

# The effect of intra-abdominal hypertension on gastrointestinal function

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**Introduction.** Intra-abdominal hypertension (IAH) is a frequent occurrence in critically ill patients. Raised intra-abdominal pressure negatively affects gastro-intestinal (GI) function and may reduce the success of enteral nutrition support, which in turn is associated with adverse clinical outcomes.

**Aim.** To evaluate the impact of raised intra-abdominal pressure (IAP) on GI function and success of enteral nutrition support in an adult intensive care unit (ICU) population at risk of abdominal compartment syndrome (ACS).

**Methods.** In a prospective observational study, critically ill patients in whom the IAP was monitored routinely for clinical indications were assessed for GI symptoms, methods of nutrition support and enteral feeding success on a daily basis.

**Results.** In total, data from 17 patients for a total of 98 patient days were included in the study. The mean IAP was 14.0 mmHg (standard deviation (SD) 3.7) on admission to the ICU. There were 10 patients with grade I, 2 with grade II and 2 with grade III IAH. Seven patients (41%) developed ACS. GI symptoms were common in patients with IAH, and days of IAH correlated positively with number of GI symptoms ( $r=0.85$ ,  $p=0.000$ ). Exclusive enteral feeding was possible on 32% of study days. There was a 12% incidence of enteral feeding intolerance and a 59% incidence of enteral feeding failure. Enteral feeding failure was not significantly associated with IAH ( $r=0.43$ ,  $p=0.08$ ), but was associated with number of GI symptoms ( $r=0.67$ ,  $p=0.003$ ). Days of IAH were positively associated with longer ICU stay ( $r=0.65$ ,  $p=0.005$ ), as was prevalence of IAH combined with concurrent GI symptoms ( $r=0.71$ ,  $p=0.001$ ). Days with IAH and multiple GI symptoms combined was associated with worse subsequent sequential organ failure assessment (SOFA) score ( $r=0.64$ ,  $p=0.005$ ). The worst SOFA score in those who died was significantly higher than that of survivors (11.7 (SD 3.05) v. 6.86 (SD 3.2),  $p=0.03$ ), and was also significantly higher in those who developed ACS than in those who did not (10.9 (SD 2.5) v. 5.5 (SD 1.1),  $p=0.0005$ ). The mortality rate was 17%, and only patients who developed ACS died.

**Conclusion.** Raised IAP was associated with poor GI function, enteral feed intolerance, prolonged hospital stay and death.

Intra-abdominal hypertension (IAH), defined as an intra-abdominal pressure (IAP)  $>12$  mmHg, is a frequent though somewhat under-recognised occurrence in critically ill patients.<sup>1</sup> IAH is associated with morbidity and places patients at risk for abdominal compartment syndrome (ACS), which in turn is associated with multiple organ dysfunction and several-fold increased mortality.<sup>2-4</sup> Risk factors for IAH include major abdominal surgery, major trauma, damage control laparotomy, intra-abdominal sepsis, mechanical ventilation, obesity and large-volume fluid resuscitation, among others.<sup>1,5</sup>

IAH has been shown to induce various deleterious effects on gastro-intestinal (GI) physiology, from gut micro-circulatory hypoperfusion, bowel ischaemia and oedema to infectious risk associated with mucosal hyperpermeability.<sup>6,7</sup> There is a perception that clinically apparent GI symptoms are also associated with IAH. This idea may be somewhat speculative, as GI dysfunction manifested by symptoms such as vomiting, regurgitation, diarrhoea, constipation and distension is common among patients in intensive care units (ICUs).<sup>8</sup> The clinical conditions that increase risk for IAH are also risk factors for the development of

GI symptoms, and in patients with IAH enteral feeding itself can aggravate bowel ischaemia or worsen IAH due to fermentation and bowel distension.<sup>9</sup> The precise link between IAH and GI symptoms is therefore currently unclear, including whether GI symptoms might be the cause or the effect of raised IAP.<sup>10</sup>

The question of a possible association between IAH and GI symptoms is relevant, as both IAH and GI symptoms are related to ICU outcomes<sup>8,11</sup> and both are associated with a lower enteral feeding success rate. Since enteral feeding is considered the standard of care for critically ill patients, and failure of successful enteral nutrition delivery is itself associated with unfavourable clinical outcomes,<sup>12,13</sup> there is increasing interest in the clinical impact of IAP on gut function and enteral feeding. A recent study showed that most patients with IAH had GI symptoms, but the relationship between IAH, GI symptoms and enteral feeding remains elusive.<sup>14</sup> We therefore decided to examine this association.

## Materials and methods

A prospective study was conducted in an 8-bed general surgical ICU of a university teaching hospital over a 6-month period. Records

of adult patients ( $\geq 18$  years) who were in the ICU for more than 24 hours and were having their abdominal pressure monitored for clinical reasons were included in the study. Patients not expected to survive for 24 hours were excluded. Data were recorded daily throughout the period during which the IAP was monitored or until the IAH resolved, or the patient was discharged from the ICU or died.

Patient demographics, supine length, estimated body mass index (BMI), caloric requirements (25 - 30 kCal/kg), relevant clinical data and IAP measurements were recorded on admission to the ICU. Acute Physiology and Chronic Health Evaluation II (APACHE II)<sup>15</sup> and Sequential Organ Failure Assessment (SOFA)<sup>16</sup> scores were calculated from relevant clinical variables in the first 24 hours. Length of ICU stay and outcome were recorded for each patient. Intravesical measurement of IAP was performed in the supine position, using a water manometer and an infusion volume of 25 ml of 0.9% saline with the zero level in the mid-axillary line.<sup>17</sup> This was performed routinely by the ICU nursing staff every 2 - 12 hours as clinically indicated. IAP was measured in cm H<sub>2</sub>O, which was converted to mmHg (1 cm H<sub>2</sub>O = 1.36 mmHg). IAH was defined as an IAP of  $\geq 12$  mmHg, while ACS was defined as IAP sustained above 20 mmHg combined with a new organ dysfunction.<sup>1</sup> The unit policy was to surgically decompress the abdomen in such cases. The abdominal perfusion pressure (APP) was calculated by subtracting the IAP from the mean arterial pressure (MAP).

Variables that were recorded daily included: SOFA score, maximum IAP, MAP and APP simultaneous with maximum IAP, worst arterial pH and serum lactate, nasogastric drainage/aspirate volume, total enteral nutrition volume delivered, and GI symptoms, as defined below. Volume of enteral feed delivered was monitored and recorded daily. Early enteral feeding was routine practice, using a standard enteral feeding protocol. The following definitions were used: *diarrhoea*: 3 or more loose/liquid stools in a 24-hour period; *constipation*: less than 2 stools per week occurring on separate days where the stool is neither liquid nor loose, or where laxatives are required; *vomiting*: regurgitation of gastric contents in any volume; *abdominal pain/discomfort*: the subjective report of pain/discomfort by the patient, or subjective signs of pain or tenderness noted by the doctor when performing an abdominal examination; *abdominal distension*: the subjective assessment by the doctor that the abdomen is enlarged for reasons unrelated to anthropometric features such as adiposity; *high gastric residual volume*: a volume exceeding the amount of feed infused over the previous 4-hour period; *high nasogastric drainage*: free drainage volume of  $>400$  ml in 24 hours; *absent bowel sounds*: the doctor's subjective assessment of very infrequent, pathological or completely absent bowel sounds on abdominal auscultation; *enteral feed intolerance*: inability to increase feeds according to protocol due to one of the above GI symptoms; *enteral feeding failure*: enteral nutrition stopped for clinical reasons or enteral feeding entirely clinically inappropriate and parenteral nutrition therefore utilised.

The study was approved in writing by the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town and was conducted in accordance with the principles of the Declaration of Helsinki (2008) and Good Clinical Practice (GCP). Verbal informed consent was obtained retrospectively from

each patient or their relatives to utilise their clinical records for the purpose of the study audit. Patient confidentiality was maintained.

Statistical analysis was conducted using the STATISICA 10 (Statsoft, USA) software programme. Descriptive data were presented as mean (standard deviation (SD)). Parametric correlations were tested using Pearson's correlation coefficient, *t*-tests and ANOVA were used to test differences in means, and Fisher's exact test was used to test differences in proportions. A *p*-value of  $<0.05$  was considered statistically significant.

## Results

Data from a total of 17 patients over 98 patient days were analysed from clinical records selected during a 6-month period between March and August 2010. The diagnoses and characteristics of the study sample are shown in Tables I and II.

### Intra-abdominal pressure

On admission 14 patients had IAH. Of those, 10 had grade I (mean 12.6 (SD 1.6) mmHg), 2 had grade II (mean 19.7 (SD 0.85) mmHg)

**Table I. Diagnosis and injury characteristics**

Case	Diagnosis
1	Thoraco-abdominal gunshot, trauma laparotomy
2	Motor vehicle accident, blunt abdominal trauma
3	Gunshot abdomen, trauma laparotomy
4	Thoraco-abdominal gunshot, trauma laparotomy
5	Motor vehicle accident, blunt chest and abdominal trauma
6	Thoraco-abdominal gunshot, trauma laparotomy
7	Gunshot abdomen, trauma laparotomy and sub-xiphoid window
8	Thoraco-abdominal gunshot, trauma laparotomy
9	Severe acute pancreatitis, laparotomy
10	Severe acute pancreatitis
11	Severe acute pancreatitis
12	Perforated gastric ulcer, intra-abdominal sepsis, laparotomy
13	Perforated gastric ulcer, intra-abdominal sepsis, laparotomy
14	Bowel infarction, laparotomy
15	Sigmoid volvulus, laparotomy
16	Repair leaking aortic abdominal aneurysm
17	Bowel obstruction, laparotomy

**Table II. Patient characteristics (N=17)**

Age (yrs) (mean (SD))	42.1 (15.6)
Males (N (%))	12 (71)
Estimated BMI (kg/m <sup>2</sup> ) (mean (SD))	26.3 (4.1)
Patients with BMI $>30$ kg/m <sup>2</sup> (N (%))	5 (29)
APACHE Score (first 24 hours) (mean (SD))	18.1 (6.8)
Initial SOFA Score (first 24 hours) (mean (SD))	7.4 (3.5)
IAP on admission (mmHg) (mean (SD))	14 (3.7)
MAP on ICU admission (mmHg) (mean (SD))	89 (17.8)
APP on admission (mmHg) (mean (SD))	73.8 (17.8)
ACS (N (%))	7 (41)
Days in ICU (mean (SD))	12.9 (9.9)
ICU Mortality (N (%))	3 (17.6)

and 2 had grade III IAH (17.6 (SD 6.3) mmHg) IAH. No patient had grade IV IAH on admission to the ICU. The mean (SD) IAP for the entire study period for all patients was 14 (3.4) mmHg. Seven patients (41%) developed ACS during their ICU stay, of whom 4 underwent decompressive laparotomy. The highest measured IAP was 28 mmHg and the lowest 5 mmHg. The 3 patients who did not have IAH on admission all experienced at least one period of IAH during the monitoring period. IAH occurred on 65 of the 98 patient days (66%), with a mean (SD) number of intra-abdominal hypertensive periods of 3.8 (3.6) per patient. The mean worst IAP was 17.4 (4.4) mmHg.

### Gastro-intestinal symptoms

A total of 253 GI symptoms were recorded during the 98 study days. All patients experienced at least one symptom. The most commonly occurring symptoms were abdominal distension (62% of study days), absent bowel sounds (55% of study days), and high gastric residual volumes (36% of study days), followed by inability to advance enteral feeding (27% of study days) and constipation (26% of study days). There was a significant but weak positive correlation between IAP and nasogastric drainage volume ( $r=0.19$ ,  $p=0.048$ ) (Fig. 1). There were 19 episodes of high aspiration volumes during infusion of enteral feeds. Abdominal pain or tenderness occurred on 11 study days. Diarrhoea was uncommon, with only 6 episodes during the study, of which 5 occurred after IAH had resolved. Vomiting or regurgitation seldom occurred (5 episodes). Table III outlines the occurrence of GI symptoms in relation to IAH.

A significantly higher number of GI symptoms occurred in patients with IAH compared with those with normal IAP (Fisher's exact test  $p<0.05$  for all symptom numbers) (Fig. 2). Total days of IAH was also positively correlated with total number of GI symptoms over the study period ( $r=0.85$ ,  $p=0.000$ ).

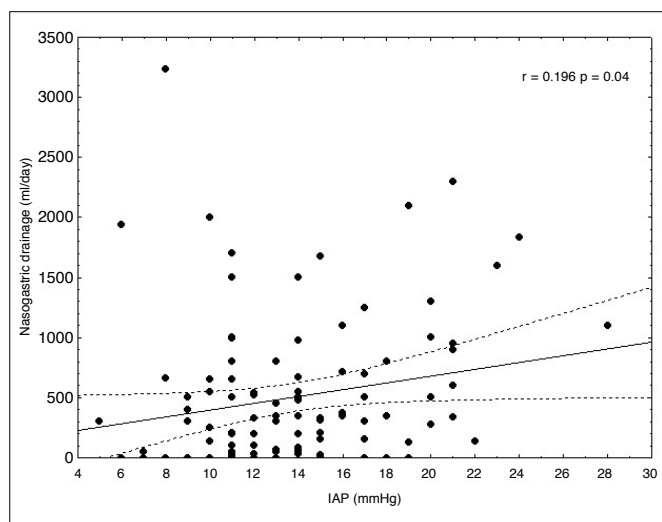


Fig. 1. IAP (mmHg) versus nasogastric drainage (ml/d).

**Table III. Number of days with GI symptoms and IAH during ICU stay**

	No IAH	IAH
No GI symptoms (N (%))	2 (2)	2 (2)
GI symptoms (N (%))	20 (20)	76 (77)
Fisher's exact test	$p=0.008$	$p=0.000$

### Enteral feed intolerance and enteral feed failure

Exclusive enteral feeding was possible during 32% of study days, but delivery of >50% of required calories via this route was only possible on 12% of study days. Enteral feeding intolerance occurred on 12% of study days, while enteral feeding failure occurred on 59% of study days. The incidence of enteral feeding failure was positively linked to number of GI symptoms ( $r=0.67$ ,  $p=0.003$ ) and days with IAH ( $r=0.43$ ,  $p=0.08$ ). Total study days where parenteral nutrition was required amounted to 41% of days. Mixed parenteral and enteral feeding occurred on 15% of study days, and on 12% of days no nutritional support was provided. Days with IAH correlated positively with days where parenteral nutrition was required ( $r=0.48$ ,  $p=0.053$ ). The combination of IAH and GI symptoms (Table III) was significantly associated with number of days requiring parenteral nutrition ( $r=0.64$ ,  $p<0.005$ ) and number of days of enteral nutrition support ( $r=0.5$ ,  $p=0.046$ ).

Fig. 3 indicates the frequency of enteral feed intolerance and failure when IAH was present compared with when IAP was normal. Fisher's exact test showed that enteral feeding intolerance and failure occurred more frequently when abdominal pressure was raised, but this effect did not reach statistical significance.

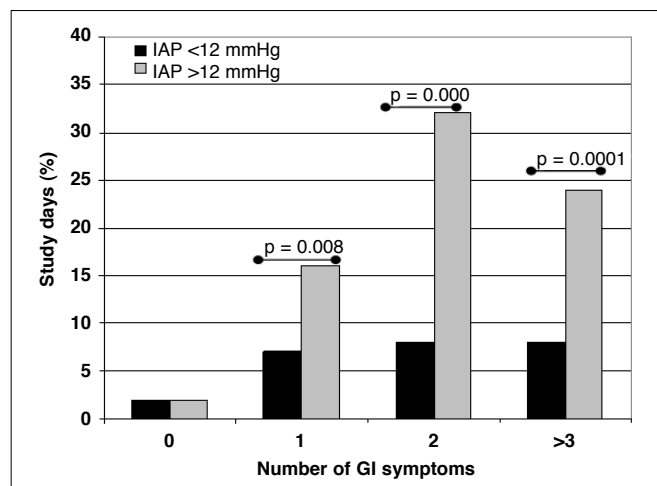


Fig. 2. Number of GI symptoms occurring with and without IAH.

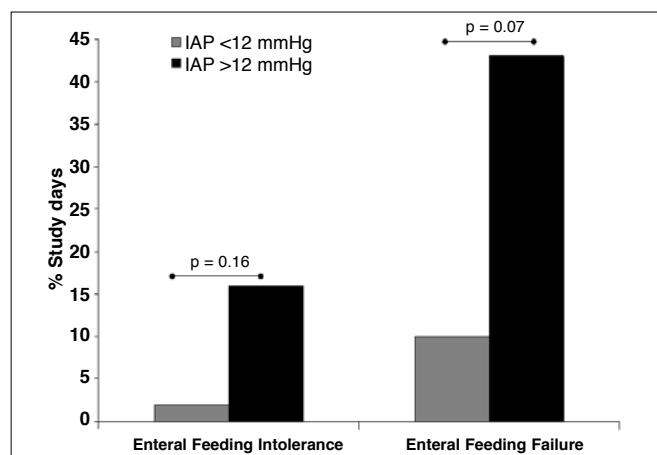


Fig. 3. Study days with enteral feeding intolerance and failure according to category of IAP.

## Clinical outcomes

Number of days during which IAH occurred correlated positively and significantly with ICU stay ( $r=0.65, p=0.005$ ). Seven patients (41%) developed ACS, of whom 3 died; all of these had undergone surgical decompression of the abdomen. The combination of IAH and GI symptoms occurring together was also positively and significantly associated with length of ICU stay ( $r=0.71, p=0.001$ ). Days with IAH combined with multiple GI symptoms was associated with a worse subsequent SOFA score ( $r=0.64, p=0.005$ ). ICU survivors had a significantly lower worst SOFA score than those who died (11.7 (SD 3.05) v. 6.86 (SD 3.2),  $p=0.03$ ). Worst SOFA score was also significantly higher in those who developed ACS compared with those who did not (10.9 (SD 2.5) v. 5.5 (SD 1.1),  $p=0.0005$ ). Deaths occurred only within the sub-group that experienced both IAH and GI symptoms.

## Discussion

In this study 66% of days were spent with IAH and 41% of patients developed ACS. The main findings were a high frequency of both IAH and GI symptoms, with GI symptoms occurring more often and in greater numbers in patients in IAH compared with those with normal IAP. Enteral feeding was possible on only 30% of study days, and there was a high incidence of enteral feeding failure. Enteral feeding failure occurred more frequently when the IAP was above 12 mmHg, but was statistically associated both with the number of GI symptoms and IAH. Unsurprisingly, the combination of IAH with concurrent GI symptoms was associated with higher use of parenteral nutrition. IAH was statistically associated with longer duration of ICU stay. ICU stay was significantly longer when multiple GI symptoms occurred together and when GI symptoms occurred concurrently with IAH. Prior duration of combined IAH and multiple GI symptoms were also associated with a worse subsequent SOFA score, which was significantly higher in patients who died and in those with ACS. Mortality approached 18%, and death occurred in ACS only when patients experienced both IAH and GI symptoms.

In general trauma and trauma followed by abdominal procedures such as laparotomy, IAH has previously been shown to have a prevalence of 30-50% and to be associated with a prevalence of ACS of up to 15%.<sup>11,18</sup> The results of this study reflect a point prevalence of IAH similar to those in other studies of a mixed ICU population.<sup>19</sup> Variations in the reported prevalence of IAH may to some extent reflect differences in defining IAH, i.e. mean IAP versus maximum IAP in different studies, and methodological differences in the frequency and mechanics of IAP monitoring. However, the high incidence of IAH in our group of patients, selected by the ICU clinicians for IAP monitoring, suggests that IAP monitoring should probably be more widely practised in this setting. Importantly, the current study specifically selected patients who were at high risk for IAH and ACS based on their diagnosis or clinical intervention, because of the aim to investigate the occurrence of GI symptoms in this group in particular.

Studies with similar aims to this one have rarely been published. Reintam *et al.*<sup>20</sup> first published the observation that many if not most patients who present with IAH also display GI symptoms. A subsequent study by the same group<sup>21</sup> showed that in a general ICU population, while the total prevalence of GI symptoms was high, the number of GI symptoms increased with increasing IAP.

The results of the current study support both these findings. It is impossible to comment on the temporal or causal relationship between IAH and GI symptoms from these study data; however, it is highly likely that the relationship between IAH and GI symptoms is bi-directional and dynamic, given the known pathophysiology associated with raised IAP. Our study demonstrates that the phenomenon of simultaneous IAH and GI symptoms is associated with worse clinical outcomes such as length of ICU stay and organ failure. This indicates that the prognostic value of gut function in the ICU may be underestimated, and that it would be important to include evaluation of the GI system as a routine part of well-validated prognostic scores, such as the SOFA score, as others have recently suggested.<sup>20,22</sup>

Previous research has consistently demonstrated that IAH correlates with poor ICU outcomes.<sup>3,11,19</sup> The addition of GI symptoms to IAH appears to magnify that effect, as supported by our results and those of others.<sup>21</sup> Of the various proxy markers for outcome in IAH, APP has been shown superior in predicting outcomes,<sup>23</sup> although not in all patient populations.<sup>24</sup> Similarly, in our clinical study, while the expected relationships between IAP, MAP and APP apply, APP was not associated with GI symptoms or length of stay, probably because it was kept high due to high MAPs. IAH reduces APP, and this negatively impacts on intestinal perfusion, compromising mucosal integrity.<sup>6</sup> In our study significant GI symptoms, enteral feeding failure and length of stay occurred with abdominal hypertension despite an adequate APP. This finding is supported by Ke *et al.*,<sup>24</sup> who have recently reported that organ failure-related outcome in severe acute pancreatitis was associated with IAP and not APP, when controlling for all other relevant clinical factors.

Certainly IAH is associated with poor tolerance of enteral feeds,<sup>25</sup> as we have again demonstrated. In this study in particular, IAH, GI symptoms and enteral feed failure occurred in a triad. Others have claimed that enteral feeding is possible in ACS, and have even placed needle catheter jejunostomies in profoundly oedematous bowel, reportedly without complication.<sup>26</sup> This group also reported that enteral feeding was tolerated in 92% of patients, in contrast to our finding of 59% enteral feeding failure. Exclusive enteral feeding was only possible on 1 day in every 3, and less than half of enteral feeding days succeeded in achieving significant calories via that route. There therefore appears to be conflicting evidence regarding enteral feeding failure under conditions of IAH. In fact, the study previously cited<sup>26</sup> really only achieved low levels of 'trophic' feed for several days. While most would not question that commencing enteral feeding early is preferable for most ICU patients, this is not necessarily equivalent to being able to deliver full nutritional requirements via the enteral route. Our study indicates that despite enteral feeding being the standard of care and despite having clinicians motivated to provide enteral feeding, it is difficult to do this with success.

Limitations of this study include the single-centre design, relatively few overall study days, and inability to standardise the definitions of the GI symptoms used against a universal guideline, since none exists. However, our data support other research findings,<sup>20,21</sup> suggesting that GI dysfunction in patients at risk for ACS indicates a worse clinical course of severe illness. As we studied selected patients, our findings cannot be generalised to all critically ill patients.

## Conclusion

In this small study we conclude that GI symptoms occur frequently in patients with raised IAP. The combination of IAH and GI symptoms is associated with low enteral feeding success and worse clinical outcomes.

The authors declare that no conflict of interests exist.

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