5.5 Strategies to Optimize the Delivery of EN: Use of and Threshold for Gastric Residual Volumes May 2015

2015 Recommendation: *Based on 3 level 2 studies, a gastric residual volume of either 250 or 500 mLs (or somewhere in between) and frequency of checking residuals either q4 or q8 hrs should be considered as a strategy to optimize delivery of enteral nutrition in critically ill patients.*

2015: Discussion: The committee noted there was no difference in nutritional outcomes and clinical outcomes in the new study (William 2014) between checking GRVS q 8 hrs vs 4 hrs. It was acknowledged that checking GRVS less frequently was associated with a significantly higher incidence of vomiting/regurgitation and although no differences in the interruption of feeds was seen, this may be a risk factor for further complications. Despite the favourable cost savings from reducing RNs times checking GRVS more frequently, the committee agreed that on the basis of this study, it could not be ruled out that less frequent checking of GRVs is without risks and hence a recommendation supporting this could not be made. The discussion pertaining checking GRVs vs not and a specific GRV from 2013 below remains the same.

2013 Recommendation: There are insufficient data to make a recommendation for not checking gastric residual volumes or a specific gastric residual volume threshold. Based on 2 level 2 studies, a gastric residual volume of either 250 or 500 mLs (or somewhere in between) is acceptable as a strategy to optimize delivery of enteral nutrition in critically ill patients.

2013 Discussion:
The committee noted that in the multicenter study (Reignier 2013), not checking gastric residual volumes was associated with increased rates of vomiting, despite no differences in clinical outcomes. Nutritional adequacy was greater in the 'not checking GRV' group but differences were minimal (111 calories over the first week). Given the concerns about the external validity of the trial (under-represents difficult to feed patients i.e. multi organ failure and surgical) and the signals associating vomiting from gastrointestinal intolerance with increased infection, length of stay and mortality in critically ill patients (1), the committee agreed not to make a recommendation for abandoning the practice of checking GRVs.

The committee noted that in Spanish multicentre trial (Montejo 2010), there was an absence of any clinical effect of increasing the gastric residual volume threshold and that the increase in nutritional adequacy with the higher GRV was minimal but statistically significant (84 vs. 88 % of goal calories). Despite the potential safety of an approach that used a high GRV threshold, as evidenced by the lack of increased gastrointestinal complications, concerns regarding potential micro aspiration were raised. Opposing views about the risk of higher gastric residual volumes exist (2, 3). Furthermore, in the Montejo et al study, patients were predominately medical patients and there was a lack of information about their hemodynamic stability. Thus, the generalizability of the results to all ICU patients that might receive a feeding protocol in a given ICU is not clear.

The committee agreed that a strong recommendation could not be made for higher GRVs of 500 mLs but it was agreed that a range of 250-500 mLs be recommended.

(1) Metheny NA, Schallom L, Oliver DA, Clouse RE. Gastric residual volume and aspiration in critically ill patients receiving gastric feedings. Am J Crit Care 2008;17:512-520.
(2) Mentec H, Dupont H, Bocchetti M, Cani P, Ponche F, Bleichner G. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med.* 2001;29(10):1955-1961.
(3) McClave SA, Lukan JK, Stefater JA, et al. Poor validity of residual volumes as a marker for risk of aspiration in critically ill patients. Crit Care Med 2005;33(2):324-330.

Semi Quantitative Scoring

Values	Definition	2013 Score (0,1,2,3) High vs Lower	2013 Score (0,1,2,3) 250ml vs none	2015 Score: (0,1,2,3) 4hr vs 8 hr
Effect size	Magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	0	0	0
Confidence interval	95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)--a higher score indicates a smaller confidence interval	0	0	0
Validity	Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes--a higher score indicates presence of more of these features in the trials appraised	1	3	2
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	n/a	n/a	n/a
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	3	3	3
Biological Plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies=1, minimal consistencies=2, very consistent=3)	2	2	2
Generalizability	Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre=1, moderate likelihood i.e. multicentre with limited patient population or practice setting=2, high likelihood i.e. multicentre, heterogenous patients, diverse practice settings=3)	1	1	1
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	3	3	3
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	3	3	3
Safety	Estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm	2	1	2

5.5 Strategies to Optimize the Delivery of EN: Threshold of Gastric Residual Volumes

Questions:
1. Does the use of higher gastric residual volume threshold (GRVs) result in better outcomes in the critically ill adult patient?
2. Does not checking gastric residual volumes compared to a GRV of 250 mls result in better outcomes in the critically ill adult patient?
3. Does less frequent checking of gastric residual volumes (q 8 hrs) compared to more frequent (q4 hrs) result in better outcomes in the critically ill patient?

Summary of evidence: There was one level 2 multicentre trial that compared a gastric residual volume of 500 mLs to 250 mLs (Montejo 2010). One study compared higher gastric residual volume threshold to lower within the context of a feeding protocol that also included motility agents (Pinilla 2001) and was included in the section 5.1 Feeding Protocols. The study by Taylor et al 1999 compared full rate EN with higher gastric residual volume thresholds vs gradual start EN with lower gastric residual volume thresholds was included in the section 3.2 Target Dose EN. There was a multicenter trial that compared not measuring gastric residual volumes to 250 mLs (Reigner 2013). The trial by Williams et al (2014) compared the frequency of monitoring gastric residual volumes up to every 8 hours vs every 4 hours.

Mortality: In the study by Montejo (2010) there were no significant difference between the two groups in ICU mortality (RR 1.25, 95% CI 0.78, 2.01, p=0.35) or hospital mortality (RR 1.01, 95% CI 0.74, 1.38, p=0.94). There were no differences in 28 day or 90 day mortality between the group that did not check gastric residual volumes vs. the group that checked GRVs > 250 ml in the multicentre study (Reignier 2013). There was also no difference in ICU or hospital mortality between the group with GRVs monitored every 4 hours vs up to every 8 hours (Williams 2014).

Infections: In the study by Montejo (2010), no significant differences were found in pneumonia between the two groups (RR 1.03, 95% CI 0.72, 1.46, p=0.88). There were no significant differences in ICU acquired infections or ventilator associated pneumonia rates between the group that did not check gastric residual volumes vs. the group that did check GRVs in the multicentre study (Reignier 2013). There was also no difference in ventilator associated pneumonia rates between the group with GRVs monitored every 4 hours vs up to every 8 hours (p=0.81, Williams 2014).

LOS & ventilator days: In the study by Montejo (2010), there were no differences in ICU length of stay between the groups (WMD 0.90, 95% CI -2.60, 4.40, p=0.61) and no significant difference in duration of ventilation (WMD 0.90, 95% CI -2.02, 3.82, p=0.55). There were no differences in ICU or hospital length of stay between the group that did not check gastric residual volumes vs. the group that checked GRVs > 250 ml in the multicentre study (Reignier 2013). There was also no difference in ICU length of stay between the group that monitored GRVs every 4 hours vs up to every 8 hours (p=0.57, Williams 2014) but there was a trend towards a reduction in hospital length of stay in the group with gastric residual volumes monitored up to every 8 hours (p=0.19).

Other: In the study by Montejo (2010), the frequency of gastrointestinal complications was significantly lower in the 500mL GRV vs 250 mLs GRV group and this was mainly due to the lower incidence of high GRVs when compared to the lower GRV group. There were no differences between these groups in the number of patients with abdominal distention (p=0.83), diarrhea (p=0.95), emesis (p=0.31), regurgitation (p=0.41) or aspiration (p=0.48). However, the amount of nutrition delivered in week 1 was significantly higher in the group with the 500ml GRVs threshold (p=0.0002). In the Reignier study, caloric target was achieved in a higher proportion of patients in the group not checking GRVs compared to the groups that did (p<0.001) and there was a lower cumulative calorie deficit from Day 0-7 than this group. There were higher rates of vomiting in the group that did not check gastric residual volumes but no differences in diarrhea. In the Williams (2014) study, there was a significant reduction is vomiting/regurgitation in the group with GRVs monitored every 4 hours (p=0.02) but no difference was found in interruption to EN due to vomiting (p=0.24), or the number of patients who received >80% of goal EN volume (p=0.39). There was a significant reduction in the number of daily tube aspirations in the group in which the GRVs were monitored every 8 hours (p=<0.001).

Conclusions:

1. GRVs of 500 mLs vs 250 mLs have no effect on mortality, infections or ICU LOS
2. Not checking GRVs vs checking GRVs > 250 ml threshold has no effect on mortality, infections, ICU/hospital length of stay
3. Monitoring GRVs every 4 hours vs up to every 8 hours has no effect on mortality, VAP or ICU LOS but may be associated with a trend in reducing hospital LOS.
4. GRVs of 500 mLs vs 250 mLs are not associated with increased gastrointestinal complications
5. GRVs of 500 mLs vs 250 mLs are associated with significantly better nutrition delivery.
6. Not checking GRVs vs checking GRVs > 250 ml threshold is associated with a significant better caloric delivery.
7. Monitoring GRVs every 4 hours vs up to every 8 hours are associated with a reduction in vomiting/regurgitation but had no effect on nutrition delivery.

Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.
Level 2 study: If any one of the above characteristics are unfulfilled.

*p-value calculated from RevMan and differs slightly from that reported in the article.

Table 1. Randomized studies evaluating gastric residual volume in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡
1) Montejo 2010	Mechanically ventilated patients from 28 ICUs requiring EN for at least 5 days N = 329	C.Random: No ITT: No Blinding: No (5)	GRV limit of 500mL vs. GRV limit of 200mL Both groups: nasogastric EN, prophylactic prokinetics X 3 days & PN, if needed	GRV 500mL ICU 31/157 (20)	GRV 200mL ICU 26/165 (16)	GRV 500mL GRV 200mL Pneumonia 44/157 (28) 45/165 (27) RR 1.03, 95% CI 0.72, 1.46, p=0.88
				RR 1.25, 95% CI 0.78, 2.01, p=0.35		
				Hospital 53/157 (34)	Hospital 55/165 (34)	
				RR 1.01, 95% CI 0.74, 1.38, p=0.94		
2) Reignier 2013	Mechanically ventilated patients from 9 ICUs requiring EN via NG within 36 hrs after intubation N= 452	C.Random: Yes ITT: Yes Blinding: No (11)	Not monitoring GRV vs. GRV limit of 250 ml Vomiting considered an intolerance to EN in both groups	No GRV ICU 63/227 (28)	GRV 250mL ICU 61/222 (28)	No GRV GRV 250mL VAP 38/227 (17) 35/222(16) ICU acquired 60/227 (26) 60/222 (27)
				Hospital 82/227 (36)	Hospital 76/222 (34)	
3) Williams 2014	Critically ill pts, single centre, LOS expected >48 hrs, EN expected >72 hrs N=357	C.Random: Yes ITT: Yes Blinding: No (9)	Monitoring GRVs for gastric feeds up to every 8 hrs vs every 4 hrs. For both groups, GRVs were returned if the volume was ≤300 mL and for GRV exceeding 300 mL, the first 300 mL was returned to the stomach and the remainder discarded.	GRVs q8hr GRVs q4hr ICU 32/178 (18) 25/179 (14) Hospital 39/178 (22) 34/179 (19)		Pts with VAP (p=0.81) 13.2% 14.1%

Table 1. Randomized studies evaluating gastric residual volume in critically ill patients (continued)

Study	Length of Stay	Mechanical Ventilation	Other
1) Montejo 2010	GRV 500mL ICU 20.7 ± 16.2 (157) GRV 200mL ICU 19.8 ± 15.8 (165) WMD 0.90, 95% CI -2.60, 4.40, p=0.61	GRV 500mL 15.6 ± 13.6 (157) GRV 200mL 14.7 ± 13.1 (165) WMD 0.90, 95% CI -2.02, 3.82, p=0.55	GRV 500ml GRV 200mL GI Complications 75/157 (48) 105/165 (64), p=0.004 High GRV 42/157 (27) 70/165 (42), p=0.003 Abdominal distention 16/157 (10) 18/165 (11), p=0.83 Diarrhea 31/157 (20) 33/165 (20), p=0.95 Emesis 17/157 (11) 24/165 (15), p=0.31 Regurgitation 8/157 (5) 12/165 (7), p=0.41 Aspiration 1.157 (1) 0/165 (0). p=0.48 Mean Diet Volume Ratio in 1st week of EN 88.2% 84.48%, p=0.0002
2) Reignier 2013	No GRV GRV 250mL ICU 10 (6-17) 10 (7-17) Hospital 17 (9-31) 19 (10-32)	No GRV GRV 250mL 7 (4-13) 7 (5-13)	No GRV GRV 250mL Vomiting 90/227 (40) 60/222 (27) Diarrhea 51/227 (23) 51/222 (23) EN intolerance 90/227 (40) 141/222 (64)
3) Williams 2014	GRVs q8hr GRVs q4hr ICU 9 (6-14) 9 (5-15) Hospital 23 (12-38) 25 (13-41)	NR	GRVs q8hr GRVs q4hr Vomiting/regurgitation (p=0.02) 3.6% 2.1% EN interruption due to vomiting (p=0.24) 2.1% 1.5% Tube aspirations per day (p=<0.001) 3.4 (1.3) 5.4 (1.3) ≥80% EN volume received (p=0.39) 50% of pts 48% of pts

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
ITT: intent to treat; NA: not available
± ( ) : mean ± Standard deviation (number)
‡ refers to the # of patients with infections unless specified