every termination of feeding that exceeded one hour. The day of initiation and the duration of support was recorded if total PN was used. Complications were noted in terms of sepsis or pneumonia, including the cause and focus of the infection.

Results

Of the 1 091 consecutive patients treated from 26 March 2007 to 31 December 2011, 1 014 patients were included in the study. Of these patients, 12 were ineligible (Figure 1). The final study sample comprised 1 002 patients. Of these patients, the largest cohort was involved in a motor vehicle collision (61.0%). The mechanisms of injury are shown in Figure 2. Five patients (“other”) had injuries that were not classified by the other groups, namely a shark attack, a snake bite, being gored by cattle and nearly drowning. One patient had a combination of gunshot and stab injuries. The mean age of the patients was 29.1 years, and the mean length of stay 13.4 days (Table III). There were 746 (74.4%) men, in keeping with the normal distribution of trauma patients which shows a male predominance.

Early enteral feeding was possible in 639 patients (63.7%). Overall, 633 patients (63.1%) reached the early enteral feeding goal rate. Eighty-one patients (8.0%) were given PN at some point during their stay either owing to non-tolerance of 50% of the enteral goal by day 6, or owing to enterocutaneous high-output fistula. There was no statistically significant difference in the ISS between the groups



ICU: intensive care unit

Figure 1: The selection of patients presented in a consort diagram

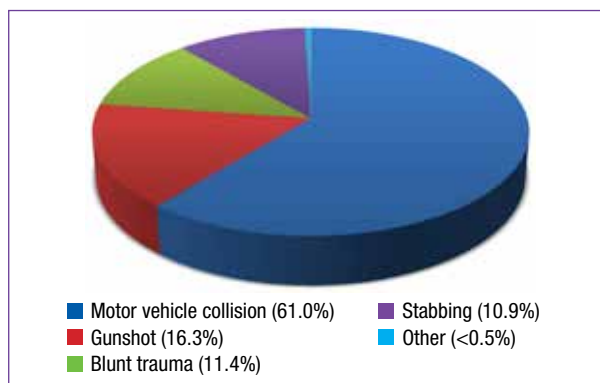


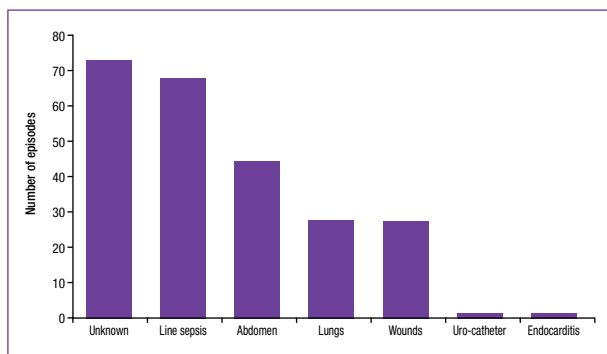
Figure 2: Mechanisms of injuries in the study population

who required PN (alone or before tolerating 50% of the enteral goal) and the group who did not receive any PN. However, there was a significant difference in the AIS for the abdomen. The group who did not receive PN had a median abdominal AIS of 1, while the group who was given PN had a median abdominal AIS of 3 (p-value < 0.001). This indicates more severe abdominal injuries that precluded or delayed enteral feeding. There was a difference in the mean ICU length of stay of 12.1 days (SD 12.0) for the group who

Table III: Characteristics of the study population*

Variable	Mean \pm SD (median)	Range
Age	29.1 \pm 15.1 (27)	0.5/90.0
ISS	22.3 \pm 11.9 (20)	1.0/66.0
AIS (abdomen)	1.3 \pm 3.6 (3)	1.0/5.0
Length of stay	13.4 \pm 13.7 (9)	1.0/110.0

AIS: Abbreviated Injury Score, ISS: Injury Severity Score, SD: standard deviation
 * Male: 746 (74.4%), female: 256 (25.6%)

**Figure 3:** Septic foci in the study population

never received PN, and 27.4 days (SD 21.5) for those requiring PN at some point (p -value < 0.001).

On reviewing the complications, 346 (34.5%) experienced either sepsis or pneumonia episodes during their course of stay at the hospital. Two hundred and eight (20.7%) patients had at least one episode of sepsis, with up to four episodes of sepsis. Each episode of sepsis was counted as one case. Therefore, there were 244 confirmed cases of sepsis in total. The distribution of the septic foci is shown in Figure 3.

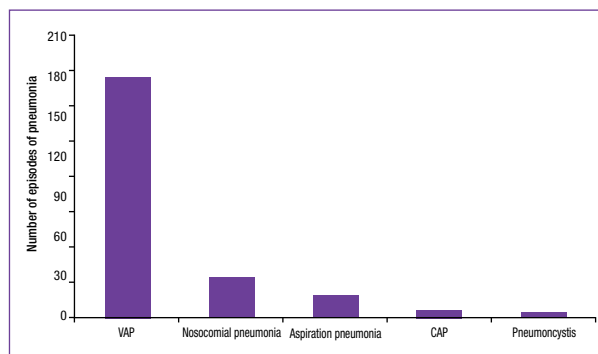
Three nutritional parameters increased the risk of developing sepsis: the use of PN during some point of the patients' stay, irrespective of the duration of PN; patients achieving their feeding goal late, and patients having a late EN start. The use of PN is an integral risk factor, which increases the hazard ratio for the development of sepsis by 9.11 (Table IV). The results were adjusted for the plausible confounding factors, namely a high ISS, AIS (abdomen) and age.

The omnibus test of mode coefficients was used to test the predictive ability of the different variables in relation to the development of sepsis. The duration of PN was shown to be the most heavily weighted variable concerning the development of sepsis. The risk of developing sepsis increased 7.38 times [p -value < 0.001, 95% confidence interval (CI): 4.46-12.20] for every day of PN. Mechanical ventilation was the second most important predictor of the development of sepsis. The sepsis risk increased 10.29 times for every ventilation day (p -value < 0.001, 95% CI: 4.12-25.70). The trauma score on arrival was the third strongest predictor of the development of sepsis. Each additional ISS point increased the sepsis risk by 1.9% (p -value < 0.05, 95% CI: 1.00-1.03). This may not appear to be significant, but bearing in mind that the ISS is a scale from 1-75, there is a substantially increased risk of sepsis for a patient with a higher ISS than that for a patient with a low ISS.

Table IV: Risk factors for the development of sepsis, connected to nutrition

Nutrition details	Hazard ratio	Statistical significance (p-value)
TPN	9.11	< 0.001
Late-feeding enteral nutrition goal	2.67	< 0.001
Late enteral nutrition start	2.41	< 0.001

EN: enteral nutrition, TPN: total parenteral nutrition



CAP: community-acquired pneumonia, VAP: ventilator-associated pneumonia

Figure 4: Types of pneumonia in the study population

Two hundred and thirteen patients (21.2%) developed pneumonia during the course of their stay. Some patients had repeated pneumonia. These cases were counted as one episode, resulting in 239 episodes in 213 patients. The different types of pneumonia, and the incidence thereof is outlined in Figure 4. The vast majority were VAP. Statistically significant results were noted with regard to enteral and parenteral feeding and pneumonia. Patients who reached their individual feeding goal late had a 17.9% increased risk of developing pneumonia, compared to those who had early nutritional goal achievement (p -value < 0.001). The results were adjusted using logistic regression for the number of days with mechanical ventilation, the AIS for chest injury, a high ISS and age. A significant relationship was not noted between the use of PN and pneumonia, nor between the timing of the feeding initiation and pneumonia. Each day of the mechanical ventilation increased the risk of developing pneumonia by 11% (p -value < 0.001). The result was adjusted for AIS for chest injury and a high ISS, independent of feeding, using logistic regression.

Of the 63.7% of patients who received early enteral nutrition, intolerance occurred less in the group with an early EN start than it did in the group with late initiation of feeding, i.e. 16.7% versus 32.8%, respectively.

The median ISS was 20 (range 1-66). The majority of patients (76.8%) had a high ISS score ranging from 15-66. None of the patients with a score higher than 66 survived the first 24 hours after admission to the ICU. A comparison was made of the patients with a high ISS, i.e. above 15, with the group of patients with a low ISS, i.e. 1-14, for the purposes of a subgroup analysis. There were a number of statistically significant differences between the two groups (Table V).

Table V: Differences between the groups with a high and low injury severity score

Characteristics	A high ISS (%)	A low ISS (%)	Statistical significance (p-value)
Mortality rate	19.6	5.6	< 0.001
Early enteral nutrition initiation	60.6	74.1	< 0.005
Reaching the enteral nutrition goal early	58.5	78.4	< 0.001
Pneumonia	24.6	9.9	< 0.001
Sepsis	23.2	12.5	< 0.001

ISS: Injury Severity Score

Table VI: The differences between the patients who were discharged and those who died in the intensive care unit

ISS	Discharged	Died	Statistical significance (p-value)
	21.2 (SD 11.5)	28.2 (SD 12.2)	
Length of stay (days)	13.9 (SD 13.8)	10.9 (SD 12.4)	< 0.05
Early enteral nutrition start	69.4%	34.7%	< 0.001
Use of TPN	6.6%	14.6%	< 0.001
Sepsis	15.5%	47.5%	< 0.001
Pneumonia	20.0%	27.4%	< 0.05

ISS: Injury Severity Score, SD: standard deviation, TPN: total parenteral nutrition

There was a significantly higher mortality rate in the group with a high ISS, who also experienced a lower frequency of early enteral nutrition initiation, significantly later attainment of the goal rate and an increased number of complications. One hundred and sixty-four patients (16.3%) died in the ICU, and 838 (83.6%) were discharged. The outcome of the patients (dead versus discharged) was used to divide the patients into two groups in order to perform further subgroup analyses (Table VI). Patients who were discharged were more likely to have received early EN, to have less need for PN, and to have experienced less sepsis and pneumonia, compared to those who died. A statistically significant difference was not observed between the two groups with regard to attaining the enteral feeding goal rate.

The omnibus test of mode coefficients was used to test the different variables to predict outcomes. ISS was shown to be the most important predictor of outcome. The risk of dying increased by 5.1% per each point of the ISS (p-value < 0.001, 95% CI: 1.03-1.06). The risk of dying increased in patients aged 27 years and older by 98.5% compared to that in the younger patients (p-value < 0.001, 95% CI: 1.39-2.83).

Discussion

The most remarkable results of this study were that a hazard ratio of 9.11 for the development of sepsis was shown in patients in need of PN at some point during their length of stay at the trauma

unit, compared to the group of patients in whom enteral feeding met their nutritional requirements. Furthermore, late attainment of the enteral feeding goal was associated with an increased hazard ratio of 2.67 for the development of sepsis, compared to that in patients who met their feeding goal early. There was an increased sepsis rate, i.e. a hazard ratio of 2.41, in patients in whom enteral feeding was initiated later, compared to that in patients in whom it was commenced early. The late achievement of the goal rate was shown to increase the incidence of pneumonia by 17.9%. PN was also shown to be the strongest predictor of the development of sepsis, irrespective of the presence of abdominal injury, but not for pneumonia, whereas mechanical ventilation was associated with the development of pneumonia.

This study confirms the findings of previous studies, in which it has been suggested that a reduced sepsis rate applies to patients whose nutrition can be supplied via the enteral route, as compared to a patient population in need of PN.⁸ Many authors advocate the use of enteral nutrition rather than PN, and both the ESPEN and ASPEN guidelines support this view. However, the underlying condition of the patient has to be considered, and not all patient populations are comparable.^{6,7,24}

However, a significant difference in septic complications between EN and PN was not found in a prospective randomised trial performed by Woodcock et al in the UK at a large district general hospital.²⁴ Overall catheter-related sepsis in that study was 11%, compared to an incidence of 6.78% in the present study. This difference may relate to the local use of SMOF-based PN and standard enteral feeds, with good protocol-based glucose control, although not all cases of suspected line sepsis were proven on microbiology culture.

Only a small number of trauma patients were included in the Woodcock et al study.²⁴ It has been shown that trauma patients are a specific group that differs from other patients in terms of age, and physiological and nutritional status, and who are not always comparable with other groups of critically ill patients.^{13,15,24}

The successful initiation of early EN may be a prognostic factor for a decreased risk of sepsis. In the present study, a hazard ratio of 2.41 was given for the development of sepsis with a late start. This is supported by the literature which demonstrates a threefold decrease in sepsis in this regard.⁸ The literature is sparse with regard to the effect of early versus late feeding initiation as a predictor of sepsis, and the present study suggests that this is important.

Regarding the risk of developing pneumonia in relation to feeding, it has been shown that an early EN start is associated with a decreased risk of pneumonia.¹³ Kompan et al performed a randomised study on trauma patients which showed that patients in whom EN was initiated within 24 hours had a lower incidence of pneumonia than those in whom EN was initiated after 24 hours.³² Statistical significance was not shown in the present study with respect to early EN initiation. However, late-goal achievement was shown to correlate with an increased incidence of pneumonia. The present study used EN commenced within the first 48 hours, while Kompan et al,³² as well

as Doig et al,¹³ shows benefit if EN feeding was commenced within 24 hours. However, most of the study patients were commenced on feeds on day 1, rather than day 2.

There may have been under-reporting regarding the difference in the incidence of line sepsis in the present study compared to that reported in the Woodcock et al study,²⁴ since 29.9% of the sepsis episodes were from unknown foci and some may have been line sepsis, but the associated peripheral blood culture was not confirmatory. A slightly higher sepsis rate in late initiation has been reported in earlier studies, possibly owing to the lack of a uniform definition of early EN feed initiation. For example, Genton, Romand and Pichard defined the early initiation of EN as occurring within 72 hours, while the definition was initiation within 48 hours in the present study.⁸ Doig et al suggest that initiation should be within 24 hours for a survival benefit in the trauma subgroup, which may explain the disparate findings in this study, albeit with a retrospective patient cohort.¹³

The need for PN in the present study was defined as the strongest predictor of the development of sepsis, but there is an interrelation between sepsis, PN and inotropic support. If an enterally fed patient with sepsis progresses to septic shock, with the need for inotropic support, enteral feeding may be contraindicated above a certain level of inotropic support owing to the potential complication of gut necrosis, as mentioned in the introduction.^{18,19,27,33} This level was recently determined in a pragmatic study as being anything over 12.5 µg/minute of the noradrenaline equivalent. We used a level of 13.4 µg/minute of adrenalin locally as the safe cut-off where feeding enterally was either held, or commenced (once weaning the inotrope) during inotrope administration.²⁷

Therefore, it is relevant to define what came first; i.e. sepsis leading to the use of high-dose inotropes and PN, or whether PN was a predisposing factor to the development of sepsis. There were 70 episodes of sepsis in the present study population in the patients who received PN at some point during their course of stay in the ICU. The inotropic support preceded the use of PN in only 11 of these cases. There were other reasons for the use of PN in the remaining cases. Most commonly, these were intolerance or a gastrointestinal fistula. The plausible confounding factor of sepsis leading to the use of PN, rather than PN leading to the development of sepsis, could be considered, but does not explain the strong relationship between PN and sepsis. There was no association between mechanical ventilation and the development of sepsis. However, it was associated with a risk of pneumonia, while PN did not increase the pneumonia risk.

Additionally, patients who receive PN may be prone to sepsis owing to severity of the injury, which necessitates a longer ICU length of stay and increases the risk of infection. Using logistic regression with adjustment for ISS, the group who receives PN continues to have a hazard ratio of 9.11 for sepsis, compared to patients who are fed enterally.

Limitations

This was a retrospective, single-centre study, and only included data from the trauma intensive care unit. While patients were only stabilised at a referring hospital briefly before being referred to Inkosi Albert Luthuli Central Hospital, the final outcome and length of hospital stay after the ICU period (after a step down to the referring base hospital) is unknown. ISS may not reflect the full clinical picture as it is an anatomical scoring system. The use of physiological scoring could have improved the outcome prediction. However, this would not have distinguished between the patients who were initially stabilised at another hospital, and those who arrived directly from the scene of their injury, which has been previously studied in this population.¹

The results of the present study can be considered relevant to critically ill trauma patients, provided similar feeding protocols are used and similar intensive care management is practised. Further generalisation to other populations should be made with caution. Trauma patient outcomes appears to differ from those of other critically ill patients.

Conclusion

This study confirms former findings that PN in critically ill trauma patients is a risk factor for the development of sepsis. It reinforces the concept that early successful EN and early EN feeding goal attainment is beneficial to the patient, and associated with less complications, compared to late EN initiation and late achievement of this goal.

Declaration

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