

**THE RELATIONSHIP BETWEEN DISTURBED
GASTRIC MOTOR FUNCTION AND ENTERAL
NUTRITION IN CRITICALLY ILL PATIENTS**

A thesis submitted by

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THESIS SUMMARY

Delayed gastric emptying, that manifests clinically as intolerance to enteral feeding, occurs in over 50% of critically ill patients and has a major impact on patient morbidity and mortality. Despite the recognition that the proximal stomach has a major role in gastric emptying of liquids, only the motor activity of the antro-pyloro-duodenal region has been evaluated in detail. In addition, many of the proposed risk factors for the gastric dysmotility, particularly a prior history of diabetes mellitus, have not been evaluated formally but have been extrapolated from data from non-critically ill patients. The currently available prokinetic drugs, erythromycin and metoclopramide, are considered to be the first line treatment for feed intolerance. However, neither data comparing the effectiveness of these agents nor the data on the effects of combination of therapy in the treatment of feed intolerance are available. The aims of this thesis were, therefore, to examine: (i) proximal gastric motor activity and the association between proximal and distal motility; (ii) the relationship between entero-gastric humoral responses to nutrients, gastric emptying and feed intolerance; (iii) the impact of admission diagnoses, choice of sedations, timing of initiation of feeding, and pre-existing history of diabetes mellitus on gastric emptying and feed intolerance; and (iv) the efficacy of erythromycin, metoclopramide and combination of these drugs in treatment of feed intolerance in critically ill patients.

The current thesis indicates that motor activity is impaired in multiple regions of the stomach in the critically ill. When compared to healthy humans, proximal gastric relaxation was prolonged and fundic wave activity was reduced during small intestinal

nutrient infusion in critically ill patients. In addition, simultaneous assessment of proximal and distal gastric motility demonstrated a possible disruption of the motor integration between the proximal and distal stomach. In light of the recent data that suggested a significantly greater proportion of meal distributed proximally in critically ill patients with delayed gastric emptying (Nguyen, *et al.* 2006), the disruption of the gastric motor integration and the prolonged gastric relaxation in response to duodenal nutrients may play a significant role in the pathogenesis of slow gastric emptying during critical illness, especially as liquid formulae.

The entero-gastric hormonal feedback responses were also disturbed during critical illness. Both fasting and duodenal nutrient-stimulated plasma CCK and PYY concentrations were significantly higher in critically ill patients, particularly those who did not tolerate gastric feeds. The rate of gastric emptying of a liquid meal was inversely related to both fasting and postprandial plasma CCK and PYY concentrations, supporting the potential role of plasma CCK and PYY in the pathogenesis of gastric dysmotility in critically ill patients.

Admission diagnosis, choice of sedative drug and blood glucose control but not the timing of enteral feeds were important factors for delayed gastric emptying and feed intolerance in these patients. In particular, delaying enteral feeding by 4 days had no impact on the rate of gastric emptying, intra-gastric meal distribution, or plasma CCK and PYY concentrations. Contrary to traditional belief, critically ill patients with a pre-existing diagnosis of type 2 DM have only a minor disturbance to the proximal stomach, a relatively normal gastric emptying and are at no higher risk of feed intolerance than those

without DM, suggesting the presence of pre-existing DM 2 in critically ill patients should not influence the standard practice of gastric feeding.

Therapeutically, short-term treatment with low dose erythromycin was more effective than metoclopramide, but the effectiveness decreased rapidly overtime at similar rate as observed with metoclopramide. In patients who failed to response to either agent, treatment with both agents was highly effective in re-establishing feeding success. The use of combination therapy as the initial treatment for feed intolerance was also more effective than erythromycin alone and had less tachyphylaxis. Treatment with erythromycin and metoclopramide, either as a single agent or in combination did not associated with major cardiovascular adverse side effects. Although diarrhoea was a common side effect and was highest with combination therapy, it was not associated with *Clostridium difficile* infection and settled quickly after the cessation of the prokinetic therapy.

In summary, the work performed in the current thesis has provided substantial insights into the understanding of the nature, risk factors, pathogenesis and treatment of disturbed gastric motor function in critically ill patients. Not only do these findings stimulate further research into the mechanisms responsible for gastric dysmotility in critical illness, they also lead to the development of new strategies for optimizing the management of feed intolerance.

STATEMENT OF ORIGINALITY

The work presented in this thesis has been submitted to the University of Adelaide for the degree of Doctor of Philosophy. The studies reported herein are entirely original and were performed by the author between 2004 and 2006. This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution. To the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except when due reference has been made in the text.

I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provision of the Copyright Act 1968. The author acknowledges that copyright of published works contained within this thesis (as listed in the “Publications from this thesis”) resides with the copyright holders of the journals.

Nam Q. Nguyen

August 2007

DEDICATION

I dedicate this thesis to my dearest parents, Mai and Lưu Nguyễn.

To my dearest wife, Lisa Tang, I am forever grateful for your unconditional love and support.

Kính thưa Cha Mẹ,

Con cảm ơn công nuôi dưỡng và dạy dỗ của Cha Mẹ bao năm qua.

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PUBLICATIONS FROM THIS THESIS

PUBLISHED ORIGINAL PAPERS:

Nguyen NQ, Chapman M, Fraser RJ, Ritz M, Bryant L, Butler R, Davidson G, Zacharakis, B Holloway RH. Longstanding type II diabetes mellitus is not a risk factor for slow gastric emptying in critically ill patients. *Intensive Care Medicine* 2006; 32(9):1365-70.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Vozzo R, Holloway RH, Feinle-Bisset C, Horowitz M. Proximal gastric response to small intestinal nutrients is abnormal in mechanically ventilated critically ill patients. *World Journal of Gastroenterology* 2006; 12(27):4383-8.

Nguyen NQ, Fraser RJ, Chapman M, Bryant LK, Wishart J, Holloway RH, Horowitz M. Fasting and nutrient-stimulated plasma peptide-YY levels are elevated in critical illness and associated with feed intolerance: an observational, controlled study. *Critical Care* 2006; 10: R175.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Wishart J, Holloway RH, Horowitz M. Feed intolerance in critical illness is associated with increased basal and nutrient-stimulated plasma cholecystokinin concentrations. *Critical Care Medicine* 2007; 35:82–88.

Nguyen NQ, Ng MP, Chapman M, Fraser R, Holloway RH. The impact of admission diagnosis on gastric emptying in critically ill patients. *Critical Care* 2007; 11; R16.

- Nguyen NQ**, Chapman M, Fraser R, Bryant L, Holloway RH. Erythromycin is more effective than metoclopramide in the treatment of feed intolerance in critical illness. *Critical Care Medicine* 2007; 35: 483-9.
- Nguyen NQ**, A Chapman M, Fraser R, Bryant L, Holloway RH. Prokinetic therapy with erythromycin has no impact on the hemodynamics of critically ill patients. *British Journal of Clinical Pharmacology* 2007; 63: 498-500.
- Nguyen NQ**, Holloway RH. Erythromycin as a prokinetic: Is the overall benefit corroborated? *Critical Care Medicine* 2007; 35; 1446-1447.
- Nguyen NQ**, Chapman M, Fraser R, Bryant L, Holloway RH. Proximal gastric motility in critically ill patients with type 2 diabetes mellitus. *World Journal of Gastroenterology* 2007; 13; 270-275.
- Nguyen NQ**, Lam SW, Ching K, Chapman M, Fraser R, Holloway RH. Gastric feed intolerance is not increased in critically ill patients with type 2 diabetes mellitus. *Intensive Care Medicine* 2007; 33; 1740-45.
- Nguyen NQ**, Chapman M, Fraser R, Bryant L, Holloway RH. Functional association between proximal and distal gastric motility during fasting and duodenal stimulation in humans. *Neurogastroenterology & Motility* 2007; 19; 638-645.
- Nguyen NQ**, Chapman M, Fraser R, Bryant L, Holloway RH. Prokinetic therapy for treatment of feed intolerance in critical illness – one or two drugs. *Critical Care Medicine* 2007; 35; 2561-67.

Nguyen NQ, Ching K, Fraser R, Chapman M, Holloway RH. Risk of Clostridium difficile diarrhea in critically ill patients treated with erythromycin based prokinetic therapy for feed intolerance. *Intensive Care Medicine* 2008; 34; 169-73.

Nguyen NQ, Ching K, Fraser R, Chapman M, Holloway RH. The relationship between blood glucose control and intolerance to enteral feeding during critical illness. *Intensive Care Medicine* 2007; 33; 2085-92.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Burgstad C, Ching K, Bellon M, Holloway RH. The effects of sedation on gastric emptying and intra-gastric meal distribution in critical illness. *Intensive Care Medicine* 2007 (December 4, Epub ahead of print).

Nguyen NQ, Fraser R, Bryant L, Chapman M, Wishart J, Holloway RH, Butler R, Horowitz M. The relationship between gastric emptying, plasma CCK and PYY in critically ill patients. *Critical Care Medicine* 2007; 11(6); R132.

Nguyen NQ, Fraser R, Bryant L, Chapman M, Holloway RH. Diminished functional association between proximal and distal gastric motility in critically ill patients. *Intensive Care Medicine* 2008 (March 4, Epub ahead of print).

Nguyen NQ, Fraser R, Bryant L, Chapman M, Bellon M, Wishart J, Holloway RH, Horowitz M. The impact of delaying enteral feeding on gastric emptying, plasma cholecystokinin and peptide YY concentrations in critically ill patients. *Critical Care Medicine* 2008 (April 3, Epub ahead of print).

REVIEW ARTICLES:

Chapman M, **Nguyen NQ**, Fraser RJ. Gastrointestinal motility and prokinetics in the critically ill. *Current Opinion in Critical Care* 2007; 13; 187-94.

Deane A, Chapman M, Fraser RJ, Bryant L, Burgstad C, **Nguyen NQ**. Mechanisms underlying feed intolerance in the critically ill: implications for treatment. *World Journal of Gastroenterology* 2007; 13; 3909-17.

PUBLISHED ABSTRACTS:

Nguyen NQ, Chapman M, Fraser R, Bryant L, Burgstad C, Wishart J, Holloway RH, Horowitz M. Elevated plasma CCK and PYY concentrations are associated with delayed gastric emptying in critical illness. *Gastroenterology* 2007; 132; A379.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Burgstad C, Wishart J, Holloway RH, Horowitz M. Impact of delayed enteral feeding on gastric emptying and plasma CCK in critically ill patients. *Gastroenterology* 2007; 132; A380.

Nguyen NQ, Fraser R, Ching K, Chapman M, Holloway RH. Risk of Clostridium difficile diarrhea in critically ill patients treated with erythromycin-based prokinetic therapy for feed intolerance. *Nutrition in Clinical Practice* 2007; 22(1); 126.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH. Prokinetic therapy for feed intolerance in critical illness: the role of combination therapy? *Journal Hepatology & Gastroenterology* 2006; 130(4S); A610.

Nguyen NQ, Fraser R, Chapman M, Bryant L, Holloway RH. Relationship between intra-gastric meal distribution and delayed gastric emptying in critical illness. *Neurogastroenterology & Motility* 2006: 18(8); 663.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH, Horowitz M. Peptide YY (PYY) Release is increased in critical illness during intestinal nutrient stimulation. *Gastroenterology* 2006: 130(4S); A607.

Nguyen NQ, Ching K, Fraser R, Holloway RH. Relationship between blood glucose control and feed intolerance in critical illness. *Gastroenterology* 2006: 130(4S); A607.

Nguyen NQ, Chapman M, Bellon M, Fraser R, Butler R, Bryant L, Holloway RH. The role of ¹³C-octanoic acid breath testing in the assessment of gastric emptying in critically ill patients. *Gastroenterology* 2006: 130(4S); A247.

Nguyen NQ, Fraser R, Chapman M, L Bryant, C Burgstad and Holloway RH. Disruption to the interaction of proximal and distal gastric motor activity in critically ill patients. *Gastroenterology* 2006: 130(4S); A430.

Bryant L, Nguyen NQ, Burgstad C, Fraser R, Chapman M, Holloway RH. Lack of effect of elevated plasma CCK concentrations on proximal gastric motor activity in critically ill patients. *Gastroenterology* 2006: 130(4S); A429.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH. Relationship between proximal and distal gastric motor activity in humans. *Gastroenterology* 2006: 130(4S); A130.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH. Prokinetic therapy for feed intolerance in critical illness: one drug or two? *Gastroenterology* 2006: 130(4S); A610.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH. Rapid gastric emptying of a liquid meal in critically ill patients with DM II. *Gut* 2005; 54(SVII); A254.

Nguyen NQ, Fraser R, Chapman M, Bryant L, Holloway RH, Vozzo R, Feinle-Bisset C. Relationship between feed intolerance and fundic slow volume wave abnormalities in critically ill patients. *Gut* 2005; 54(SVII), A15.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH, Vozzo R, Feinle-Bisset C, Horowitz M. Impaired proximal gastric relaxation in response to small intestinal nutrients in critically ill patients. *Gastroenterology* 2005: 128(4); A548.

Nguyen NQ, Fraser R, Chapman M, Bryant L, Holloway RH, Vozzo R, Feinle-Bisset C, Horowitz M. Delayed proximal gastric relaxation in response to small intestinal nutrients in critically ill patients with type II diabetes mellitus *Gastroenterology* 2005: 128(4); A554.

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH, Wishart J, Feinle-Bisset C, Horowitz M. Elevated plasma cholecystokinin concentrations and feed intolerance in critically ill patients. *Gastroenterology* 2005: 128(4); A610.

NQ Nguyen, AA Mangoni, M Chapman, R Fraser, Creed S, L Bryant, C Burgstad, Bland K and RH Holloway. Prokinetic therapy with erythromycin has no significant impact on the hemodynamics of critically ill patients. *Anaesthesia and Intensive Care* 2005

NQ Nguyen, R Fraser, M Chapman, L Bryant, C Burgstad and RH Holloway. A lack of coordination between proximal and distal stomach - a contributing factor to delay gastric emptying in critically ill patients? *Anaesthesia and Intensive Care* 2005

Nguyen NQ, Chapman M, Fraser R, Bryant L, Holloway RH, Horowitz M, Vozzo R. Impaired proximal gastric relaxation in response to duodenal nutrients in critically ill. *Journal of Gastroenterology and Hepatology* 2004; 19, A257.