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Review

Measuring gastric residual volumes in critically ill burn patients — A systematic review

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ABSTRACT

Purpose: Measuring gastric residual volumes (GRV) is common in intensive care units (ICU) in patients receiving enteral nutrition (EN) and are a common source of feeding interruptions. Interruptions in EN yield adverse outcomes and are an area of improvement in burn care. The objectives of this study are to summarize the literature's ICU GRV practices and offer practical suggestions to GRV management in the burn patient.

Methods: PubMed, SCOPUS, and OvidSP Medline were systematically reviewed using the keywords: burns; thermal injury; gastric residual volume; enteral feeding; tube feeding; enteral nutrition; gastric intolerance; ICU; critical illness. Reviews, case reports, and consensus and opinion papers were excluded.

Results: 26 articles were identified. Six burn-specific studies were identified. GRV practices vary widely and are a common cause of EN interruption. Elevated GRVs do not equate to gastrointestinal intolerance and do not always reflect aspiration risk.

Conclusions: We advocate a GRV threshold of 500 mL should be used to optimize the benefits of EN in burn ICUs. A single incident of elevated GRVs should not mandate immediate EN rate reduction or cessation but should prompt a thoughtful examination of secondary causes of gastrointestinal intolerance. Randomized controlled trials are needed to define the ideal GRV threshold and re-evaluate its role in burn care.

Contents

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1. Introduction

The provision of robust nutritional support to severely burned patients is a tenet of modern burn care. Patients with extensive partial-thickness and full-thickness burns develop a hyper-inflammatory response to injury that drastically elevates basal metabolic rates [1] (BMR) with subsequent protein catabolism, lipolysis, and glycogenolysis. Early, sustained enteral nutrition (EN) with calorically dense and protein rich formulations is proven to facilitate improved wound healing, strengthen the immune system, provide the requisite energy for supporting the catecholamine-derived stress response, and is entero-protective. [1]. The goal is to reach full caloric alimentary support of critically ill burn patients early while minimizing EN discontinuations.

On the whole, EN in intensive care unit (ICU) patients has been extensively studied to determine optimal timing for initiating EN, safe practices for advancing EN to goal, and accurate biomarkers for measuring nutritional status as well as caloric estimations. Specifically, the measurement of gastric residual volumes (GRV) practices has been studied and guidelines have been developed by the American Society of Parenteral and Enteral Nutrition (ASPEN) [2]. While many studies have been performed in medical, surgical, and trauma intensive care unit (ICU) patients; there are few studies that have specifically addressed critically ill burn patients.

Prior studies that have investigated various methods for safely advancing tube feeds often implement GRV as a surrogate for feeding tolerance, or lack thereof. However, the practice of measuring GRV is controversial and varies among healthcare providers. While some centers have abandoned routine GRV measurements unless clinically indicated (i.e. development of nausea, vomiting, or distension), others continue to employ protocol-driven GRV checks in their ICU patients. In critically ill patients, there are no universally accepted guidelines that specify which patients are appropriate for GRV tailored EN, the optimal sampling frequency, a clinically relevant GRV threshold indicative of intolerance, and what is the appropriate modification for an EN regiment once this threshold is crossed [3].

In the U.S., up to 97% of ICU nurses use GRVs [4] to assess for gastrointestinal (GI) intolerance, the presence of which has been shown to be predictive of poorer outcomes [5–7]. This correlation between GI intolerance and adverse outcomes has also been shown to occur in the burns population as well [8]. A potential drawback of routine GRV checks is they may result in inappropriate discontinuation of enteral nutrition, which would predispose patients to other complications associated with inadequate nutritional intake. Frequent discontinuation of enteral feeding due to measuring GRVs is especially detrimental in critically ill burn patients whose hypermetabolic states create a 118% to 210% increase in BMR. Given the degree to which the caloric and protein estimations increase in severely burned patients, it is vital that studies elucidate the role of GRV in guiding EN in this patient population. However, to date, the vast majority of studies on EN management in critically ill patients are from non-burn populations who have drastically disparate post-injury physiological states.

Early EN, which is now standard-of-care [9], has been shown to be associated with improved outcomes in burn patients [9] and believed to blunt the hyper-metabolic response [10]. However, a known consequence of EEN is elevated GRVs in the initial periods of starting EN [1]. This is further complicated by the fact that patients with large burn injuries (>20% total body surface area (TBSA)) already have a high prevalence of GI intolerance (up to 80%) [11] likely due to the hyper-adrenergic response to thermal injury resulting in decreased mesenteric blood flow [12], high fluid resuscitation use causing bowel edema [13], and high opioid delivery [13] that are present regardless of nutritional support methods. Despite this concern, some authors have proposed that initiating feeds within the first 18 h of thermal injury may reduce the incidence of GI intolerance (40% vs. 60%) [14].

The existence and adherence to EN protocols has been shown to be associated with significant improvements in EN delivery [15]. Therefore, protocols that use elevated GRVs as an indicator to reduce or terminate EN must optimize their cessation thresholds to minimize the risks of aspirating gastric contents while maximizing nutritional supplementation. Because a balance exists between prevention of aspiration complications and providing adequate supplementation, clinicians must examine the practices surrounding GRVs in burn patients. Although prior studies [16–21] have systematically reviewed the topic of GRV monitoring and management, none have focused specifically on the critically ill burn population. With respect to burns, some studies have detailed nutrition protocols [8,22–27] but did not focus on the techniques employed to adjust EN rates. Despite the paucity of studies addressing the optimal timing of GRV measurements, clinically-relevant thresholds, and the appropriate response to elevated GRVs in burn patients, this study will review the current literature on GRV practices as it relates to critically ill burn patients.

2. Methods

A systemic search of the literature was performed using PubMed, SCOPUS, and OvidSP Medline databases. All subsequently identified reference lists of retrieved articles and reviews were manually reviewed. Permutations of the

following keywords and free text were included in all search engine strategies: burns; thermal injury; gastric residual volume; enteral feeding; tube feeding; enteral nutrition; gastric intolerance; ICU; critical illness. The search was restricted to English language, those with English translations, full text availability, primary source (including randomized controlled trials, prospective observational, and retrospective studies), and human subject only (including both adults and children). The final search was completed in October 2017 to include all articles published between January 1, 1900 and October 31, 2017.

Articles were included if they:

1) presented original quantitative data.
2) defined the patient population being evaluated with respect to demographics and mechanism of injury.
3) involved critically ill patients.
4) defined the GRV threshold used to identify EN intolerance.
5) clearly defined GRV-dependent management protocols and/or algorithms.
6) incorporated statistical analysis to support conclusions.

The titles, abstracts, and full text of identified articles were independently reviewed by four researchers (CP, ZC, CK, JG) to determine eligibility. Excluded studies included: reviews, case reports, independent abstracts, consensus and opinion papers. Studies focusing on EN in non-critically ill patients were also excluded.

Data were extracted regarding study design, patient demographics and burn injury characteristics (e.g., age, race, gender, TBSA, number of subjects,), type and terminal location of feeding tubes, GRV thresholds, GRV management protocols, nutritional outcomes (calories received/prescribed), medical outcomes, and complications.

3. Results

3.1. *Study selection*

The electronic database search initially produced 94 articles, which were reduced to 83 after duplicates were removed (Fig. 1). Screening titles and abstracts for eligibility to the research question resulted in the exclusion of 19 articles. After full text review of the remaining 64 articles, 38 were excluded and 26 were included for data extraction and analysis.

These 26 original articles addressed GRV monitoring and management in critically ill patients of all mechanisms (Table 1). Only six of these studies examined burn patients. We aim to address the conclusions and limitations of the 20 non-burn and 6 burn studies as well as their applicability to the evidence-based care of the burn patient.

4. Discussion

Underfeeding in the ICU is common [28,29] and can be due to many factors, including under-prescribing by physicians [28] and feeding cessations (i.e., due to high GRV, frequent surgical procedures with prolonged perioperative fasting, increasing administration requirements, etc.) [28]. Many ICUs now implement a multidisciplinary approach to patient care,

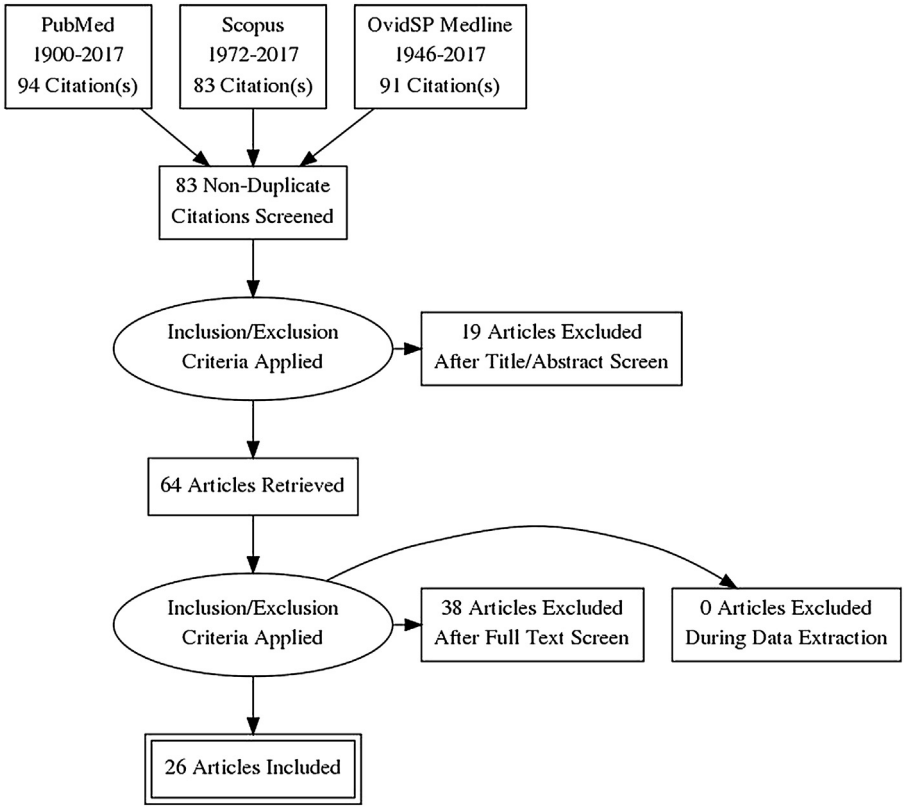

Fig. 1 – PRISMA diagram.

Table 1 – Study summaries.

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
Conrad et al., 2017 [48]	Prospective (P)	Yes (Y)	Group 1 (pre-protocol) =6.24%	Group 1 (pre-protocol, retrospectivel) =26	39.65 (22.37)	19 (59%; 73%)	~	~	Group 1: variable–variable sampling	Group 1: no refeeding or catch-up rate	% of patients who received 100% goal feeds: group 1: 61.6% of prescribed days group 2: 85.4% of prescribed days (P<0.001) Hours TFs held for surgery (13.4 vs 13.3), procedures (4 vs 4.4), clogged (5.9 vs 4.9) or dislodged tubes (5.7 vs 5.5): equivocal
			Group 2 (post-protocol) =18.4%	Group 2 (post-protocol, prospective)=21	34.56 (22.12)	13 (41%; 62%)			Group 2: 0-14 yrs: 2.5x infusion rate – q4h 15+ yrs: 400 mL – q4h	Group 2: refeed GRVs with fresh formula, catch-up rate is 2x prior rate	No statistically significant differences in length of stay (23.5 vs 21 days), ventilator days (7.5 vs 6), or mortality despite significant difference in burn size (6.24 vs 18.39%, P=0.01) 6 (7%) patients had EN interruptions 2/2 large GRVs.
Czapran et al., 2015 [34]	Retrospective (R)	Y	~	88	41(~)	~	Nasogastric tube (NGT), NOS	70 (81%) =gastric tubes	60 (67%) of study pts belonged to ICUs that used GRVs as part of their feeding protocol.	~	
								6=post-pyloric	Median threshold was 200 (100-400)		No association bw mortality and GRVs when comparing ICUs that had GRV protocols and those that did not (P=0.533)
								10=gastric→postpyloric			No sig diff in caloric deficits bw pts belonging to ICUs that had GRV protocols compared to those that did not have a protocol (P=0.056)
Kesey et al., 2013 [24]	R	Y	Group 1 (study)=27%	Group 1 (study): 42 study	Group 1 (study) =45.6 (~)	~	NGT, NOS	Gastric	New protocol=400– q4h	>400 1st time→replace and maintain, check again in 4 h→still elevated→replace and decrease by 20 mL/h and check in 4 h	Total daily GRV was similar bw groups on Day 1 but higher in study group from Day 2 onward.
			Group 2 (control) =30%	Group 2 (control):34 control	Group 2 (control) =47.7 (~)						No sig diff in clinical outcomes (total LOS, mortality, ±pressors, antibiotic days) More ileus in study group than controls (P=0.037).

Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
											No diff in use of prokinetics or bowel regimens.
Hogan et al., 2012 [51]	R	Y	Group 1 (positive blood culture): 40 (~)	Group 1 (positive blood culture): 101	Group 1 (positive blood culture): 27 (~)	Group 1 (positive blood culture): 91:10	~	~	2x feeding rate-sampling interval not specified	~	High residuals correlated with positive blood cultures only 6.9% of the time
			Group 2 (negative blood culture): 22 (~)	Group 2 (negative blood culture): 95	Group 2 (negative blood culture): 31 (~)	Group 2 (negative blood culture): 84:11					Non-high residuals correlated with negative blood cultures 5.9% of the time (P=0.717)
Wolf et al., 1997 [50]	R	Y	>80%	91	~		NGT, NOS	Postpyloric only	150	~	In each episode of epsis, EFI was ID'ed before a positive blood cx in 70% of pts, thrombocytopenia in 64%, hyperglycemia in 66%, No differences ID'ed among these 3 indicators of sepsis and that each indicator did not develop in all patients and none of the indicators were present in some patients.
Raff et al., 1997 [14]	R	Y	44.2±17.4	55	37.6 (17.3)	45:10	12-14F NGT	Gastric	Used the rate as a threshold– q2h	If RV > EN rate, then reduce rate and gradually titrate up	81.8% of pts could be fed within 72h and met nutritio~l needs
Ozen et al., 2016 [42]	RCT	No (N)	~	Group 1 (no routine GRV monitoring) =26	Group 1=68 (18)	Group 1=17:9	NGT, NOS	~	Group 1: no monitoring	If >250, then stop feeding for 4h and repeat GRV in 4h.	Feeding goals reached more quickly in "not checking" group with no increase in complications (15.7 vs 18.8h; P<0.05)
				Group 2 (routine GRV monitoring) =25	Group 2=65 (15)	Group 2=10:15			Group 2: 250– q8h	If still >250, hold feeds for 6 more hours and measure again.	No significant relationship between GRVs and reflux (P>0.05)
Blaser et al., 2015 [6]	R	N	~	1712 patients on EN	Survivors=59	Survivors=945:546	NGT, NOS	~	500mL/24h– QD	~	GRVs above 500mL/24h associated with increased mortality (17.6 vs 9.2%, P<0.001)
					Non-survivors=63	Non-					Defining "feed intolerance" with 3/5 GI markers was most

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Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
						survivors=134:87					strongly related to ICU mortality (6.3% prevalence in survivors; 23.5% in non-survivors, P=0.001, OR=3.39)
Gungabissoon et al., 2015 [5]	R	N	~	1888 patients	57.6 (17.6)	1145:743	NGT, NOS	Gastric only	~	~	EN interruption 2/2 "intolerance" occurred 576 occasions High GRVs was cited as a "reason for intolerance" in 355/576 occasions Examined GRVs and nutritional outcomes showed that "tolerant" patients had significantly more % calories/protein, fewer VFDs, shorter ICU stays, and shorter time-to-discharge
Reignier et al., 2013 [41]	RCT, multi-center	N	~	Group 1 (intervention)=452	Intervention=61 (15)	Intervention=159:68	NGT, NOS	Gastric	Group 1: no monitoring	<250=replaced	Hazard ratio of cumulative VAP incidence in intervention vs control was 1.06 (90% CI, 0.72–1.55; P=0.80) in the modified ITT population and 1.09 (90% CI, 0.74–1.60; P=0.80) in the per-protocol population.
				Group 2 (per-protocol)=423	Control=62 (14)	Control=156:66			Groups 2 & 3: 250–q6h	>250=not specified	OR of VP in intervention was 0.98 (90% CI, 0.66–1.43) in ITT and 1.01 (90% CI, 0.68–1.49) in per-protocol. Significantly more vomiting in intervention group than control (OR 1.86; P=0.003) but no sig difference in VAP, new infections, ICU stay, total LOS, organ failure scores, or mortality rates.
				Group 3 (intention-to-treat)=449							
Metheny et al., 2012 [4]	Survey	N	~	2298	~	~	~	~	~	~	97% of respondents used GRVs to assess for GI tolerance to tube feeding. Most common threshold was between 200-250 mL 25% of respondents interrupted feeding for thresholds below

Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
											150 mL 12.6% of respondents allowed threshold of 500 mL before interrupting feeding.
Ahmad et al., 2012 [47]	Survey	N	~	582 respondents	~	~	~	~	~	~	89% of nurses said they stop TF at volumes <300 mL Only 3% of nurses said they stop TF at volumes >400 mL Top 3 reasons for TF holding: 1) risk of aspiration 2) potential feeding intolerance 3) risk of regurgitation
Hsu et al., 2011 [7]	P	N	~	Group 1 (survivors)=43 Group 2 (non-survivors)=18	67.9 (2)	43:18	NGT, NOS	Gastric	Two definitions of elevated GRV–q4h 1) >500 2) 200–500 PLUS abd distension,--BS, n/v	Held if reached criteria. Restarted once GRV <200	Non-survivors=higher mean GRV (74±31) Survivors=lower mean GRV (38±6.9)
Quenot et al., 2010 [40]	P, multi-center	N	~	203	62 (18)	134/69	~	~	~	~	MV days=12 (9) ICU stay=15 (13) Total LOS=28 (19) ICU mortality=25% In-hospital mortality=32% GRV was measured in 135 patients; not measured in 68 patients +GRV=68% prescribed/required -GRV=77% prescribed/required P=0.002 +GRV=83% delivered/prescribed −GRV=95% delivered/prescribed P=0.01
Montejo et al., 2010 [39]	P	N	~	Group 1 (control)=165 Group 2 (study)=157	Group 1 (control)=60 (25) Group 2 (study)	Group 1 (control)=63:37 Group 2	8, 10, 12F NGT	Gastric only	Group 1 (control): 200 Group 2 (study): 500	Measured q6h on Day 1, q8h on Day 2, and qd after the 3rd day of tolerated EN. Measure with gravity	No sig diff in MV days, ICU days, P~, VFD, ICU mortality, hospital mortality

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					=65 (27.5)	(study) =71:29				drainage for 10 min or 50 mL syringe aspiration through gastric tube Pro-kinetic given on Day 1 at time of EN initiation	
Heyland et al., 2010 [15]	P+R	N	~	20=pre-protocol 30=post-protocol	Before=59.5 (17.3) After=64.4 (16.7)	Before=9:11 After=13:17	~	~	200– q4h=Old protocol 250– q4h=New protocol	Old protocol: If below 200, advanced by 25 mL/h every 4 h. If 2 or more high consecutively high GRVs, feeds reduced by 25 mL/h and prokinetics ordered (start with reglan, then erythro) New protocol: If >250, add erythro on top of the already prescribed reglan	No sig diff in vomiting, regurgitation, macro-aspiration, or P~ (48 h after ICU admission)
Soroksky et al., 2010 [43]	P	N	~	Group 1 (high GRV, >500 mL)=10 Group 2 (low GRV, <500 mL)=42	Group 1 (high) =52.9 (25.8) Group 2 (low) =61.5 (20.6)	Group 1=8:2 Group 2=24:18	NGT, NOS	Gastric	500– measured 4 h after initiation then QD if below threshold.	If >500, feeds held for 4 h and reglan started. At second assessment, if still elevated, then held until next day. If elevaetd on the 3rd day, then EN stopped and TPN started. EN withheld when: 1) 3 consecutive GRV >500 2) 2 consecutive vomiting/regurg within 24 h 3) UGIB 4) GI surgery	Average daily GRV in both groups similar except for Day 3 and Day 4 in which GRV was significantly higher in the high GRV group. 10 regurg/vomiting events in low GRV group 3 regurg/vomiting events in high GRV group Of the 13 regurg/vomiting events, only 1 developed VAP More pts with vomiting in the low GRV group; however, statistical significance not reached. Pts with and without VAP had similar GRVs and similar paracetamol absorption.
Poulard et al., 2010 [44]	P	N	~	Group 1 (routine GRV measurements)=102 Group 2 (no	Control=62 (16) Exp=63 (15)	Control=66:36 Exp=73/30	14F NGT	Gastric only	Group 1: 250– q6h Group 2: no monitoring	If >250, rate decreased to previously well-tolerated rate and erythromycin started. Monitored again in 6 h and	No sig diff in MV days, ICU stay, total LOS, ICU mortality, or hospital mortality. Sig. higher EN/day in intervention group (1489 vs 1381,

Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
				routine GRV measure-ments)=103						increased by 25 mL/h to goal.	P=0.002). Median daily EN volumes greater in intervention group than controls on Days 1 and 2 of the 7-day study period but did not differ bw groups on Days 3–7 Intolerance recorded in 47 (46.1%) of controls and 27 (26.2%) of intervention patients (P=0.004). Control group had higher mean cumulative erythromycin dose (1593 vs 888, P<0.05). No sig diff in rates of vomiting (24.5% vs 26.2%, P=0.87) Rates of VAP not sig diff bw groups (20.9 vs 16.9/1000 pa-tient-days of intubation in control group and intervention groups, respectively, P=0.9) In the control group, of those that had VAP, there was no sig diff between those that had elevated GRVs and those that did not
Cahill et al., 2010 [46]	Audit of best prac-tices at different sites and ICUs	N	~	2946 (18.6 pa-tients per site)	59.7 (17.6)	1729:12-17	~	~	Audit threshold=250 or greater	~	Mean (actual) threshold in the study=217 (50-500) Only 24 ICUs (15.2%) used the recommended CPG threshold of 250 or greater. Found that elevated GRVs oc-curred 782 (27%) had high GRVs. Prokinetic agents used on av-erage 58.7% (461/782) and SB feeds (14.7%, 115/782). Of the 158 participating sites, only 34 (21.5%) used promotility agents and 4 (2.5%) used SB feeds when high GRVs occurred (i.e., 100% compliance with

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Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
											guidelines) In contrast, 24 (15.2%) and 92 (58.2%) of sites did not utilize promotilty of SB feeds (i.e., 100% noncompliance)
Metheny et al., 2008 [37]	P	N	~	206	51.9 (18.1)	126:80	10F NGTs	~	Group 1: 150– q4h Group 2: 200– q4h Group 3: 250– q4h	<200=replaced. EN holding protocol not specified.	3286 GRVs measured (mean=37.1±36.6) GRVs and aspiration did not have a consistent relationship with aspiration occurring fairly often when GRVs were consistently low (33.7% occurred when GRV between 0 and 50mL). However, aspiration occurred more frequently when GRVs increased (F=7.7, P<0.001) 3 heavy predictors of aspiration: 1) 2 or more GRVs > 200mL 2) 1 GRV >250 3) 2+ GRV >250
McClave et al., 2005 [36]	P	N	~	40	44.6 (18-88)	28:12	NGT, NOS	Gastric only	Group 1: 400– q2h Group 2: 200– q2h	Group 1: Held for RV >400 Group 2: Held for RV >200	RV≤50mL on 83% of bedside evals RV≤150mL on 93.2 of bedside evals RV≤400mL on 1.5% of bedside evals Over the wide range of RVs, frequency of aspiration or regurgitation did NOT change, suggesting virtually no relationship between RV and these clinical events Estimated that the PPV of elevated RVs is only 18-25% of the time depneding on the threshold for RV No sig correlation between presence of suspected or confirmed P~ at any time during hospitalization and %

Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
											regurgitation (r=0.123; P=0.502) or % aspiration (r=0.139; P=0.442)
Elpern et al., 2004 [30]	P	N	~	39	60.6 (~)	21:18	OGT, NGT, PEG	Not specified	150– q8h	<150=replace and continue >150=replace, hold, recheck in 1 h. a) >150 after 1 h and no vomiting=do not replace, continue to hold and notify MD. b) <150 after 1 h and no vomiting=replace and continue feeding If +vomiting, do not replace and notify MD.	GRVs exceeded the 150 mL threshold on 28 measurements in 11 patients 5 pts experienced episodes of n/v feeding aspiration occurred in 4/276 feeding days Mean fasting duration for tests and procedures was 6.5 h
Roberts et al., 2003 [29]	R	N	~	50	57.5 (17.5)	27:23	NGT, NOS	93% gastric 7% postpyloric	Varied by provider– not standardized	Not specified	38% prevlalence of elevated GRVs
Pinilla et al., 2001 [35]	P+R	N	~	Group 1 (old protocol): 36 Group 2 (new protocol): 44	Group 1=49.1 (21.6) Group 2=56.7 (16.9)	Group 1: 21:15 Group 2: 23:21	14-18F NGT	Gastric only	Group 1: 250– q4h until goal feed rate reached; q12h once goal reached Group 2: >250	If elevated 1x, held for 4 h then restarted later at 25 mL/h and then increased by 25 mL/h q4h until goal reached If elevated 2x, then held for 6 h then restarted at 50% and increased by 25 mL/h q4h until goal	19/36 (0.53) (old) had more elevated GRVs than new 10/44 (0.23) (new) (P<0.005) No sig diff in emesis, diarrhea, time-to-goal, and calories received. Pts in group 1 9x more likely to have high GRVs
Mentec et al., 2001 [32]	P	N	~	153	Not specified	Not specified	NGT, NOS	Gastric only	Not specified threshold but defined "upper digestive intolerance": 1) 150-500 at 2 times 2) >500 1 time 3) Emesis	~	32% (49 pts) had increased RV after median EN of 2 days 46% (70 pts) had UGI intolerance Independent risk factors for high RV were: 1) RV >20 mL before start of EN (OR=2.16, 1.11–4.18, P=0.02) 2) RV >100 mL during EN (OR=1.49, 1.01–2.19, P<0.05) 3) Sedation during EN (OR=1.78, 1.17–2.71, P=0.007) 4) Use of catecholamines during

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Table 1 (*continued*)

Study-author, year	Study design	Burns (yes/no)	TBSA (%)	Sample size (N)	Age (SD)	M:F	Type of feeding tube	Location of feeding tube	GRV threshold (mL) and interval qxh=every x hours	GRV management	Outcomes/complications
McClave et al., 1992 [33]	P	N	~	Group 1 (study): 10 critically ill (8/10 on ventilator) Group 2 (control): 8 stable pts with PEGs 20 healthy volunteers	69.6 (~)	Group 1 (study) 18 men Group 2 (control) 10 men 10 women	NGT, NOS	Gastric	Threshold not specified – q2h	Aspirate re-introduced. Authors did not specify elevated GRV protocol	EN (OR=1.81, 1.21–2.70, P=0.004) High RV associated with: 1) Lower feed intake (15 vs 19 kcal/kg/day, P=0.0004) 2) Emesis (53% vs 23%, P=0.0002) UGI intolerance associated with: 1) Higher P~ risk (43% vs 24%, P=0.01) 2) Longer ICU stay (23 vs 15 days, P=0.007) 3) Higher ICU mortality (41% vs 25%, P=0.03) No patients suffered overt GI intolerance.

~ denotes that the information was not provided in the original article.
Gastric residual volume (GRV); Not otherwise specified (NOS).

which includes routine dietician participation in patient care. The routine involvement of dieticians may help reduce delayed initiation of EN, and under-prescription of nutrition. The larger issue is interruptions of EN; this is extremely concerning for the critically ill burn patient population. One of the factors that contribute to inadequate nutrition is the routine measurement of GRV, as a surrogate for feed tolerance. McClave et al. found that when elevated GRVs were documented as a cause for feeding cessation, up to 70% of these feeding cessations were likely avoidable [28]. Similarly, Elpern et al. and Reid showed that elevated GRVs were the cause of 11.5% of all EN cessations and 14% of all instances of underfeeding in their critically ill cohorts, respectively [30,31].

In the burn population, early EN is associated with a significant decrease in mortality [14]. In addition, GI intolerance can be prevented if patients are fed within the first 18 h post-burn [14]. This 18-h critical threshold, then, becomes relevant in the discussion of GRVs when one considers delayed gastric emptying in burn patients (i.e., higher GRVs) [11] and varying GRV protocols/algorithms that may obstruct EN delivery within this timeframe.

Elevated GRVs are believed to be an early sign of GI intolerance [32], which itself is associated with a higher incidence of nosocomial pneumonia, longer ICU stays, and higher ICU mortalities [7,32]. McClave et al. [33] challenged the utility of GRV measurement as a marker of GI intolerance in a prospective study comparing GRVs to both physical exam (nausea, vomiting, and/or aspiration) and radiographic findings. They reported that GRV $\geq$150 mL did not correlate with objective scores on radiography or physical exam. They found that abnormal physical exam findings and abnormal radiography did not correlate with GRVs. While 13.1% of their cohort (N=38) had GRVs $\geq$150 mL, none of them had overt signs of GI intolerance such as vomiting or aspiration. Their findings were one of the first to challenge the utility of GRVs, and they made the thoughtful argument that a single elevated GRV should warrant suspicion but not cessation of feeding [33].

High GRVs have been associated with increased mortality but this has been challenged. A study of medical ICU survival showed that increases in sequential organ failure assessment (SOFA) scores were significantly associated with elevated GRVs, with non-survivors having nearly double the GRVs of survivors [7]. However, a retrospective burn study reported that cohort experienced a 7% incidence of elevated GRVs, which was not associated with an increase in mortality [34]. In addition, Gungabissoon et al. performed a sensitivity analysis (N=1441) of routine monitoring of GRVs at a threshold of 200 mL and its effects on nutritional outcomes and mortality and found that while it was associated with poorer nutritional outcomes ($P<0.0001$) it was not associated with changes to mortality ($P=0.19$) [5]. With this in mind, there is a need to dichotomize "elevated GRVs" from "GI intolerance". In other words, high GRVs alone do not necessarily indicate GI intolerance. This careful use of language was demonstrated in Blaser et al.'s findings [6], which indicated that GI intolerance was associated with increased mortality but the strength of that relationship depended on the definition used. They found that, while not immediately generalizable, their "best" definition for GI intolerance was patients receiving <23% of their prescribed EN [6]. This new evidence suggests that much of the evidence toward revising our GRV monitoring practices is in the interest of preventing avoidable feeding cessations and its effects on nutritional outcomes. Therefore, a single incident of high GRV in and of itself, may not be indicative of GI intolerance and should increase surveillance but not precipitate EN reduction or cessation.

High GRVs were previously considered to be associated with higher rates of aspiration, regurgitation and pneumonia, and even used as a predictor of aspiration [2]. This prompted clinicians to study which cutoff value of GRV should be used to suspend EN [2,24,35–39]. Pinilla et al. performed a randomized controlled trial and compared GRV thresholds of 250 mL versus 150 mL and examined patient outcomes [35]. The elevated threshold group did not experience differences in emesis, diarrhea, and volume of nutritional support received but did show a trend toward earlier time-to-goal feeds ($P=0.09$). It is worth noting that their 250 mL GRV cohort was prescribed mandatory pro-kinetics, which is a common practice and appears in the "Enhanced Protein-Energy Provision via the Enteral Route in Critically Ill Patients (PEPuP) protocol" [38].

McClave et al. later demonstrated that increasing the GRV threshold from 200 mL to 400 mL did not significantly increase the risk of aspiration between intervention and control groups (22.6% vs. 21.6%, $P>0.05$) [36]. Interestingly, they found no correlation between regurgitation and aspiration events and GRVs. These authors then argued that low GRVs did not assure the absence of aspiration or regurgitation because 23% of their cohort's aspiration events occurred when GRVs were less than 150 mL. They agreed with Mentec et al. and asserted that elevated GRVs may have clinical meaning only when combined with vomiting, sedation, sepsis, or need for vasopressor support [36]. In addition, McClave et al.'s findings were later corroborated by Metheny et al. [37], who agreed that there is no consistent relationship between GRVs and aspiration [37]. While these studies [35–38] suggest that monitoring GRVs may be for naught, they were not focused in the burn population.

Eliminating GRV monitoring has also been examined [40–44]. In a multi-center prospective study Quenot et al. followed 135 medical-surgical ICU patients that received GRV monitoring and 68 who did not and found that patients who did not receive routine GRV monitoring went on to receive more delivered/prescribed EN (95% vs. 83%, $P=0.01$). The multicenter randomized controlled trial of 9 ICUs (medical and medical-surgical ICUs) by Reignier et al. demonstrated that their critically ill cohort could forego GRV monitoring without an increase in the incidence of ventilator associated pneumonia (VAP) compared with those who underwent routine GRV monitoring [41]. While they also showed that the non-monitoring group had significantly more vomiting ($P=0.003$) than the group that received monitoring, it was not associated with an increase in infectious complications, ICU days, total length-of-stay, or mortality [41]. In addition, the group who did not undergo routine GRV monitoring also had quicker 'time-to-goal' EN rates [41]. Similar findings were also reported in a study by Ozen et al. [42]. Soroksky et al. (GRV threshold up to 500 mL) and Poulard et al. (no GRV monitoring) performed prospective studies and reported that patients who developed VAP and those who did not had similar GRVs [43,44] and similar rates of paracetamol absorption (a test for delayed gastric emptying) [43], further suggesting minimal correlation

between an elevated GRV and the development of a VAP [43,44]. Even the process of aspirating and monitoring GRVs is not without consequence because small-bored nasogastric feeding tubes are frequently used for nutritional support in burn patients, and it has been shown that aspirating small-bore tubes can cause tube occlusion [45]. Tube occlusion, then, delays feeding in the forms of direct occlusion or time spent replacing the tube.

Through the years, as more studies [41–44] continued to challenge the necessity of routine GRV monitoring, the guidelines surrounding the practice have evolved. The 2013 Canadian Critical Care Practice Guidelines assert that a GRV threshold of 250-500 mL [3] should be the point at which one considers holding EN, and the 2016 ASPEN guidelines [2] recommend that EN should not be stopped unless GRV $\geq$ 500 mL with all GRVs below that to continue unless there are other signs of GI intolerance [2]. Despite this, many institutions have adopted different thresholds [46] at which to discontinue feeds. A survey of critical care nurses across the U. S. indicated that 97% of respondents (N=2298) reported measuring GRVs and most commonly using thresholds of 200–250 mL [4]. Cahill et al. performed an international observational study of the ICU nutrition practices of 158 various types of ICUs (surgical, medical, cardiac, neurologic, burns, etc.) and 2,946 total patients and found that the mean GRV threshold was 217 mL, with only 15.2% of ICUs having used a threshold of 250 mL or greater [46]. While not specifically examined, it is imaginable that any feeding cessations attributable to 84.8% of the ICUs that used GRV thresholds below 250 mL were largely avoidable. A U.S.-based survey of ICU (medical and surgical) nurses similarly found that 89% [47] of respondents held EN at volumes below 300 mL and reported that the top three reasons for this were: fear of aspiration, potential feeding intolerance, and risk of regurgitation. These fears are likely over-estimated as high level evidence suggests that elevated GRVs do not correlate well with feeding intolerance, aspiration, or pneumonia [35,36,41,43,44].

A majority of the studies reviewed were performed in medical or surgical ICU patients, with only a small subset of burn ICU patients included in some of the study populations. New feeding algorithms that incorporate standardizing high GRV thresholds have recently been examined as a means to increase the amount of days burn patients receive 100% of their prescribed EN [48]. Conrad et al. prospectively examined feeding algorithms (determined by age) [48] to significantly increase the amount of days that burn patients received 100% of prescribed calories. A central component of their study algorithm was increasing GRV thresholds and the GRV threshold for patients ages 0–14 was 2.5x the EN hourly rate and the GRV threshold for their patients older than 15 years old was 400 mL. Both groups had their GRVs monitored every 2–4 h and the protocol dictated continuous feeding at the current rate if the threshold was exceeded once. It was only after exceeding the threshold twice that the EN rate was decreased and exceeding it three times that EN was ceased completely [48].

Compared to patients under the old protocol, patients under the new protocol experienced significantly more days receiving 100% of prescribed EN (59.9% vs. 76.5%, $P=0.003$). There were no significant differences in adverse outcomes, including infections between groups. This study, however, is limited by its small sample size (N=37 in both groups) and may be underpowered to detect statistically significant differences.

Regardless, their results do corroborate the idea that adopting higher GRV thresholds in burn patients can effectively increase the amount of time patients spend receiving 100% of their prescribed EN rates, which has the metabolic and wound healing benefits previously described.

The connection between opioids and gastroparesis are well-known and, unfortunately, few of the studies [7,32,37] in this review systematically detailed their use of opioids and its direct effects on GRV. Mentec et al. demonstrated that patients receiving sedation had an increased odds of having elevated GRVs (OR=1.78, 95% CI=1.17, 2.78, $P=0.007$) [32]. Because of the high pain medication use often seen in burn patients, examining opioid use in conjunction with elevated GRVs in future burn studies would be prudent and further clarify their relationship.

Many practitioners use pro-kinetic agents (e.g., metoclopramide, erythromycin, cisapride) as a response to or as prophylaxis to feeding intolerance and these drugs were used variably across studies [4,24,32,35,38–42,46]. Because many of these studies were not designed to measure the effect of pro-kinetic agents on GRVs, few of them could draw firm conclusions about the efficacy of pro-kinetics on lowering GRVs. Only one of the studies [35] in this review directly examined the effects of pro-kinetics on GRVs (i.e., what is the change to GRV after introducing a pro-kinetic agent?) and found that pro-kinetics are significantly associated with lower GRVs ($P<0.0001$). In contrast, Kesey and Dissanaike found that their burn patients that received pro-kinetics did not experience a significant difference in feed intolerance [24]. They argue that perhaps starting pro-kinetics early instead of on an as-needed basis may have resulted in a noticeable improvement in feed tolerance. This early use of pro-kinetics is embodied in the PEP uP protocol [38], which advocates the use of pro-kinetics in all patients while starting them at goal feed rate. The results of these studies suggests that early and routine use of pro-kinetic agents may be beneficial in reducing GRVs and an appropriate response to isolated incidences of elevated GRVs in lieu of interrupting feeds.

The incidence of and indications for small bowel feeding varied across studies [3,5,34,46] from 6% [34] to 100% [49]. Others were designed specifically to exclude patients receiving small bowel feeding [35]. Like the use of pro-kinetics and its effects on GRVs, many of these studies were not designed to meaningfully examine the relationship between small bowel feeding and GRVs. However, the Canadian Clinical Practice Guidelines [3] advocate the use of small bowel feedings in patients with multiple bouts of elevated GRVs at a threshold between 250-500 mL. Similarly, the 2016 ASPEN guidelines state although that there are no differences in LOS or mortality between gastric versus small bowel feeding, they recommend small bowel feeding whenever possible due to meta-analysis data showing improved nutrient delivery ($P<0.00001$) and reduced rates of pneumonia (RR=0.75, $P=0.01$). In regard to responding to isolated incidences of elevated GRVs, we would argue against the routine advancement of post-pyloric tubes because elevated GRVs do not always indicate GI intolerance [6].

In burns, elevated GRVs have long been used as a marker of sepsis [50], perhaps prolonging their use in burn care. Wolf and colleagues [49] used retrospective data of 91 pediatric burn patients with ≥80% TBSA involvement to show that enteral feeding intolerance was significantly associated with sepsis ($P<0.001$). They found that 71% of episodes of sepsis were preceded by enteral feeding intolerance, which was closely correlated with positive cultures, thrombocytopenia, and hyperglycemia, the traditional markers of burn sepsis. It is worth noting that the authors defined feeding intolerance as having at least one of the outcomes: GRVs ≥150 mL, diarrhea (≥2.5 L/day), and/or abdominal distention [49]. Although it is unclear how many patients fit intolerance criteria due to elevated GRVs alone, it demonstrates the use of GRVs as a relatively non-invasive method to detect sepsis, which could herald changes to management.

The premise of Greenhalgh et al.'s findings is currently reflected in the American Burn Association (ABA) sepsis criteria [50]. Feeding intolerance is defined by the ABA sepsis criteria as GRVs greater than two times the feeding rate, abdominal distension, and/or diarrhea ≥2.5 L/day. However, the concept of feeding intolerance and high GRVs as predictors of sepsis has been recently challenged as they did not correlate strongly with bacteremia [51]. In a study challenging the sensitivity of the ABA sepsis criteria against the gold standard of blood cultures [51], high GRVs were not shown to be associated with predicting sepsis when considered as both a categorical (high versus low) or continuous variable. If, in fact, GRVs lack the historic association with sepsis that earned it its place in the ABA sepsis criteria, it is one argument in favor of discontinuing the practice.

Although several non-burn studies suggest that foregoing GRV monitoring could increase the amount of EN received, which would be favorable in burn patients, it would be imprudent to generalize these recommendations to the burn population without further research. Burn patients have different physiologies from standard medical and surgical ICU patients. For example, Kesey and Dissanaik showed that aggressive feeding in burn patients is significantly associated with developing ileus and no difference in tube feed volume received [24]. Also, the REGANE study [39], although not focused on burn patients, showed that increasing GRV thresholds from 200 mL to 500 mL significantly increased EN volume received during the first week ($P=0.0001$) but did not significantly increase the amount of EN received after the second week The authors then argued that 500 mL may be recommended as a normal limit for GRV. In the context of burns, early feeding is essential to blunt the hyper-metabolic response [10] and is safe [8]. Early feeding (~11.5 h after burn) was associated with decreased mortality and gastric stress ulcers [14,52]. Raff et al. also reported that GI intolerance due to early feeding could be prevented if patients were fed within the first 18 h after burn [14]. It is possible that the results of the REGANE study, which advocate 500 mL GRV thresholds, may be applied to burn patients, but further investigations are needed.

In summary, there is likely enough evidence to support abandoning routine monitoring of GRVs in medical ICU patients [2,26,27]; however, similar recommendations cannot be made for burn ICU patients due to the paucity of data. Based on our findings in this systematic review of limited studies which do not focus on burn patients, we would recommend continuing routine GRV monitoring. Although one study advocates using a threshold of 500 mL in burn patients, there is insufficient data to provide definitive recommendations on the cutoff value of GRV. Due to the increased metabolic needs of burn patients, we would advocate that in patients with GRV ≥500 mL, without other signs of GI intolerance, the EN rate should be decreased rather than completely discontinued, but more studies are needed to support this recommendation.

There is a pronounced need for randomized controlled trials to investigate optimal GRV practices in critically ill burn patient population. Areas of further research include designing RCTs to compare eliminating routine GRV monitoring to routine GRV monitor on the effects of complications and mortality, and the optimal GRV cut-off values. Further studies on using GRV as predictors of sepsis in burn patients are also required.

Conflict of interest

None.

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