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CONTINUATION OF ENTERAL NUTRITION IN THE HAEMODYNAMICALLY UNSTABLE BURNS PATIENT ON HIGH DOSE INTRAVENOUS VASOPRESSOR SUPPORT: A FIVE YEAR RETROSPECTIVE STUDY

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DEPARTMENT OF PLASTIC AND RECONSTRUCTIVE SURGERY

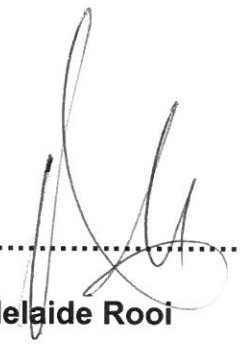
SUPERVISORS

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DECLARATION

I, Adelaide Rooi, am submitting this research dissertation for the degree of Masters of Medicine at the University of the Witwatersrand, Johannesburg.

I declare that this research report has not been submitted for examination to this or any other university before.



.....

Adelaide Rooi

08 **Day of** November **2017**

DEDICATION AND ACKNOWLEDGEMENTS

- This work is dedicated to my mother, Lilian Rooi, for her unconditional love and her unfailing faith in me. Her prayers, guidance and support kept me motivated and grounded in difficult times. It is also written in honour and memory of my late father, Johannes Rooi, who I miss dearly every single day.
- I would like to thank all my supervisors: Professors Muganza and Ndobe and Dr. Nel. Their patience, supervision and support made this project possible.
- I never expected that a question I asked Prof. Muganza on a teaching ward round would be the foundation for my MMed research. For this reason I want to express my gratitude to him, and also thank him for helping me to do research at the Bara Burns Unit.
- A very special thanks to the HOD of Wits Department of Plastic and Reconstructive Surgery, Prof. Elias Ndobe. His support and guidance made this research possible. I can only pray to be a great surgeon like him.
- This project took a very long time and all my supervisors, especially Dr. Marietha Nel, never gave up on me. Words cannot explain how grateful I am for that.
- I would also like to express my gratitude to Dr. Michel Muteba, a biostatistician in the postgraduate research office, who helped greatly with the statistical analysis of the results.

ABSTRACT

Introduction

Early enteral nutrition and the continuation of enteral nutrition are critical factors in burn patients, who typically have higher nutritional needs due to their post-injury hypercatabolic state and their additional need for nutrients to aid in the healing of wounds and skin grafts. In the critically ill patient, enteral nutrition is the preferred mode of administration. However, disagreement exists regarding the simultaneous use of enteral nutrition and intravenous vasopressor agents in the haemodynamically unstable patient- which is the current protocol at the Chris Hani Baragwanath Academic Hospital. Nonetheless, the general consensus is to withhold enteral nutrition whilst the patient is receiving vasoactive substances, because of the risk of gut hypoperfusion, which increases the chances of tissue hypoxia and intestinal ischaemia. Thus, the aim of our retrospective study was to determine if it is safe, and whether patients would be negatively affected by having enteral feeds administered to them while receiving high doses of adrenalin. The objectives for this study were: 1) to determine the safety, and 2) the tolerability of enteral nutrition in these patients.

Methodology

A retrospective medical record review was conducted at the Adult Burns Unit of the Chris Hani Baragwanath Academic Hospital, which included all adult burn intensive care unit patients receiving concomitant enteral nutrition and vasopressor support for at least two hours or more. The patient register was used to identify the patients admitted to the intensive care unit during 01/09/2010 to 31/12/2015. The number of patients during this period totalled 1109, of which 475 had been admitted to the intensive care unit of the Chris Hani Baragwanath

Academic Hospital. From this group, 44 met the inclusion criteria for participation in this retrospective study.

Results

Of the 44 participants, 25% (11/44) experienced gastrointestinal tract upset in the form of moderately high gastric aspirates (> 200 ml/6 hours) on high doses of adrenalin. Only 9% (4/44) experienced vomiting, while 20% (9 patients) experienced diarrhoea. In only 7% (3/44) were the enteral feeds stopped (one patient experienced simultaneous vomiting and diarrhoea, another one had high gastric aspirates > 500 ml/6 hours, and one had high gastric aspirates together with diarrhoea). Only 44 patients met the inclusion criteria Total Body Surface Area > 20%, and/or inhalation injury, mechanical ventilation) in addition to receiving concomitant enteral nutrition and intravenous vasopressor support (i.e. adrenalin). Moreover, in the sample of 44 patients, not one patient experienced clinical or radiological signs of bowel ischaemia or necrosis.

Conclusion

Based on this local retrospective review study conducted at the Adult Burns Unit of the Chris Hani Baragwanath Academic Hospital, it was found that in the majority of the haemodynamically unstable burns patients in the intensive care unit who received vasopressor support (i.e. high doses of adrenalin), enteral nutrition was well tolerated. Even in the patients who experienced intolerance, there were no complications such as ischaemia or bowel necrosis. As such it would appear that the administration of vasopressors in haemodynamically compromised burn patients is not a contraindication in carefully monitored early and ongoing enteral nutrition. In this study, the simultaneous use of enteral nutrition and vasoactive support did not place the patients at increased risk for ischaemia or non-occlusive

bowel necrosis. However, larger samples would need to be investigated to enable generalisation of the findings to the larger/general population of critically ill burns patients.

LIST OF ABBREVIATIONS

ABU	Adult Burns Unit
A.S.P.E.N.	American Society for Parenteral and Enteral Nutrition
CHBAH	Chris Hani Baragwanath Academic Hospital
EEN	Early Enteral Nutrition
EN	Enteral Nutrition
GIT	Gastrointestinal Tract
NOBN	Non-Occlusive Bowel Necrosis
PN	Parenteral Nutrition
SCCM	Society of Critical Care Medicine
TBSA	Total Body Surface Area
WITS	University of the Witwatersrand

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TITLE

CONTINUATION OF ENTERAL NUTRITION IN THE HAEMODYNAMICALLY UNSTABLE BURNS PATIENT ON HIGH DOSE INTRAVENOUS VASOPRESSOR SUPPORT: A FIVE YEAR RETROSPECTIVE STUDY

CHAPTER 1

1. INTRODUCTION

Critically ill burn patients in Intensive Care Units (ICU) have unique requirements, in that their need for nutrients is higher than in patients who have only experienced trauma or shock or surgery. This increased need for nutrients is as a result of the critically ill patients' post-injury hypercatabolic and hypermetabolic states and their need for nutrients to assist in the healing of burn wounds and skin grafts. However, administering nutrients via enteral feeds places more pressure on the Gastrointestinal Tract (GIT) system, in that the absorption of the nutrients in the feeds increases the oxygen requirement of the gut (GIT) mucosa, and if this increased demand for oxygen is not met, bowel necrosis may occur (Turza, Krenitsky and Sawyer, 2009). Therefore, although the benefits of early and ongoing Enteral Nutrition (EN) in critically ill patients are well documented, there are certain risks and complications associated with enteral feeding (Yang, Wu, Yu, and Li, 2014). An additional challenge exists in haemodynamically unstable burns patients who are given intravenous vasopressor support (e.g. adrenalin) to increase their cardiac output and blood pressure. In these cases, the vasoactive substance can decrease the splanchnic blood supply to the gastrointestinal organs (Lasierra, Pérez-Vela, and González, 2015), resulting in hypoperfusion, thereby increasing the chances of tissue hypoxia and intestinal ischaemia (Wells, 2012).

Although research has confirmed the existence of some cases of Non-Occlusive Bowel Necrosis (NOBN) in Early Enteral Nutrition (EEN), the causal relationship between EEN and NOBN (Non-Occlusive Bowel Necrosis) has not been verified, contributing to the lack of consensus regarding the concomitant use of vasopressors in haemodynamically compromised patients (Yang *et al.,* 2014). This places clinicians in a predicament as to when to start EN in the hemodynamically compromised and unstable patient receiving vasopressor support (Yang *et al.,* 2014), and especially the hemodynamically compromised/unstable burns patient.

In addition to the above challenges, intolerance is a further risk associated with EN. According to Wells (2012), intolerance to EN is a possibility in patients who are seriously ill, and thus the introduction of EN in these patients needs to be wisely approached and cautiously monitored. In spite of these concerns, Wells is of the opinion that providing EN together with low dose vasopressors, while carefully monitoring the patient for feeding intolerance and changes in haemodynamic status, should present "very little risk for bowel necrosis" (Wells, 2012).

In the light hereof, this study investigated the safety and tolerability of EEN and ongoing EN in haemodynamically compromised burn patients receiving simultaneous vasopressor support. This topic is of particular interest for the Chris Hani Baragwanath Academic Hospital (CHBAH) burns patients admitted to the ICU, as the administration of relatively high doses of vasopressor substances (e.g. adrenalin) form part of their treatment plan at some point during their ICU stay.

CHAPTER 2

2. LITERATURE REVIEW

2.1 The splanchnic circulation and the impact of shock on gut integrity

The splanchnic circulation involves circulation to the visceral organs in the abdominal cavity (stomach, intestines, colon, liver, pancreas, spleen) and originates in the celiac trunk and the mesenteric artery (both inferior and superior) (Takala, 1997). A strong relationship exists between splanchnic blood flow and cardiac output, evidenced by the fact that under normal conditions, about 25% of the cardiac output is present in the splanchnic circulation (Takala, 1997). However, in the presence of shock, the blood flow to these "splanchnic" organs is redistributed in order to ensure that blood reaches the brain and heart (Takala, 1997). The consequence thereof is vasoconstriction in the splanchnic circulatory system with the resultant hypoperfusion of the gastrointestinal organs and peripheral tissues supplied by the splanchnic network (Lasierra *et al.,* 2015). This splanchnic hypoperfusion alters the circulation in the gut. The resulting intestinal hypoperfusion reduces the oxygen supply to the highly vascularized intestinal villa, contributing to tissue hypoxia and possible intestinal ischaemia (Wells, 2012). At the same time, the decreased circulation to the gut reduces the oxygen supply to gut mucosa, thereby affecting the mucosal barrier which acts as a mechanical barrier to pathogens (Turza *et al.,* 2009). Thus splanchnic hypoperfusion places the seriously ill/critically ill patient at risk not only for intestinal ischaemia and bowel perforation (Turza *et al.,* 2009), but also for bacterial translocation and multiple organ dysfunction (Khalid, Doshi, and DiGiovine, 2010).

In the light of these facts, the critically ill patient is in a vulnerable, haemodynamic condition and mostly requires haemodynamic support. However, in this vulnerable

state, giving the patient vasopressors to increase their cardiac output and blood pressure can exacerbate the gut perfusion problem. The vasoconstrictive action of some vasopressors leaves the gut mucosa under-perfused and susceptible to mucosal inflammation and injury, and in so doing, predisposes the patient to bowel necrosis (Turza *et al.,* 2009). As such, the critically ill patient, who is haemodynamically unstable and on vasopressors, is susceptible to a further decrease in splanchnic perfusion and the associated possibility of bowel necrosis (Cresci, 2015). The issue of bowel necrosis and vasopressors will be discussed (Section 2.8).

An additional challenge exists in the case of critically ill, haemodynamically compromised and unstable patients. These patients need nutrients to maintain the strength and integrity of the gut and also to facilitate the healing process (grafts and donor sites) especially in the case of burn patients who have higher nutritional needs due to the hypercatabolic (increased breakdown of protein) and hypermetabolic state following the injury (Allen, 2012). For patients who are critically ill, enteral feeding and having their nutritional needs met is vital because "malnutrition has been linked to increased morbidity and mortality " as well as increased duration in ICU (Hegazi & Wischmeyer, 2011; Khalid *et al.,* 2010). Thus it is imperative that the critically ill patient receives feeding. However, a decision needs to be made regarding the route of administration of the feeding, whether parenteral or enteral.

Parenteral Nutrition (PN) used to be the primary choice, but due to its complications it has been displaced as the favoured route of administration. PN is associated with immunosuppression, sepsis and/or septic shock, longer stays in ICU and complications due to infections (Simpson & Doig, 2005; Khalid *et al.,*

2010). Moreover, PN has an adverse effect on the intestinal mucosal barrier, reducing the small bowel's mucosal thickness, and thereby reducing the mucosal mechanical barrier against pathogens (Cresci, 2015). PN is also linked to increased gut permeability and this, together with the inflammatory changes in the intestinal mucosa and the reduction in the mucosal barrier, supposedly predisposes the patient to systemic infections (Takala, 1997; Cresci, 2015). Additionally, PN increases the intestinal pro-inflammatory mucosal cytokines, resulting in inflammation and injury to the intestinal mucosa, thereby contributing to hypoxia in the intestinal villi, the latter which predisposes the patient to bowel necrosis (Takala, 1997 and Cresci, 2015). According to Turza *et al.,* (2009) PN is also associated with increased metabolic stress response compared to EN.

With these reported complications associated with PN, EN appears to be the obvious choice, especially due its favourable effects on the gut. The favourable effects include the maintenance of gut integrity (including its flora), the prevention of mucosal damage, and the protection of the gut's mucosal mechanical barrier (Turza *et al.,* 2009). Other recorded benefits of EN include enhanced immuno-competence (Khalid *et al.*, 2010), improved nitrogen balance and reduction in the metabolic response to stress (Wells, 2012) as well as increased visceral protein synthesis and enhanced visceral blood flow (Takala, 1997 and Cresci, 2015). Enteral feeding therefore protects against under-perfusion by enhancing blood flow to the internal organs as well as to the intestinal mucosa. This is important because a reduction in this blood flow (e.g. in trauma, shock and surgery) results in bacterial overgrowth and has been linked to increased "microbial translocation" (Kazamias, Kotzampassi, Koufogiannis, and Eleftheriadis, 1998). Thus, EN is also associated with a reduction in bacterial translocation (Khalid *et al.*, 2010).

2.2 Benefits of enteral nutrition in haemodynamically unstable burns patients

According to Revelly, Tappy and Berger (2001) and also Lavrentieva, Kontakiotis, and Bitzani (2014), in critically ill and haemodynamically compromised postoperative patients, enteral feeding was associated with an increase in the patients' "cardiac index" as well as the enhanced splanchnic blood flow (to the viscera and mucosa). EN was also linked to the increase in absorption and utilisation of nutrients, without any having any negative effect on the heart, blood pressure and blood volume. Moreover, EN has shown to reduce deaths caused by post-surgery septicaemia (Zaloga, Roberts and Marik, 2003).

Additionally, in patients who have experienced trauma/shock, EN not only provides the necessary nutrients, but also supports the gut in functioning effectively i.e. in maintaining gut integrity (Scaife, Saffle, and Morris, 1999; Wasiak, Cleland & Jeffery, 2006). Besides, EN reinstates "splanchnic perfusion and oxygenation" in the hemodynamically compromised patient as well as in those patients who are administered vasoactive drugs/substances intravenously (Zaloga *et al.,* 2003; Wasiak *et al.,* 2006). With regard to EN, Revelly *et al.,* (2001) found an improvement in the haemodynamic condition of postoperative patients having undergone heart surgery and who were receiving vasopressor support.

Zaloga *et al.,* (2003) found that enteral feeding improves intestinal motility in critically ill, postoperative burn patients, the latter who had improved gut blood flow and gut motility. In fact it was found that those patients who received EN had decreased infections compared to the non-fed group (Zaloga *et al.,* 2003). In addition, EN in burn patients within the first day of injury showed less absorption of toxins from the gut when compared to those who were fed after two days (Zaloga

et al., 2003). This is understood to be due to the fact that EN stimulates peristalsis and thus biliary secretion and helps counter gut dysmotility, thereby preventing bacterial overgrowth (Takala, 1997; Cresci, 2015). Finally, intestinal blockages and tissue death/necrosis, consequential to early and intense feeding, is an uncommon complication (Scaife *et al.,* 1999).

Based on the aforementioned, EN appears to be the preferred feeding method in critically ill and also in burn patients. However, there are also risks involved with EN which will be discussed (Section 2.4) after the issue of early enteral nutrition has been addressed.

2.3 Benefits of early enteral nutrition

The main difference in the literature between early and late enteral feeding pertains to the clinical condition and haemodynamic stability of the patient, and in some instances, the efficiency of the gut's functioning (Khalid *et al.,* 2010). Both Khalid *et al.,* (2010) and (Wells, 2012) found that in critically ill patients, EEN reduced spread of infection, as well as duration in hospital and also deaths In support hereof, Zaloga *et al.,* (2003), in their meta-analytic review of EEN in critically ill patients, found that EEN benefitted these patients. Furthermore, Zaloga *et al.,* (2003) specified that EEN maintained gut and mucosal integrity, improved gastrointestinal blood flow, and decreased gut permeability. Moreover, they noted in their review of seriously patients, that EEN was found to be helpful and linked to septicaemia. In addition, their review found that the nitrogen balance also improved in EN nutrition patients and decreased permeability and less severe organ failure (Zaloga *et al.,* 2003). What is more, in their extensive meta-analytic review, Zaloga *et al.,* (2003) found that critically ill patients and burns patients

received EEN well and also showed a reduction in infection quicker. Other resaerchers in support of these findings include Gottschlich, Jenkins, Mayes, Khoury, Kagan & Warden (2002) and Lee, Jang, Kim, Jung & Lee (2014) as well as Wasiak, Cleland & Jeffery (2006).

According to Khalid *et al.,* (2010) EEN can minimize the effects of oxidative stress after surgery and can decrease post-operative mortality in patients who have had gastrointestinal surgery. In fact, in the patients receiving EEN deaths in ICU were lower than those who were fed later. Similarly, Khalid *et al.,* (2010) found that the benefits of EEN were more evident in those patients who were more haemodynamically unstable and who were treated with multiple vasopressors.

In spite of the recorded advantages of EEN in critically ill patients (Gottschlich *et al.,* 2002; Lee *et al.,* 2014; Wasiak *et al.,* 2006), there is still a risk involved in EEN, which is linked to some complications (Yang *et al.,* 2014). For example, there has been a link with NOBN in patients on vasopressos who are given EEN simultaneously (Yang *et al.,* 2014). Although the causal relationship between EEN and NOBN has not been verified, controversy surrounding EEN and the concomitant use of vasopressors in the haemodynamically unstable patient still persists (Yang *et al.,* 2014). This places clinicians in a difficult position as to how soon they should administer EN in the patient who is receiving vasopressor support and is hemodynamically compromised (Yang *et al.,* 2014). In an attempt to resolve this dilemma, Yang *et al.,* (2014) reviewed the animal and clinical data pertaining to the concurrent administration of EEN and vasoactive agents in the presence of hemodynamic instability and found that in the presence of vasopressors, EEN is able to reinstate bloodflow to the splanchnic organs, thereby

facilitating perfusion/oxygenation in patients who have reduced blood pressure and blood volume (Yang *et al.,* 2014). Moreover, they found that when patients receiving EEN and vasopressor support are carefully observed there are no complications. With regard to non-occlusive bowel obstruction they reiterated the need for caution as it is a serious complication with a high mortality rate (Yang *et al.,* 2014). Moreover, with regard to the safety of EEN in the haemodynamically unstable patient on vasopressors, they emphasized the need for more randomized clinical trials, because existing studies pertain mostly to cardiac surgery, whereas traumatic and septic shock are more common in ICU (Yang *et al.,* 2014). Similarly, Gottschlich et al., (2002) and Wasiak et al., (2006) confirm the benefits of EEN in critically ill patients. .

2.4 Risks and complications associated with enteral nutrition

Since intolerance to EN is a possibility in critically ill patients, these patients needs to be carefully and closely monitored when administering EN (Wells, 2012). Besides intolerance, in patients being fed enterally, bowel necrosis could occur, especially when the route of administration is via the jejunum (Wells, 2012). Scaife *et al.,* (1999) upon hearing about a burn patient who had sustained a bowel obstruction and perforation after receiving EN, decided to review the complications associated with tube feedings. They found bowel obstruction and ischemic necrosis to be an uncommon complication after early and intensive enteral feeding (Scaife *et al.,* 1999).

Similarly, Lasierra *et al.,* (2015), who confirmed that intestinal ischemia is the most feared complication of EN in the hemodynamically unstable patient, found that when EN, when started in the first 2 to 3 days of admission to ICU, was not

associated with intestinal ischemia. Lasierra *et al.,* (2015), reiterated that intestinal ischemia is an "infrequently described complication" in patients having undergone heart surgery. However, they drew attention to the reports of non-occlusive bowel obstruction after the administration of EN, and in cases where post-pyloric feeding tubes were used together with rich nutritional formulas containing non-fermentable fibre (Lasierra *et al.,* 2015). Furthermore, Lasierra *et al.,* (2015) reiterated that in most of the NOBN cases, the EN was not given early and moreover, specific details pertaining to the hemodynamic condition of the patients at the start of EN, the mode of EN administration, and also the details pertaining to the daily monitoring of the clinical condition of the patients, were not provided. needless to say, Montejo (1999) reported GIT complications in critically ill patients receiving EN, and other authors have written on and reported EN intolerance in critically ill patients (Deane, Chapman, Fraser, Bryant, Burgstad, and Nguyen, 2007) and also in critically ill septic burn patients (Lavrentieva, Kontakiotis, and Bitzani, 2014).

Zaloga *et al.,* (2003) stated that the etiology of bowel necrosis (intestinal ischemia) in the presence of enteral feeding is not clear. Needless to say, they identified the following correlations between feeding and bowel necrosis: (i) the majority of patients had undergone surgery, and (ii) the cell/tissue death in the intestines took place post-laparotomy. With regard to the etiology bowel necrosis Turza *et al.,* (2009) offered the following explanation: the impact of EN on the GIT is paradoxical because the increased supply of nutrients increases splanchnic blood flow; however, the absorption of these nutrients also increases mucosal oxygen requirements, and this increased demand for oxygen if not met, can result in bowel necrosis.

In support of Turza *et al.,* (2009), Lasierra *et al.,* (2015) confirmed the explanation of the etiology of NOBN, stating that it arises as a consequence of increased oxygen requirements which are not met by the increase in splanchnic blood flow, resulting in the "alteration of the supply/demand ratio at intestinal mucosa level," thereby predisposing the patient to bowel necrosis. In agreement with Turza *et al.,* (2009) and also Lasierra *et al.,* (2015). In addition, Wells (2012) stated that vulnerability of the intestine to tissue death/necrosis is increased when patients, who receive vasopressors, have experienced shock/trauma, or have undergone surgery or are severly burnt. Moreover, Wells (2012) emphasized that when EN is administered via jejunal or naso-jejunal routes, the patients are vulnerable to tissue death/necrosis in the intestines. These literature findings, justified further research on EN in burn patients who are haemodynamically unstable and on vasopressors.

Interestingly, despite the inconsistent findings pertaining to the specific role of vasopressors on splanchnic circulation and gut perfusion/oxygenation, Wells (2012) is of the opinion that the danger of intestinal tissue death/necrosis can be reduced in most critically ill patients who receive EN while on vasopressors, if these patients are well managed and closely observed for EN intolerance and haemodynamic instability. In support hereof, Wells (2012) backed this opinion by reminding that there are only a small number of reported cases of bowel necrosis linked to the simultaneous use of EN and vasopressors in the haemodynamically unstable patient.

2.5 Protocol for enteral nutrition in haemodynamically unstable patients

Both A.S.P.E.N. (The American Society for Parenteral and Enteral Nutrition) and SCCM (Society of Critical Care Medicine) recommend withholding EN in patients who display haemodynamic instability/fluctuation, and who are receiving high doses of vasoactive substances. Furthermore, they recommend the the cautious use of EN in patients receiving low doses of vasoactive substances (Allen, 2012). Despite the suggested protocol/guidelines, many clinicians continue to feed patients who are hemodynamically unstable (Khalid *et al.,* 2010). In the light hereof, it is imperative to be aware of the dangers associated with EN in the seriously ill, hemodynamically unstable patients on vasopressors.

2.6 The risk of giving enteral nutrition in the presence of vasopressors

Sperry, Minei, Frankel, West, Harbrecht, Moore, Maier, and Nirula (2008) caution against the early use of vasopressors after injury, while Meier-Hellmann, Reinhart, Bredle, Specht, Spies, and Hannemann (1997) reiterate that epinephrine (adrenalin) impairs splanchnic perfusion in septic shock. Dünser, Mayr, Ulmer, Ritsch, Knotzer, Pajk, Luckner, Mutz, and Hasibeder (2001) outline the effects of vasopressin on patient hemodynamics (BP, etc.) in septic shock and Herget-Rosenthal, Saner, and Chawla (2008) recommend an approach to hemodynamic shock and the concomitant use of vasopressors. Turza *et al.,* (2009) cautions about starting EN while a patient is hemodynamically compromised and on vasopressors, as these vasoactive agents might cause reduced splanchnic perfusion and thus the possibility of bowel necrosis.

Although the mode of action of vasopressors is to increase blood pressure and blood volume and thus reduce hypotension, the different types of vasopressors act on different receptors and thus appear to have different actions on the splanchnic circulation and also on the gut. As such, sometimes the vasoactive substances raised blood pressure and increased cardiac output (thereby increasing splanchnic perfusion), and at other times vasopressors decrease splanchnic perfusion.

Furthermore, Turza *et al.,* (2009) stated that the shock itself alters splanchnic circulation, resulting in reduced perfusion to the gastro-intestinal areas, so that even if the vasopressor did restore the blood pressure and volume, this does not mean that the gut perfusion is simultaneously restored. Moreover, Turza *et al.,* (2009) reiterated that changes in gastrointestinal blood flow not only differ according to the vasoactive agent used, but also depend on the patient's clinical condition (i.e. sepsis, haemorrhagic/cardiogenic shock, burns). As such, both Turza *et al., (*2009) and Zaloga *et al.,* (2003) are of the opinion that it is difficult to predict what the effect of the vasoactive agent will be.

2.7 Vasoactive agents and splanchnic perfusion

Meier-Hellmann, Reinhart, Bredle, Specht, Spies and Hannemann (1997) confirm and explain how epinephrine/adrenalin impairs splanchnic perfusion in critically ill patients with septic shock. Within the gut, the small intestine is very vulnerable to changes in perfusion (especially in the villi), such that a reduction in splanchnic blood flow from shock or sepsis could contribute to mucosal ischemia (Wells, 2012). Administering vasopressors in this situation may amplify/exaggerate the changes in splanchnic perfusion/oxygenation which resulted from the

shock/sepsis, thereby increasing the chances of mucosal ischemia (De Backer, Creteur, Silva and Vincent, 2003).

Nonetheless, low-doses of catecholamines such as dopamine are thought to be relatively safe during enteral feeding (Wells, 2012). In support of this last statement, Mancl, and Muzevich (2013) also found in their review, that most patients receiving EN together with vasopressors did not present with problems. Indeed, they found that only three cases (0.9%) of bowel perforation/intestinal ischemia had occurred with EN in haemodynamically unstable patients in the presence of vasopressors.

With regard to vasoactive agents and septic shock, several authors have written on the topic. Some authors detail the effects of vasopressors (e.g. dopamine, norepinephrine, and epinephrine/adrenalin on the splanchnic circulation in septic shock (De Backer *et al.,* 2003). Other authors have written about vasopressor and inotropic support in septic shock (Beale, Hollenberg, Vincent, and Parrillo, 2004), while others such as Herget-Rosenthal et al., (2008) advocate a specific approach to managing hemodynamic shock while on vasopressors.

2.8 The risk of enteral nutrition in burn patients on vasopressors

Several researchers have found risks associated with EN in critically ill burn patients receiving vasopressor support (Beale, Hollenberg, Vincent, and Parrillo, 2004; De Backer *et al.,* 2003; Herget-Rosenthal, Saner and Chawla, 2008). Scaife *et al.,* (1999) in their retrospective review, found that bowel blockage had occurred when burn or trauma patients (who were haemodynamically unstable) received EN and vasopressors simultaneously. Likewise, Turza *et al.,* (2009) identified four

patients who presented with bowel/intestinal obstruction after receiving EN. Three of these four enterally fed patients had septic shock and were given vasopressors for hemodynamic fluctuations/instability. The three patients were nutritionally fed with a high-fibre formulation administered via naso-jejunal tubes. In these patients, intestinal necrosis took place within two weeks of injury/trauma. Wells (2012) attributed the cause of this intestinal necrosis to (i) the high-fibre content of the EN, while the patients, who were (ii) haemodynamically compromised and (ii) on vasopressors, and also (iv) experienced GIT dysmobility. Therefore, although intestinal necrosis has been found during EN (administered via jejunal tubes)- there is not enough documented evidence linking the use of EN in the presence of vasopressors (for hemodynamic instability) to the intestinal necrosis (Wells, 2012).

2.9 The protocol for critically ill patients on vasopressors

Wells (2012) reiterated that there is insufficient evidence to provide clinicians with evidence-based (valid and reliable) instructions as to how to deal with the challenge of providing EN in the patient who is hemodynamically compromised and on vasopressors. In light of the lack of evidence, Allen (2012) recommended cautionary use of EN with vasoactive substances, while Turza *et al.,* (2009), suggested that since haemodynamically unstable patients who need vasopressors will benefit from EN, each patient should be carefully evaluated and fed when the risk is not too great. Tsuneyoshi, Yamada, Kakihana, Nakamura, Nakano, and Boyle (2001) suggested low-dose vasopressin infusions in vasodilatory septic shock. Furthermore, Turza *et al.,* (2009) postulated that when a thorough, four-phase process is followed in order to select patients suitable for enteral nutrition, then EN is a relatively safe intervention in haemodynamically compromised patients on vasopressors. Against this backdrop, Turza *et al.,* (2009) provide the

clinician with "experience-guided recommendations" for introducing EN to the hemodynamically unstable patient on vasopressors. They restated that in the case of critically ill patients on vasopressors, the dangers and advantages of EN should be carefully evaluated in the context of each individual patient's clinical status and nutritional needs (Turza *et al.*, 2009).

Based on this literature review, it is apparent that additional research studies need to be conducted in order to investigate the effect of EN in critically ill patients (including burn patients) who are haemodynamically unstable and on vasopressors. Currently the debate pertaining to the safety and tolerability of EN in critically ill patients on vasopressors is currently ongoing, as no agreement/consensus has been reached, and not enough studies have been conducted. With this in mind, our present study was undertaken.

CHAPTER 3

3. MOTIVATION

3.1 Problem Statement

Inconsistent and inconclusive results have been found in studies involving the administration of EEN and the continuation of EN in critically ill patients on high doses of vasoactive substances, who demonstrate haemodynamically instability. The safety and tolerability of this mode of feeding in the haemodynamically compromised burns patient on high dose vasopressor support has not been verified, resulting in a lack of consensus among medical practitioners. An investigation of the literature confirmed the need for additional research to be carried out in order to conduct a comprehensive and in-depth evaluation of the consequences of administering EN in patients who are seriously ill, especially in burn patients, who are haemodynamically unstable and on vasopressors. Currently the lack of consensus between practictioners about a suitable protocal is driven by the ongoing debate about the safety and tolerability of EN in critically ill patients on vasopressors. In a three-year retrospective study, intestinal obstruction secondary to EN was identified in four burns patients, emphasising the need for further research to verify the safety and tolerability of EN in critically ill burns patients.

3.2 Aim

The main aim in doing this retrospective study was to determine if eternal feeding is safe in critically ill burn patients who are haemodynamically unstable and on high doses of vasopressors. In other words, our aim was to determine whether

patients would be negatively affected by having enteral feeds administered to them while receiving high doses of adrenalin.

Another aim was to determine whether EN should be continued in the haemodynamically unstable burns patient on high dose intravenous vasopressor support, which is the current protocol in the CHBAH, Adult Burns Unit (ABU). All patients admitted to the CHBAH Burns Unit receive enteral feeds on admission.

3.3. Study objectives

1) To assess the safety of EN in haemodynamically unstable burns patients requiring high dose intravenous vasopressor support.
2) To assess the tolerability of EN in haemodynamically unstable burns patients requiring high dose intravenous vasopressor support.

Importantly, for the purposes of this study high dose intravenous support is defined as administering adrenaline 0.5 ug/kg/minute (or more), because no clear consensus exists in the literature as to the exact definition.

3.4. Hypothesis

3.4.1 The null hypothesis

The null hypothesis states that there is no significant difference between the tolerant group and intolerant group of participants in the study sample. In other words, there is no significant different between the group of patients who tolerated EN and the group who did not tolerate EN.

CHAPTER 4

4. RESEARCH METHODOLOGY

4.1 Setting

This study took place at the ABU of the CHBAH.

4.2 Study design, study population and sampling procedure

4.2.1 The design: A retrospective review design

A retrospective records review was conducted at the ABU of the CHBAH, and included all adult burn ICU patients receiving concomitant EN and vasopressor support for at least two hours or more.

4.2.2 The study population

The patient register was used to identify the ICU patients admitted during the five year period from 01/09/2010 to 01/05/2016. The number of burns patients during this period totalled 1109, of which 42.8% (475 patients) were admitted to ICU.

4.2.3 The sample selection procedure

From the total number of patients admitted to ICU (i.e. critically ill patients), the sample was selected for the study, based on the following criteria:

a) Inclusion criteria:

- Adults 10 years and above (protocol at CHBAH)
- TBSA > 20% and or inhalation injury
- Concomitant EN and high dose intravenous vasopressor support (adrenaline 0.5ug/kg/min or more)

- Admission to the Burns Unit ICU
- Mechanical ventilation
- In-patients (burns ward) requiring ICU care

b) Exclusion criteria:

- Oral feeds
- Parenteral nutrition

The study sample thus consisted of patients who were admitted to the A.B.U. ICU, between 01/09/2010 to 01/05/2016, and who also received EN and simultaneous vasopressor support (i.e. high doses of adrenalin).

4.3 Data collection

4.3.1 Participant identification

Each participant's record selected for the study was assigned a study number. These participants met the inclusion criteria and received concomitant EN and vasopressor support. A total of 44 patients were selected for our study.

4.3.2 Data capturing

All the data collected was entered into the attached data sheet and finally into an Excel spreadsheet (Microsoft Corporation Version 2010).

4.3.3 Assessing tolerability

Feeding intolerances were noted and the tolerability of EN on patients receiving vasopressor support was assessed using the following feeding intolerance criteria, as per clinical guidelines used at the ABU at the CHBAH:

- High gastric aspirates 500ml or more per 6 hours
- Vomiting
- Diarrhoea
- Distended abdomen/acute abdomen

4.4 Data analysis

The data was analysed using Stata statistical software (StataCorp. 2015, Release 14 College Station, TX) and MS Excel software (Microsoft Office Version 2010). The mean and standard deviation were used to summarize variables with age and TBSA used as continuous variables. Frequencies and proportions were calculated to describe the distribution of patient's gender, age category, TBSA burns category, and feeding intolerance. Graphs (histogram, pie charts, frequency distribution) were used to provide a visual representation of the findings.

For the categorical variables, a two-sample test of proportions was used to assess the equality of proportions among the groups compared. The cut-off point was 0.05% (p value less than 0.05) with a 95% confidence interval. For numerical variables such as age and TBSA%, a Wilcoxon Sum Rank test was used to determine the p-values, when comparing the medians between the groups.

4.5 Sources of Error

4.5.1 Sources of Bias and Confounding Data

The findings in a sample of patients seen in a single unit were used, which may bias the outcomes of the study to the broader local experience.

4.5.2 Potential threats to validity

In order to achieve high internal validity a research design should control as many extraneous variables as possible and in so doing minimise the threats to validity, which include amongst other things, history, maturation, regression to the mean, test effect, experimental mortality and selection bias (Graziano and Rualin, 2000). As this was a retrospective study carried out using records, test effect is not relevant and neither is selection bias as only those patients (records) who met the criteria were included. Needless to say, the selection criteria could have been different, affecting the outcome and thus the validity of this study. With regard to the other potential threats to validity, there is no way of ascertaining whether history or maturation had an influence on the patiennts while they were in the burns unit. Experimental mortality or dropout could have influenced this study's validity, but the records were not examined with this in mind. Likewise regression to the mean was not investigated when the statistical analysis was conducted.

4.6 Ethics

Even though no direct research was carried out on patients (only their hospital records were accessed) – the privacy of the participants was still respected. Although their names and hospital file numbers were entered onto the datasheet,

only the research candidate and supervisors had access to this information. In this way, the identification of the participants was protected. As such, the findings were treated ethically and with confidentiality. It was however, not possible or practical to obtain permission/consent from the patients whose records were used in this study. Nonetheless, no participant was negatively affected by having his or her hospital records form part of this study. Finally, ethical approval for conducting this research was obtained from the Human Research Ethics Committee of the University of Witwatersrand (see Appendix). Furthermore, medical approval was obtained from the CEO of CHBAH, in order to access the relevant burn patients' hospital records (see Appendix C).

CHAPTER 5

5. RESULTS

The number of patients admitted to the ABU over an approximately five year period, totalled 1109 of which 42.8% (475 patients) were admitted to ICU. Of the aforementioned group of patients, ICU admission was due to haemodynamic instability, severity of injury or direct ward transfers. In the latter situation, some of the main reasons for transfer from the burns ward to the ICU were septic and haemodynamic shock in the previously stable burns patient. As shown in Figure 5.2, the sample size of patients (number of patients who met the inclusion criteria) was 9.3% (44 out of 475 patients admitted to the ICU). In terms of gender distribution, the sample of 44 patients consisted of 18 females and 26 males.

5.1 Patient Characteristics

The following details pertain to the 44 patients who met the inclusion criteria for this study. In terms of **age,** the group of 18 females ranged between 25 years and 83 years, while the group of 26 males ranged between 14 and 65 years. The average age of the burns patients in this study was 36.5 years (IQR 28-52.5). In terms of **gender**, the majority of patients were male (26/ 44), with females forming the smaller group (18/44 patients). Thus in this study population 61.4% (26/44 patients) were male, versus the 38.6% of the females (18/44). In terms of **TBSA** the females had a minimum of 10% total body area burnt and a maximum of 63%, while the males had a minimum of 11% and a maximum of 70%. The total surface area injured was higher in males, especially in the 20 to 29 years age group (Figure 5.4). In this study, female patients were older than the males and of poorer

health. All of this aforementioned data is represented in Table 5.1 below, which is a summary of the characteristics (i.e. age, gender and TBSA) of the 44 patients who met the inclusion criteria.

Table 5.1: Summary measures of patients characteristics

Characteristics	Sex	N	'Median (IQR)*	Min	Max
	Female	18	37.5 (33-53)	25	83
Age (years)	**Male**	26	33.5 (26-43)	14	65
	Total	**44**	**36.5 (28-52.5)**	**14**	**83**
	Female	18	26.5 (20-36)	10	63
TBSA Burn (%)	**Male**	26	39 (22-50)	11	70
	Total	**44**	**33 (22-50)**	**10**	**70**

*IQR: interquartile range

In terms of the number of patients who formed part of the study, Figure 5.2 depicts the 9% of patients (rounded off) who met the inclusion criteria and thus formed the sample. The sample consisted of 44 patients (9.3%) out of a total of 475 ICU patients (over an approximate five year period).

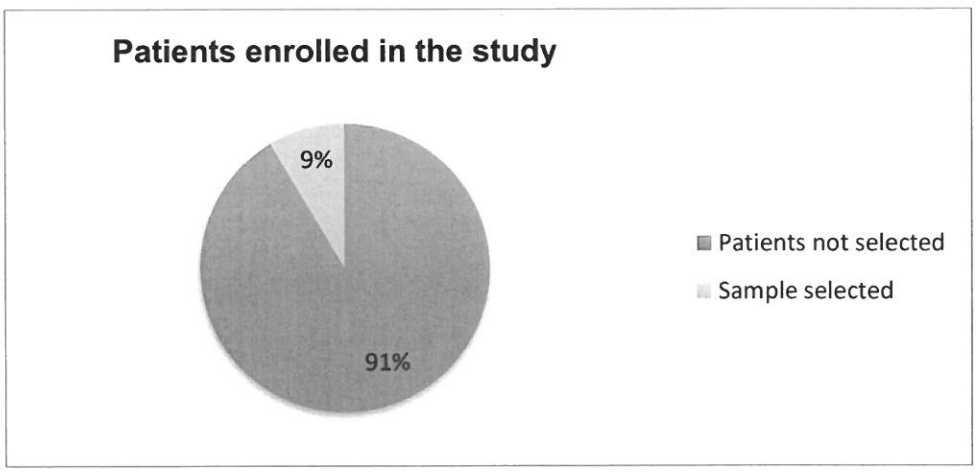


Figure 5.1: Sample selected

The frequency distribution of patients in terms of the categories age and gender is seen in Figure 5.3 where there is an absence of females in two of the age categories (10-19 years and 40-49 years).

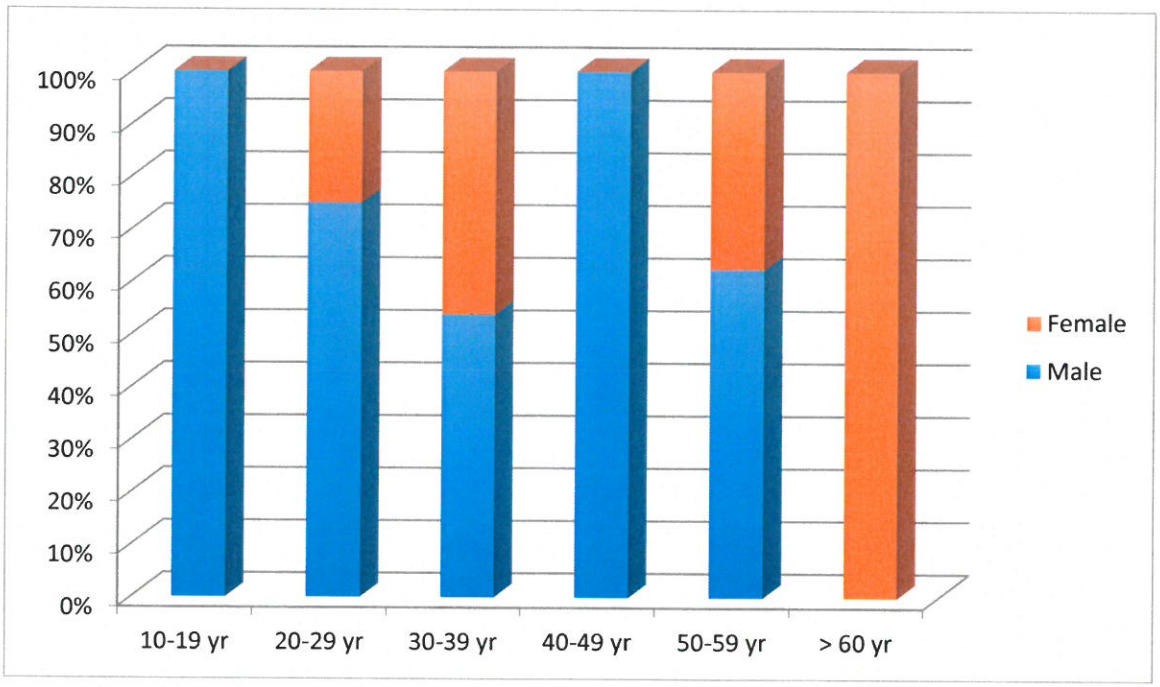


Figure 5.2: Frequency distribution of patients by age category and gender

In burns patients, the TBSA affected is one of the major predictors of outcome for the patient admitted to a specialised burn care centre. Higher TBSA burn injuries are associated with poorer survival and an increased need for interventions, as demonstrated in our study. These interventions include admission to the ICU and the subsequent need for organ support by mechanical ventilation, together with the administration of high dose vasopressors. The frequency distribution of the TBSA percentages in the total sample of 44 patients is portrayed in Figure 5.4 below.

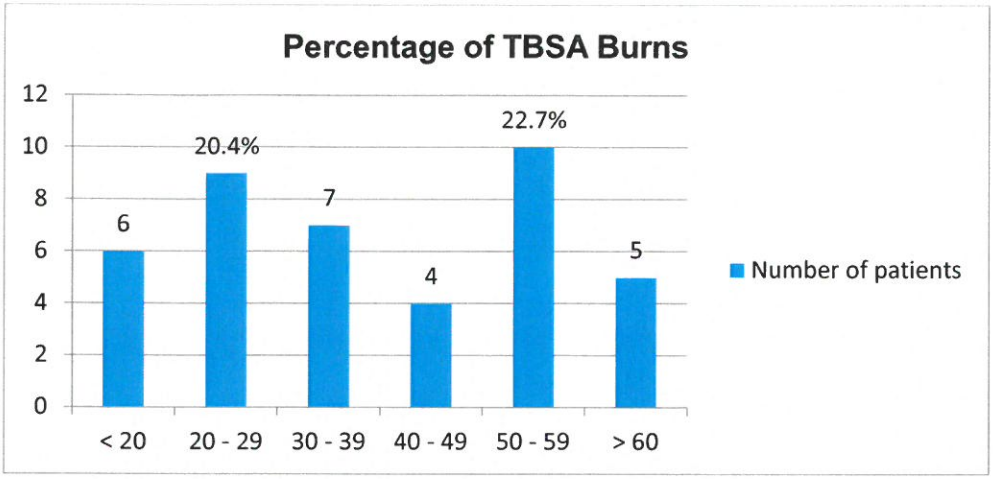


Figure 5.3: Frequency distribution by percentage TBSA burns

[The highest TBSA burns in this study were found in the younger and older age groups (20.5% aged 20–29 years and 22.7% aged 50–59 years) (Figure 5.3].

With regard to feeding intolerance, when patients demonstrated the clinical signs of feeding intolerance (as listed in **Table 5.4)**, feeds were stopped and the patients were then monitored to assess for persistent enteral feeding intolerance.

Table 5.2: Clincal signs of feeding intolerance

Feeding Intolerance	**Number of Patients (n)**
Moderately high gastric aspirates (>200 ml/6 hours)	11 out of 44 (0.25%)
Vomiting	4 out of 44 (0.01%)
Diarrhoea	9 out of 44 (0.21%)
Acute abdomen	0 (0%)
Distended abdomen	0 (0%)

As shown in **Figure 5.6** below, only 7% of the study patients had persistent intolerance to enteral feeds. Out of the 44 patients studied, a total of 41 patients

(93 % rounded off) tolerated enteral feeding whilst on high dose vasopressor support, whilst only three of the study patients (7%) were intolerant and had their feeding stopped in its entirety.

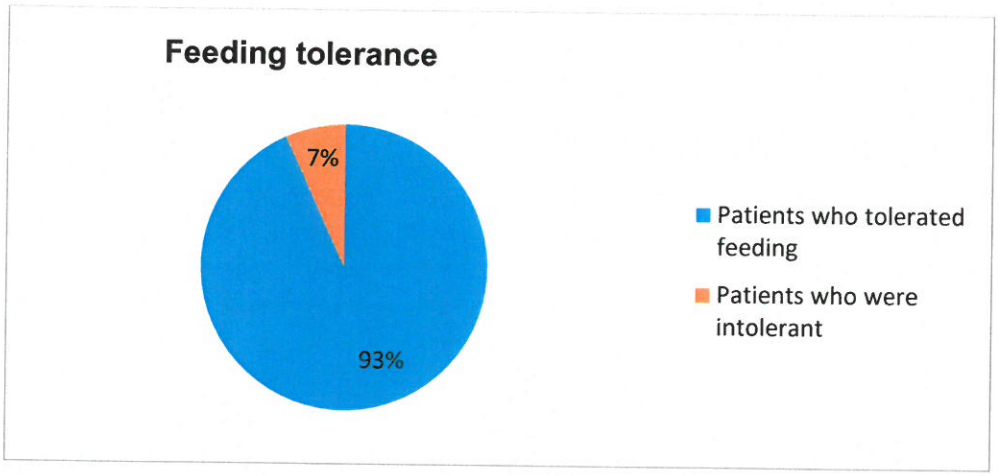


Figure 5.4: Persistent feeding tolerance/intolerance

The reasons for stopping enteral feeds in the previously mentioned three patients (7% of the study sample) are tabulated below in **Table 5.7.** The reasons included (i) high gastric aspirates, (ii) vomiting with diarrhoea and (iii) high gastric aspirates with diarrhoea.

Table 5.3: Reasons why feeding was stopped

Enteral Feeds stopped	**Number of Patients (n)**
High gastric aspirates (>500ml / 6 hours)	1 (0.02%)
Vomiting and simultaneous diarrhoea	1(0.02%)
High gastric aspirates with diarrhoea	1(0.02%)
Total	**3 (0.07%)**

The next table (Table 5.8) depicts the comparison of participants' proportions by feeding tolerance.

The patients reviewed in our study received early enteral naso- or orogastric feeds on admission to the burns ICU. This was coupled with continuous monitoring of their feeding tolerance or lack thereof. Enteral feeds were only stopped in 7% (3 of the 44 patients). In these three patients, one (1) patient experienced vomiting with simultaneous diarrhoea, one (1) had aspirates greater than 500 ml/6 hours, and another one (1) had high aspirates together with diarrhoea.

Table 5.4: Comparison of participants proportions by feeding tolerance (N = 44)

Characteristics	Level	Feeds stopped		Total	Pvalue
		No	Yes		
		41 (93.18)	3 (6.82)	44 (100)	
Sex (N %)	Female	17 (94.44)	1 (5.56)	18 (40.91)	0.7822
	Male	24 (92.44)	2 (7.69)	26 (59.09)	0.7822
median Age (years) (IQR)		34 (28-52)	56 (42-78)		0.056
median TBSA Burn % (IQR)		34 (22-50)	28 (25-55)		0.8339
Gastric aspiration (N %)	<50	10 (100)	0	10 (22.73)	0.3305
	50-100	6 (85.71)	1 (14.29)	7 (15.91)	0.3927
	100-200	15 (100)	0	15 (34.09)	0.1969
	>200	10 (83.33)	2 (16.67)	12 (27.27)	0.1125
GIT Upset (N %)	No	32 (96.97)	1 (3.03)	33 (75.00)	0.0842
	Vomiting	1 (100)	0	1 (2.27)	0.7844
	Diarrhoea	6 (85.71)	1 (14.29)	7 (15.91)	0.3927
	Vomiting& Diarrhoea	2 (66.67)	1 (33.33)	3 (6.82)	0.0591

5.2 Interpreting the results

The null hypothesis states that there is no significant difference between the tolerant group and intolerant group of participants in the study sample.

- A statistically significant difference was not found between the median age of those whose feeding had to be stopped and those whose feeding could continue ($p= 0.056$) as this is greater than $p = 0.05$.

- The difference between proportions of those who had vomiting and diarrhoea in the GIT upset group was also found to be not statistically significant as the p value was greater than 0.5 ($p= 0.0591$). These results should be treated with caution since the sample size was small, and therefore inferences about the general population of burns patients on EN cannot be made.

- The rest of the variables were also found to be not statistically significant ($p>0.05$). This means there was not a statistically significant difference when comparing the proportions between the group of those who had their feeding stopped and those who continued feeding ($p>0.05$). Although the majority of patients tolerated EN, the findings were not significant, most likely due to the small sample size.

CHAPTER 6

6. DISCUSSION

This limited and local study, with a relatively small sample size of 44 patients, shows that EN is well tolerated in the majority of the haemodynamically unstable burn patients who received vasopressor support (i.e. high doses of adrenalin) in the ICU of the ABU at CHBAH. The development of systemic sepsis is one of the main reasons why our patients required inotropic support. Importantly, this made our study somewhat different to the studies reviewed in the literature with regard to the patient population. Most of these studies were either done on postoperative cardiac patients, general ICU patients, or patients provided with post-pyloric tube feeding (Revelly et al., 2001). One example of the different patient profile is the retrospective review of data by Khalid *et al.,* (2010). Even though Khalid and his team looked at the outcome of EEN on the critically ill and heamodynamically unstable patient requiring mechanical ventilation and inotropic support, all their patients were non-surgical.

Another major difference is the primary and secondary outcomes (ICU and hospital mortality being the main objectives). Furthermore, the secondary outcomes they evaluated were the length of ICU stay, the development of ventilator - associated pneumonia, as well as ventilator and vasopressor free days. However, some of our research questions about continuing feeding in the haemodynamically unstable burns patients were answered by referring to Khalid's outcomes. Due to the aforementioned we were able to extrapolate the Khalid study findings to our study, as well as to other studies evaluated earlier, as part of the literature review.

The patients reviewed in our study received early enteral naso- or orogastric feeds on admission to the burns ICU. This was coupled with continuous monitoring of their feeding tolerance or lack thereof. Enteral feeds were only stopped in 7% (3 of the 44 patients). In these three patients, one patient experienced vomiting with simultaneous diarrhoea, one had aspirates greater than 500 ml/6 hours, and another one had high aspirates together with diarrhoea. As per our CHBAH burns unit protocol, feeds were immediately stopped in these three patients. In the patients with the high gastric aspirations of more than 500ml/6hr, additional aspirations were done after six more hours elapsed. In the patient with simultaneous vomiting and diarrhoea, feeds were withheld to monitor if tolerability improved.

These patients were then monitored for further intolerance and if it resolved, feeding was reintroduced at a lower initiating rate of 20ml/hour. The nursing sister slowly increased the feeds six hourly to the maximum rate as predetermined by the unit's registered dietician. Pro-kinetik drugs (e.g. metoclopramide and erythromycin) were also prescribed to the patient with concomitant diarrhoea and vomiting.

Feeding intolerance usually improved in most cases when these steps were taken, as reflected in the patients who initially did not tolerate their feeds (Table 5.7). However, none of these measures proved helpful in all three of the aforementioned patients. As a result of this outcome, feeds were stopped altogether. Most importantly, in all the patients who experienced signs of feeding intolerance, there were no clinical or radiological signs of complications such as bowel ischaemia, thrombosis or necrosis.

In the review of the literature, the authors mentioned below concluded that one of the most feared complications of EN, namely NOBN, is not common with enteral feeding. Lasierra *et al.,* (2015) pointed out that NOBN was associated with the insertion of post-pyloric feeding tubes. Feeds provided in this manner also contained non-fermentable fibre with rich nutritional formulas. Similarly, Wells (2012) corroborated that the NOBN cases mentioned earlier in the literature, were those who had enteral feeds given via surgically placed tubes. The majority of the feeding tubes were placed in the jejunum and feeds were supplemented with fibre.

On arrival in our unit, the unit's dietician assesses the patient's caloric/nutritional requirements. If there are no contraindications to enteral feeding, nasogastric or oro-gastric tube feeds containing nutritionally complete, peptide-based liquid are initiated. After twenty-four hours of receiving the feed without any clinical signs of intolerance, the feeds are changed to a liquid consisting of protein, fat, carbohydrate, vitamins, minerals and trace elements. By following these steps we ensure that the risk of NOBN, in our patients is significantly reduced. Lastly, Scaife *et al.,* (1999) also reviewed the complications related to tube feeding after hearing about bowel obstruction and perforation in a burns patient who received enteral feeding. However, Scaife *et al.* (1999) and his co-workers concluded that intestinal blockage and ischaemic necrosis after early and intense EN, feeding is not a common complication.

Our main aim in doing this retrospective study was to determine whether our patients would be negatively affected by having enteral feeds administered to them simultaneously with high doses of adrenalin. There are no specific, clear-cut guidelines in the literature for providing EN in the patient who is haemodynamically

unstable and on vasopressors. Moreover, there are mixed opinions about initiating and withholding enteral feeds. A number of societies and authors suggest enteral feeds in the haemodynamically unstable patient requiring vasopressor support. However, according to Allen (2012), the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) and the Society of Critical Care Medicine (SCCM) recommend abstinence from enteral feeding in the unstable patient on 'high dose' catecholamines. Turza *et al.,* (2009) also warned about the initiation of enteral feeds while the patient is on vasopressors for haemodynamic instability, as these vasoactive agents may cause impaired splanchnic perfusion with the risk of potential intestinal/bowel necrosis. Needless to say, despite these potential risks and guidelines, many clinicians persist with feeds in the unstable patient (Khalid *et al.,* 2010). Mancl *et al.,* (2013) also found that the majority of patients did not have problems and that less than one percent of patients who received EN and vasopressors complicated with intestinal ischaemia/bowel perforation. Correspondingly, Turza *et al.,* (2009) theorized that EN is a relatively safe intervention in the haemodynamically unstable patient on vasopressor therapy, providing that a thorough four phase process is followed, which includes the following: (i) the importance of evaluating the dangers and benefits of providing EN (ii) analysis is performed of the patient's physiologic state while on vasopressors; (ii) once the benefits are determined to outweigh the risks of beginning EN, the type of nutrition formula should be carefully chosen (iv) after the initiation of EN, monitoring must be done for clinical signs of distress.

As such it would appear that the administration of vasopressors in critically ill, haemodynamically compromised burn patients is not a contraindication in carefully monitored early and ongoing EN. This is an important finding with regard to the

safety and tolerability of enteral nutrition in these patients. In fact, evaluating the results in terms of the study's aim and objectives, it can be concluded that EN can be continued in the haemodynamically unstable burns patient on high dose intravenous vasopressor support with careful monitoring.

In this study, the finding that 93 percent (41 of 44 patients) tolerated enteral feeds (together with high doses of adrenalin) supports the conclusion of most studies to continue feeding the haemodynamically unstable patient requiring vasopressor support. More importantly, since patients were not placed at risk for thrombosis, ischaemia or bowel necrosis, it is further concluded that the carefully managed administration of EN in the seriously ill, haemodynamically compromised burns patients (who are on high doses of adrenalin) is a safe treatment regime/procedure.

CHAPTER 7

7. CONCLUSION

In this local study, which was a retrospective review carried out on 44 patient records at the CHBAH in the ABU, it was found that the simultaneous administration of EN and vasoactive substances did not place the patients at increased risk for intestinal ischaemia or NOBN. However, the sample was not randomly selected and it was also too small to be representative of the broader burns patient population, who receive EN and vasoactive substances simultaneously. Therefore the results need to be interpreted with caution. In order to reach a conclusive decision about the safety and tolerability of EN in haemodynamically unstable burns patients on vasopressors, a larger study with a more representative sample would need to be investigated. This would enable the generalisation of the findings to the broader population of seriously/critically ill burns patients.

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9. APPENDICES

APPENDIX A:

Data Sheet

Patient name and hospital number:

Study number:

Sex	Male	□	Female	□
Age (years)	10 - 19 y	□		
	20 - 29 y	□		
	30 - 39 y	□		
	40 - 49 y	□		
	50 - 59 y	□		
	>60 y	□		
TBSA burns (%)	<20	□		
	20 - 29	□		
	30 - 39	□		
	40 - 49	□		
	50 - 59	□		
	> 60	□		
Inhalation Injury	Yes	□	No	□
Inotropic support (Adrenaline 0. 5ug/kg/min or more)	Yes	□	No	□

APPENDIX B:

Letter Requesting Permission to do Research

August 2015

Chief Executive Officer: CHBAH

I Adelaide Rooi would hereby like to request permission to access the medical records of patients admitted to the Adult Burn Unit from 2010 to 2015 for my MMed research study at Chris Hani Baragwanath Academic Hospital.

Title of the research study: Continuation of enteral nutrition in the haemodynamically unstable burns patient on high dose intravenous vasopressor support: a 5 year retrospective study

Researcher: Dr. Adelaide Rooi

Supervisors: Dr. A. Muganza, Prof. E. Ndobe, Dr. M. Nel

Department: General Surgery and Plastic Surgery

Outline of the study:

This retrospective study was conducted at CHBAH. There are no clear guidelines in the literaure and Intensive Care Units about continuation of feeds in the hemodynamically unstable patient on high dose inotropic support with the overall consensus to withhold feeds in this setting.

The objectives of the study includes:

To assess the safety and tolerability of enteral nutrition in haemodynamically unstable burns patients requiring high dose (more than 0. 5 ug/kg/min adrenaline) intravenous vasopressor support.

Study Design:

This retrospective medical record review will be conducted at the Adult Burns Unit at the Chris Hani Baragwanath Academic Hospital (CHBAH), including all adult

burn ICU patients from 2010 receiving concomitant enteral nutrition and vasopressor support for at least 2 hours or more.

Starting Date: Once ethics permission is obtained

End Date: 4-6 months after starting

Thank you for your kind assistance and I hope that the abovementioned information regarding my MMed study will be sufficient for your approval.

Yours sincerely

Dr. Adelaide Rooi

Registrar, Department of Plastic and Reconstructive Surgery

adelaiderooi@yahoo.com

072 177 3487

APPENDIX C:

Ethics Clearance Certificates

R14/49 Dr Adelaide Lilian Rooi et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M161148

NAME: (Principal Investigator)	Dr Adelaide Lilian Rooi et al
DEPARTMENT:	Surgery Chris Hani Baragwanath Adult Burn Unit (CHBABU)
PROJECT TITLE:	Continuation of Enteral Nutrition in the Haemodynamically Unstable Burns Patient on High Dose Intravascular Vasopressor Support: A 5-Year Retrospective Study
DATE CONSIDERED:	25/11/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Professor P Cleaton-Jones,Chairperson, HREC (Medical)
DATE OF APPROVAL:	17/02/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in and will therefore be due in the month of each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

18 February 2017
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX D:

Plagiarism Report

ORIGINALITY REPORT

3%	2%	2%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	&NA;. "Abstracts", Critical Care Medicine, 12/2007 Publication	1%
2	www.practicalgastro.com Internet Source	1%
3	www.guideline.gov Internet Source	<1%
4	www.idph.state.il.us Internet Source	<1%
5	Dhaliwal, R., S. M. Madden, N. Cahill, K. Jeejeebhoy, J. Kutsogiannis, J. Muscedere, S. McClave, and D. K. Heyland. "Guidelines, Guidelines, Guidelines: What Are We to Do With All of These North American Guidelines?", Journal of Parenteral and Enteral Nutrition, 2010. Publication	<1%