GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF ANAESTHESIA

PREVALENCE AND OUTCOMES OF INTRA-ABDOMINAL HYPERTENSION IN CRITICALLY ILL PATIENTS IN A MIXED INTENSIVE CARE POPULATION

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DECLARATION

I, Dr. Irene Bandoh declare that this dissertation was written by me under the supervision of Prof. Akwasi Antwi-Kusi and Dr. Wilfred Sam-Awortwi and that it has not been used for other degrees or diplomas in the past.

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Thank you

DEDICATION

To God, my family and my Boss and Mentor, Moses

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LIST OF ABBREVIATIONS

APACHE II Score	Acute Physiology and Chronic Health Evaluation (APACHE) II score
ACS	Abdominal Compartment Syndrome
AKI	Acute kidney injury
APP	Abdominal Perfusion Pressure
C_{dyn}	Dynamic compliance
CO	Cardiac output
CT	Computer tomography
CVP	Central Venous Pressure
EVLW	Extravascular lung volume
GFR	Glomerular filtration rate
GRV	Gastric residual volume
H_20	Water
IAH	Intra-Abdominal Hypertension
IAP	Intra-Abdominal Pressure
ICP	Intracranial Pressure
ICU	Intensive Care Unit
IROI study	Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients study
LOS	Length of stay
MAP	Mean Arterial Pressure
Na^+	Sodium
$Pa0_2$	Partial pressure of Oxygen
PAOP	Pulmonary Artery Occlusion Pressure
Paw	Airway pressure
$PC0_2$	Partial Pressure of Carbon Dioxide
PCWP	Pulmonary Capillary Wedge Pressure
PEEP	Positive End-Expiratory Pressure
pH	Hydrogen ion concentration

PIP	Peak inspiratory pressure
PLR	Passive leg raise
PPV	Pulse pressure variations
SIMV	Synchronised intermittent mandatory ventilation
RAAS	Renin Angiotensin Aldosterone system
RVP	Renal venous pressure
RVR	Renal vascular resistance
SAPS	Simplified Acute Physiology Score
SMA	Superior Mesenteric Artery
SOFA score	Sequential Organ Failure Assessment score
SPV	Systolic pressure variation
SVR	Systemic vascular resistance
SVV	Stroke volume variation
Vd/Vt	Ratio of dead space ventilation to tidal volume
VFD	Ventilator-free days
VVS	Ventricular venous system
WSACS	World Society of Abdominal Compartment Syndrome

STRUCTURED ABSTRACT

BACKGROUND AND AIM

Intra-abdominal hypertension (IAH) is a condition with significant morbidity and mortality risks in ICU patients, particularly when it escalates to Abdominal Compartment Syndrome (ACS). IAH and ACS can have detrimental effects like, reduced cardiac output, decreased splanchnic blood flow, and renal impairment.

Notably, the prevalence of IAH can be as high as 50.5% among ICU patients. Nevertheless, this condition still demands attention in numerous healthcare facilities, including Ghana.

The main objective of this study was to investigate the prevalence and prognostic implications of IAH in a mixed surgical and medical ICU environment

MATERIALS AND METHODS

The study participants were adult patients admitted to the Main ICU of Komfo Anokye Teaching Hospital. Intra-abdominal pressure was measured on admission and every six hours during the initial 48 hours of admission or until the patient's discharge or demise. The modified Krohn's method was employed to carry out these measurements.

The Sequential Organ Failure Assessment (SOFA) scores of the participants were calculated daily to evaluate the extent of organ dysfunction. The baseline SOFA score on admission served as the reference point for comparisons. This allowed for a comparison between the group with IAH and the group with normal intra-abdominal pressure, aiming to ascertain whether IAH significantly impacted SOFA scores as a metric for organ dysfunction.

The impact of intra-abdominal pressure on critical outcome measures such as ventilator-free days and length of stay in ICU were also measured.

RESULTS AND ANALYSIS

Ninety participants were enrolled in the study consecutively. The results of the same were analysed. The mean age of participants was 44.3(S. D 17.9, CI=40.4-48.03). Males represented the majority of participants with 53.3% while females formed 46.6%.

Intra-abdominal hypertension was defined as “IAP ≥ 12mmHg” according to the WSACS consensus guidelines while abdominal compartment syndrome was defined as “IAP ≥ 20mmHg with new onset organ failure”. The prevalence of IAH was 47% (95% CI 0.36-0.57) and that of ACS was 1.1% of the general population and 2.38% of the cohort that developed intra-abdominal hypertension.

Identified risk factors for IAH included Mechanical Ventilation (p-value 0.004), positive fluid balance (p-value 0.028), obesity (p-value 0.073) and massive fluid resuscitation (p-value 0.012). Other identified risk factors included abdominal surgery, major trauma, Acidosis and sepsis but these were not statistically significant.

The mean SOFA score on day one for all participants was 7.3±3.9 which was lower than that of the group that developed IAH and higher than the normal IAP group. Mean SOFA scores worsened significantly in the IAH group over the first 48 hours but reduced in the normal IAP group.

IAH did not significantly prolong the ICU length of stay. However, the IAH group had significantly less ventilator-free days than the normal IAP group.

CONCLUSION

The prevalence of IAH was 47% in the KATH ICU. IAH increased mean SOFA scores and increased ventilator dependence. It is crucial to have protocols for identifying and managing intra-abdominal hypertension to improve ICU outcomes.

Key Words: ABDOMINAL COMPARTMENT SYNDROME, INTRA-ABDOMINAL HYPERTENSION, INTRA-ABDOMINAL PRESSURE, PREVALENCE, OUTCOMES.

CHAPTER1: INTRODUCTION

1.1 BACKGROUND

The World Society of Abdominal Compartment Syndrome (WSACS), defines Intra-abdominal pressure (IAP) as "the steady-state pressure concealed within the abdominal cavity"[2]. In other words, it is the normal pressure inside the abdominal cavity in health. The IAP is influenced by some factors including, the density of the abdominal contents, the elasticity of the diaphragm and the abdominal wall, and the individual's anatomy[3]. It is also directly affected by the presence of space occupying structures like the gravid uterus and tumours, the mass of the solid organs and the hollow viscera, the presence of ascites, blood, and any condition that limits abdominal wall expansion like circumferential burns, obesity, tight surgical closure or prone positioning[4]. The total pressure indicates how accommodating the abdominal cavity is to some extent, and it must stay within a normal range to allow optimal function of the various organs in the body.

The normal Intra-Abdominal Pressure (IAP) can be zero to sub-atmospheric[2]. However, values up to 5mmHg are considered normal in healthy Adults whiles normal IAP in Adult critically ill patients is stated as 5-7mmHg[5]. In critically ill paediatric patients however, normal IAP is up to 10mmHg[2]. It is noteworthy however that, higher values ranging from 10mmHg to 15mmHg are acceptable in patients suffering from conditions such as obesity and pregnancy that do not have pathophysiological significance[6]. Therefore, it is essential to know the individual's steady state IAP in order to determine the clinical significance of any measured figures. Unfortunately, IAP is not measured routinely in health, making it difficult to know the steady state pressures in our patients.

Due to the fact that the abdominal compartment is a closed one, its expansions is limited. As a result of that, any elevated and sustained expansion can be detrimental. There are variations in IAP physiologically with respiration. The pressure rises with inspiration due to contraction of the diaphragm, and lowers with expiration due to the diaphragmatic relaxation[7]. Again, Intra-abdominal pressure increases transiently during coughing, laughing, straining, and sneezing[4]. Pathological elevation of IAP can occur in the presence of haemoperitonium, ascites, bowel oedema, massive fluid resuscitation, in the instance where the abdomen is packed during damage control surgery, necrotizing pancreatitis and space-occupying lesion-like tumours[8]. Raised Intra-Abdominal Pressure can lead to moderate to marked organ failure, mainly through a direct mechanical effect and if left untreated, this sustained pressure can lead to multiple

organ failure[7]. Given the restricted abdominal compliance, elevated non-physiological pressure levels can disrupt tissue perfusion, potentially causing severe ischemic or circulatory alterations. These changes are closely linked to organ dysfunction associated with increased IAP, ultimately contributing to the patient's overall health deterioration[6].

By definition, Intra-abdominal hypertension (IAH) is "a sustained or repeated pathological elevation of intra-abdominal pressure above 12 mmHg"[4]. It is frequently encountered in the critically ill and it is an independent predictor of morbidity and mortality[9]. Traditionally, IAH was thought to be a problem in patients undergoing abdominal surgery as well as trauma patients who required and had received aggressive volume resuscitation[10]. This was many years ago, now, evidence available has shown that IAH can occur in critically ill patients with medical or non-surgical conditions[7]. In fact, the current consideration is that, IAH is linked to the process of inflammation generally and resuscitation[11].

The most extreme and feared form of raised IAP is Abdominal Compartment Syndrome (ACS), and it is defined as "a sustained intra-abdominal pressure greater than 20 mmHg with or without an Abdominal Perfusion Pressure of less than 60 mmHg that is associated with new-onset organ dysfunction"[2]. Abdominal compartment syndrome occurs as a result of persistent and untreated intra-abdominal hypertension[11] and is therefore not a disease entity on its own as it occurs in a continuum with intra-abdominal hypertension. It is diagnosed after a minimum of three standardised measurements taken 4-6 hours apart[12]. When abdominal compartment syndrome results from intra-abdominal hypertension and causes organ failure, the chance of death rises even further[9]. Indeed, without prompt intervention, ACS is nearly 100% fatal[13]. In the Paediatric critical care population, IAH is defined as "a sustained or repeated pathological elevation in IAP > 10 mmHg" while ACS in children is defined as "a sustained elevation in IAP of greater than 10 mmHg associated with new or worsening organ dysfunction that can be attributed to elevated IAP"[14].

IAH and ACS have been demonstrated to negatively impact all essential organ systems in both clinical and laboratory research[11]. Some identified deleterious effects include decreased preload resulting in decreased cardiac output, alveolar atelectasis, increased intrapulmonary shunt and decreased carbon dioxide extraction, decreased mesenteric and hepatic blood flow as well as decreased renal blood flow which leads to renal impairment.

However, despite the stated deleterious effects in literature, the condition is not actively sought for and managed like other conditions and aspects of care in the intensive care unit like deep

vein thrombosis, stress ulcers, nutrition and care for pressure areas amongst others. The diagnosis is often missed in several hospitals, a fact said to be due to the lack of awareness on the part of health professionals and the lack of standardized protocols[15]. Wise et al in their 2019 study on the awareness and knowledge of intra-abdominal hypertension and abdominal compartment syndrome among ICU physicians realised, that there had been an overall improvement in awareness amongst clinicians on the WSACS guidelines as compared to a previous survey in 2007 (60.2% vs. 28.4%)[16]. However, a sizable number of responders said they never measure intra-abdominal pressure (IAP), with reliance on physical examination being the most frequent justification. Similar findings were made by Luiz Carlos Von et al, who discovered that the majority of the doctors in their study cohort (81.6%), did not measure IAP due to lack of protocols while some were not aware of the WSACS consensus definitions[15].

The reported incidence of the condition was variable in literature due to varied definitions, cut-offs and patient populations used by different researchers[17]. This was until the establishment of the World Society of Abdominal Compartment Syndrome in 2004.

The World Society of Abdominal Compartment Syndrome (WSACS) was founded to help develop standards of practice regarding the condition. In 2006, the society came out with consensus definitions for abdominal compartment syndrome (ACS) and intra-abdominal hypertension (IAH), and at its 2013 conference, the definitions were updated. The new definitions and guidelines brought uniformity with subsequent research. This study seeks to unearth the burden of the condition in our local setting using the approved WSACS standards.

1.2 RATIONALE FOR THE STUDY

There is extensive documentation of how IAH/ACS affects the body's numerous systems. Intra-abdominal hypertension affects organs within the abdominal cavity as well as organs in the retroperitoneal region and the thorax[1]. Reduced cardiac output, renal impairment, and reduced splanchnic blood flow are a few of these effects. Oliguria that is resistant to volume resuscitation can result when the increased IAP directly compresses the renal vein, cortical arterioles, or renal parenchyma[12].

IAH and ACS are prevalent in a variety of ICU patients, including non-surgical patients, despite previously being assumed to be predominantly present in trauma patients and surgical patients[18]. Malbrain et al[12] found that 50.5% of ICU patients had IAH, defined as IAP

≥12mmHg. The more recent IROI study found that the prevalence of intra-abdominal hypertension was twice as high in patients who were on the mechanical ventilator as it was in those who were breathing spontaneously[19].

In order to avoid the negative effects of intra-abdominal hypertension and the dreaded abdominal compartment syndrome, all practitioners in the ICU should be concerned with the identification and management of patients prone to having the condition or those who already have it. In Sub-Saharan Africa, there is a paucity of studies on the topics of intra-abdominal hypertension and abdominal compartment syndrome, despite recent increases in research and interest in these conditions in other areas of the world.

Results from multiple published surveys on ACS and IAH indicate that clinical knowledge of the illnesses is still generally lacking and that many Intensive care units never measure intra-abdominal pressure[20]. This may be due to either a lack of interest and/or expertise on the part of ICU physicians on the subject matter. Most ICUs like ours do not have standardised protocols or guidelines regarding the condition. Available evidence also shows that some ICU patients especially those who have received intravenous fluids, develop IAH on day one of admission[19] while others develop it later while on admission in the ICU[1]. Some high-risk patients develop IAH/ACS within 12 hours of ICU admission[21].

This study seeks to unearth the burden of the condition within our local context and provide an objective look at the condition. Findings can be used to develop protocols to improve patients' care and overall outcomes in the ICUs and also contribute to literature and knowledge in the country and the sub-Saharan Africa sub-region.

1.3 RESEARCH PROBLEM

Despite the documented deleterious effects of IAH and ACS in ICU patients, intra-abdominal pressure is not routinely measured in the majority of intensive care units, including ours. The true prevalence of the condition as well as its effects are largely unknown in our local setting and at best speculative. This is concerning especially since prevalence can be as high as 50.5% according to Malbrain et al[5]. This study seeks to find the true prevalence of the condition and observe any outcomes in patients who develop the condition in our Intensive care unit.

1.4 NULL HYPOTHESIS

The prevalence of Intra-Abdominal Hypertension in the Main ICU of the Komfo Anokye Teaching Hospital is similar to that of other mixed ICUs (45%)[22].

1.5 ALTERNATE HYPOTHESIS

The prevalence of Intra-Abdominal Hypertension in the Main ICU of the Komfo Anokye Teaching Hospital is lower than that of other mixed ICUs.

1.5 MAIN OBJECTIVE

The main objective of this study was to find out the prevalence and prognosis of patients with intra-abdominal hypertension in a mixed surgical and medical intensive care unit.

1.5.1 Specific objectives

1. To determine the prevalence of intra-abdominal hypertension within the first 48 hours of admission to the ICU.

2. To evaluate the effect of Intra-abdominal hypertension on SOFA scores as a measure of organ dysfunction.

3. To identify common risk factors for intra-abdominal hypertension at the Komfo Anokye Teaching Hospital ICU.

4. To determine the effect of intra-abdominal pressure within the first 48 hours of ICU admission on ICU length of stay.

5. To determine the effect of intra-abdominal pressure on ventilator-free days.

CHAPTER 2: LITERATURE REVIEW

In the critically ill, abdominal compartment syndrome and intra-abdominal hypertension are substantial causes of morbidity and mortality[4]. Reports from numerous researches have shown the detrimental impact of intra-abdominal hypertension (IAH) on multiple systems in the body. Patients with IAH usually stay longer in the ICU, have higher disease severity scores, have greater rates of multi-organ failure, and higher mortality[6].

2.1 HISTORY

The whole concept of the deleterious effects of increased pressure within closed compartments dates back to the year 1667 when Niels Stensen, a Danish neuroanatomist and geologist induced compartment syndrome in dogs. He ligated the abdominal aorta and observed that the tissue hypoxia from the reduced blood supply led to ischaemic paralysis of the legs, a scenario which was reversed after the aortic blood flow was restored[23].

Richard von Volkmann, a German surgeon, also identified compartment syndrome in limbs in 1811 when he reported a condition in which increasing pressure in the confined fascial area decreased blood flow to the muscles and resulted in a contracture[17]. He published his ideas that the compartmental pressure, either externally induced or internal, was what caused the restricted blood supply.

The idea of abdominal compartment syndrome was suggested by the French Scientist, Etienne-Jules Marey in 1863 when he defined abdominal compartment syndrome (ACS) as “a constellation of the physiologic sequelae of increased intra-abdominal pressure or intra-abdominal hypertension”[24]. He also hypothesized that, modifications in intra-abdominal pressure with respiration cause effects in the thorax that are opposite to those felt in the abdomen[23]. After that, Wendt reported the connection between increased intra-abdominal pressure and reduced renal function in 1867[12].

Using tubes from the rectum and the trachea to measure abdominal and thoracic pressures, another Frenchman, Paul Bert, verified Marey's earlier observations in 1870 when he documented the elevation` of IAP on inspiration and movement of the diaphragm[17].

In 1875, Ernst Odebrecht measured intra-abdominal pressure using the urinary bladder for the first time[23]. Again in 1911, Haven Emerson, a Harvard-educated physician, measured

intraperitoneal pressure directly using a device he invented and postulated that, the intra-abdominal pressure was the same in the all parts of the abdomen[23]. Based on his findings, the abdomen was thought to be principally fluid in nature, following Pascal's Law[23] which states that, "a pressure change at any point in a confined incompressible fluid is transmitted throughout the fluid such that the same change occurs everywhere". Emerson also found an association between high IAP and cardiovascular collapse and he also demonstrated that drainage of ascitic fluid led to cardiac recovery when IAH was due to ascites. However, the finding that intra-abdominal pressure was homogenous was later challenged when it was found that the pressure measured at four different sites in the abdomen was not the same in another experiment by a different researcher[25].

In 1947, Bradley reported reduced blood flow to the kidney and Glomerular filtration rate, on the average of 24.4 percent and 27.5 per cent, respectively due to increased intra-abdominal pressure in his study population[26]. This corroborated the findings by Wendt in 1867. Richardson studied the cardiorespiratory impact produced by sequential increases in IAP in dogs in 1976 and reported that there was great increase in the end-inspiratory pressure needed to transport a fixed tidal volume at pressures above 25 mm Hg. Also, there was a significant drop in cardiac output beginning at IAP of 10 mm Hg and a reduction of blood flow through the inferior vena cava suggesting reduced venous return as the reason for the reduced cardiac output[27].

The years that followed saw some work on the subject but the concept of intra-abdominal pressure and its associated conditions was generally underappreciated and not many studies were published on the subject. This was until Kron and his colleagues from the University of Virginia revisited the topic in 1984 when they studied the pathophysiological changes that followed a ruptured abdominal aortic aneurysm[28]. They popularised the monitoring of intra-abdominal pressure using a urethral catheter.

Afterwards, Fietsam invented the phrase Abdominal compartment syndrome in 1989 after describing the state of a postoperative patient with a tight abdomen who developed oliguria, high inspiratory peak pressures, hypoxemia and hypercarbia[29]. In the same year 1989, Cullen et al[13] reported on abdominal decompression surgery performed in patients with IAH/ACS and the benefits it offered to the patients. Surgical decompression or decompressive laparotomy improved cardiac output, ventilation, oxygenation, arterial filling pressures and urine output of patients with abdominal compartment syndrome within 15 minutes postoperatively according

to their study[13]. The summary of the history and Timelines of the science of intra-abdominal pressure is shown in Figure 2.1.

The last three decades have seen resurgence of interest in intra-abdominal hypertension and abdominal compartment syndrome with regards to studies and publications. With this rediscovery, abdominal compartment syndrome was seen as a condition that may occur in a variety of patient demographics and disease processes, not only as a late finding in critically ill trauma patients[29]. The syndrome may start as a mild rise in intra-abdominal pressure, which if detected early and treated, can stop the development of ACS[20].

The reported incidence however is varied in literature due to the different definitions used by various researchers and the different patient populations used[30]. Incidence is stated as ranging from 18% to 81%[7].

Using the WSACS definition of IAH and IAP≥ 12mmHg, Malbrain and his colleagues showed that prevalence of intra-abdominal hypertension 50.5% amongst ICU patients[5]. Approximately 50% of participants in the more recent WSACS Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients (IROI) study had intra-abdominal hypertension and those who were on the mechanical ventilator were affected more than those who were not ventilated[19].

Intra-abdominal hypertension and abdominal compartment syndrome are not rare in paediatric patients with the incidence of IAH in this population varying between 12.7% and 20%[31]. However, abdominal compartment syndrome is an underdiagnosed illness with numerous differences in definitions and therapeutic strategies in neonatal intensive care units (NICU) and paediatric intensive care units (PICUs) worldwide[32].

The varying definitions and the associated difference in assessing the disease burden as well as the impact of the condition led to the birth of the "World Society for the Study of Abdominal Compartment Syndrome (WSACS)" in 2004. The society's mandate was to amongst other things "promote research, foster education and improve the survival of patients with IAH/ACS"[1]. At the 2006 International abdominal compartment syndrome Consensus Definitions Conference, a multidisciplinary team of ICU doctors and nurses from all over the world developed consensus definitions to help standardise the concept of intra-abdominal hypertension and abdominal compartment syndrome.

The Society released these definitions, results and suggestions in 2007. The definitions were subsequently modified at the 2013 conference of the WSACS to cover the paediatric population as it was recognised that the condition was not peculiar to adults. Also, the new consensus definition provided a classification scheme for the open abdomen[33]. The consensus definitions from the 2013 conference are stated below and summarized in Table 2.1[28].

2.2 DEFINITIONS AND JUSTIFICATIONS (Adapted from Malbrain et al[4])

Definition 1: "The intra-abdominal pressure (IAP) is the steady-state pressure concealed within the abdominal cavity".

Definition 2: "APP = MAP – IAP"

Since it takes into account both the venous outflow constraints and the artery supply to the gut, the abdominal perfusion pressure, like the mean arterial pressure, has been proposed as a viable endpoint for resuscitation and a more reliable predictor of visceral perfusion[3]. It has been demonstrated that an abdominal perfusion pressure target of ≥60 mmHg boosts survival from intra-abdominal hypertension and abdominal compartment syndrome[12].

Definition 3: "Intra-abdominal pressure should be expressed in mmHg and measured at end-expiration in the complete supine position after ensuring that abdominal muscle contractions are absent and with the transducer zeroed at the level of the mid-axillary line".

Definition 4: "The reference standard for intermittent intra-abdominal pressure measurement is via the bladder with a maximal instillation volume of 25 ml sterile saline".

It had been realised that, there was no uniformity with regards to the amount of saline instilled into the bladder for measurements. In one study, 52.8% of respondents instilled 50 ml of saline, while 21.9% and 4.3% instilled 100 ml and 200 ml respectively. Only 16.2% of those interviewed used the recommended volume of 25 ml[17]. Definition 4 above sought to the standardise measurements.

Definition 5: "Normal IAP is approximately 5–7 mmHg in critically ill adults".

The normal IAP may be sub-atmospheric to 0mmHg[4]. However, prolonged IAP increases of 10-15 mmHg may be linked to physiological states such as morbid obesity and pregnancy, to which individuals would typically have adapted well with minimal pathophysiology[2]. The baseline steady-state IAP for each patient must therefore be considered when determining the

clinical significance of any IAP[4]. Only when there is a persistent rise in IAP indicative of a novel pathogenic event in the abdominal cavity can IAH be diagnosed[4]. IAP is commonly increased in the critically ill above the individual's normal baseline, and values between 5-7mm Hg are regarded as normal[2].

Definition 6: "Intra-abdominal hypertension is defined by a sustained or repeated pathological elevation in IAP ≥ 12 mmHg".

Definition 7: "Intra-abdominal hypertension is graded as follows: • Grade I: IAP 12–15 mmHg • Grade II: IAP 16–20 mmHg • Grade III: IAP 21–25 mmHg • Grade IV: IAP > 25 mmHg".

Definition 8: "Abdominal compartment syndrome is defined as a sustained IAP > 20 mmHg (with or without an APP < 60 mmHg) that is associated with new organ dysfunction/failure".

Definition 9: "Primary ACS is a condition associated with injury or disease in the abdominopelvic region that frequently requires early surgical or interventional radiological intervention".

Definition 10: "Secondary ACS refers to conditions that do not originate from the abdominopelvic region".

Definition 11: "Recurrent ACS refers to the condition in which ACS redevelops following previous surgical or medical treatment of primary or secondary ACS".

With clearly defined guidelines came lots of interest and research into the subject of IAH and ACS. Despite this renewed interest, however, the concept remains relatively unknown among intensive care physicians.

In their 2006 study, Kimball et al found out that a good number of clinicians were oblivious of the definitions, measurements, and present-day approaches to the management of abdominal compartment syndrome.[1] A 2014 published study by the same Author and colleagues however showed that the clinical awareness of Abdominal compartment syndrome was steadily increasing but there was still the need to come out with therapeutic bundles to standardise management.[19]

More recently in 2018, Carlos Von et al interviewed 38 physicians made up of Surgeons, Resident Physicians, Physicians and Critical care specialists in a University Hospital in Brazil and realised that just about half of the study group knew the classification of intra-abdominal hypertension and could state the onset of abdominal compartment syndrome[15]. The majority of

their respondents, 81.6% precisely, had never measured intra-abdominal pressure in their practice although some had heard about the condition a practice, they attributed to the luck of protocols by the health service or their hospital. The consensus definitions of the WSACS were unknown to seventy-nine percent (79%) of respondents[15].

Again in 2019, Wise et al. conducted a survey of 559 physicians globally, the majority of whom were from Europe, to determine their familiarity with abdominal compartment syndrome and intra-abdominal hypertension. They found that, most of the interviewees, 73.2% of them specifically, were aware of the Abdominal Compartment Syndrome society and with regards to the society's guidelines, a greater percentage than that realised in a previous global study, were aware of the current guidelines (60.2% vs. 28.4% in 2019 and 2007 respectively)[16]. Despite the increase in overall awareness and understanding, a significant portion of respondents (18%) still did not monitor intra-abdominal pressure (IAP), with reliance on physical examination being the most frequent excuse.

In the paediatric population, Rezeni and Thabet from their study, "Awareness and management of intra-abdominal hypertension and abdominal compartment syndrome by paediatric intensive care physicians" found that, although 85% of the research cohort knew about IAP/IAH/ACS, only 35% knew the WSACS definition of IAH in the paediatric population whiles, only 10% were knew for ACS[31]. Although about 70% of those interviewed said they monitored intra-abdominal pressure in their practice, they used volumes of saline that were more than the recommended volumes when using the intravesical method bringing into question, the accuracy of the values measured[31].

Again, amongst the Paediatric and Neonatal intensive care physicians, Wiegandt et al found out in a study done this year (2023) that there was still some lack of awareness amongst physicians in terms of IAH/ACS though knowledge has improved compared to findings from previous studies. More clinicians are now monitoring intra-abdominal pressure now in their practice, despite the fact that a good proportion of them are still do not measure or diagnose intra-abdominal hypertension or abdominal compartment syndrome[32]. Studies on how well-informed Physicians are with regards to intra-abdominal hypertension and abdominal compartment syndrome in sub-Saharan Africa are sparse.

From the evidence above, it is apparent that additional effort is needed to create awareness on IAH and ACS through training and education. Diagnostic algorithms need to be established to help formulate protocols concerning intra-abdominal pressure and its pathologies.

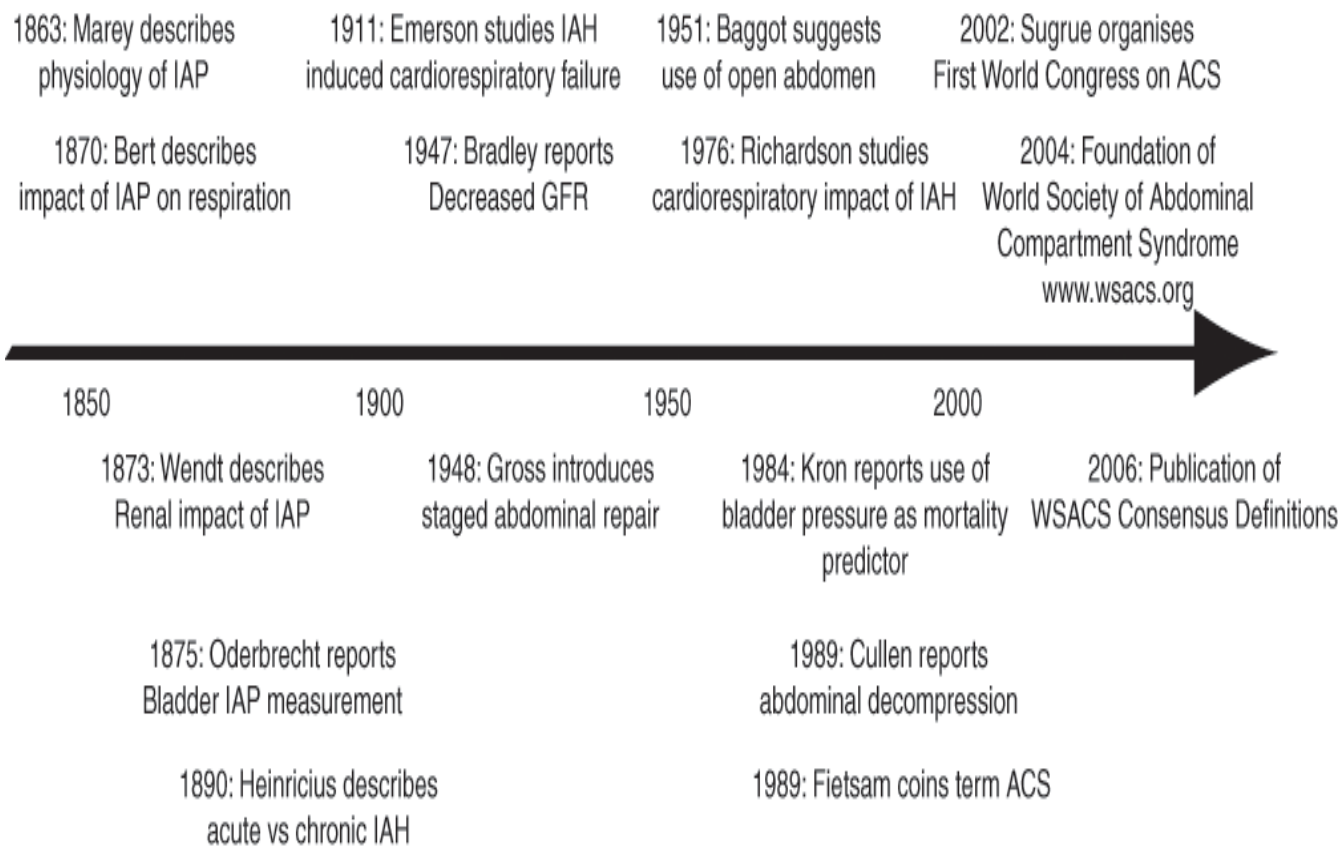


Figure 2.1- Summary of the history and timelines of the science of Intra-abdominal pressure- http://dx.doi.org/10.1017/CBO9780511667015.003. Downloaded from http:/www.cambridge.org/core.

Table 2.1: Consensus Definition of the World Society of the Abdominal Compartment Society(adapted from Malbrain et al[2]

Table 1. Final 2012 Consensus Definitions of the World Society of the Abdominal Compartment Syndrome

No.	Definition
Retained Definitions from the Original 2006 Consensus Statements [13]	
1.	IAP is the steady-state pressure concealed within the abdominal cavity.
2.	The reference standard for intermittent IAP measurements is via the bladder with a maximal instillation volume of 25 mL of sterile saline.
3.	IAP should be expressed in mmHg and measured at end-expiration in the complete supine position after ensuring that abdominal muscle contractions are absent and with the transducer zeroed at the level of the midaxillary line.
4.	IAP is approximately 5-7 mmHg in critically ill adults
5.	IAH is defined by a sustained or repeated pathological elevation in IAP ≥ 12 mmHg
6.	ACS is defined as a sustained IAP>20mmHg (with or without an APP < 60mmHg) that is associated with new organ dysfunction/failure
7.	IAH is graded as follows: Grade I, IAP 12-15 mmHg Grade II, IAP 16-20 mmHg Grade III, IAP 21-25 mmHg Grade IV, IAP > 25 mmHg
8.	Primary IAH or ACS is a condition associated with injury or disease in the abdominopelvic region that frequently requires early surgical or interventional radiological intervention
9.	Secondary IAH or ACS refers to conditions that do not originate from the abdominopelvic region.
10.	Recurrent IAH or ACS refers to the condition in which ACS redevelops following previous surgical or medical treatment of primary or secondary ACS
11.	APP=MAP – IAP
New Definitions Accepted by the 2012 Consensus Panel	
12.	A poly-compartment syndrome is a condition where two or more anatomical compartments have elevated compartmental pressures.
13.	Abdominal compliance quantifies the ease of abdominal expansion, is determined by the elasticity of the abdominal wall and diaphragm, and is expressed as the change in intra-abdominal volume per change in intra-abdominal pressure.
14.	An open abdomen is any abdomen requiring a temporary abdominal closure due to the skin and fascia not being closed after laparotomy. The technique of temporary abdominal closure should be explicitly described.
15.	Lateralization of the abdominal wall refers to the phonomenon whereby the musculature and fascia of the abdominal wall, most well seen by the rectus abdominus muscles and their enveloping fascia, move lateraly away from the midine with time.

2.3 ANATOMY AND PHYSIOLOGY OF THE ABDOMEN AND DEFINITIONS

2.3.1 The Abdominal Compartment

The abdominal compartment is surrounded by the diaphragm, the vertebral column or spine, the costal arch, the abdominal wall and the pelvis[34]. Similar to the head and other body compartments, the abdominal cavity may be thought of as a "closed box" containing major vessels, the intestines, fatty tissue, and organs[35]It has three anchorages: the costal arch above, the spine and pelvis on its hard sides, or the abdominal wall and diaphragm on its rather flexible sides[35]. The organs are located intraperitoneally and retroperitoneally.

The Gastrointestinal tract itself is a continuous hollow tube that stretches from the mouth to the anus housing about 8.5 m of intestine[36]. The diaphragm's movement, the costal arch's shifting position, the abdominal wall's contractions, the amount of gas, fluid, and faeces within the intestines, the weight of the solid organ (liver, spleen, and kidneys) as well as the amount of adipose tissue inside the wall and within the organs, all have the potential to affect the size and/or volume of the abdomen[35]. The pelvic organs, like the uterus and its adnexa, also contribute to abdominal size and volume.

The abdominal wall, muscles, and cranial (diaphragmatic) portions make up the ventral part of the abdomen, which is more flexible than the caudal and dorsal regions, which are formed by the pelvic bones and dorsal spine[37]. This makeup of the abdominal cavity determines how much it can adapt to increasing intra-abdominal volume. In order to accommodate abdominal cavity strains, the diaphragm stretches upward, which has an adverse effect on respiratory function[35].

2.3.2 The abdominal wall

The abdominal wall lies between the edges of the abdominal cavity between the iliac and pubis bones of the pelvis inferiorly and the xiphoid bone and costal margins superiorly[36]. The abdomen is divided into Anterior, lateral, and posterior walls[36].

The anterior abdominal walls play a key role when it comes to the pathogenesis of intra-abdominal hypertension. The wall is made up of skin, subcutaneous tissue, fascia, muscles, and preperitoneal adipose and areolar tissue. All these structures contain nerves, blood vessels, and lymphatic tissue. The extraperitoneal fat and peritoneal peritoneum are the deepest abdominal wall tissues[24]. Beneath them is the rectus abdominis muscle and its associated fascia[35].

The transversus abdominis, as well as the internal and external oblique muscles, form the lateral side of the anterior abdominal wall, whereas the medial rectus abdominus constitutes the central muscle[36]. The most elastic regions of the abdomen are the anterior abdominal wall and, to a lesser extent, the diaphragm. This is because the posterior muscles of the abdomen and the bone structures of the spine and pelvis are not flexible, and as a result, they have no bearing on the degree of abdominal compliance[14].

2.3.3 Intra-abdominal volume (IAV)

In a non-pathologic state, the baseline intra-abdominal volume, sometimes referred to as "the resting, starting, or static intra-abdominal volume", is approximately 13 L[35]. This baseline value changes as the intra-abdominal content increases with solid organ mass and other substances within the hollow tube and abdominal cavity like food, faeces, flatus, fat and blood and lymphatic fluid.

When the sagittal abdominal diameter, which is measured roughly at the umbilicus, is greater than a hypothetical line that runs from the symphysis pubis to the xiphoid, the abdominal is said to be distended36[36]. Abdomino-phrenic displacement, increased intra-abdominal volume (from any source), and ventro-caudal redistribution of abdominal contents are the primary causes of abdominal distention[38].

During gas insufflation procedures like laparoscopic surgeries, this is an allowable additional intra-abdominal volume that can be added to the baseline volume. This is known as the abdominal workspace and it is normally between 3 and 6 litres[35]. The baseline intra-abdominal pressure and abdominal compliance are accounted for when calculating the maximum stretched volume of the abdomen, which is equal to the baseline IAV plus the maximum workspace volume[39].

2.3.4. Abdominal compliance (C_{ab})

Abdominal compliance is defined as "a measure of the ease of abdominal expansion, which is determined by the elasticity of the abdominal wall and diaphragm"[14]. A decreased compliance, as seen in diseases like circumferential burn eschars, results in minor alterations in intra-abdominal volume resulting in larger changes in intra-abdominal pressure whiles an increased compliance suggests a loss of elastic rebound of the abdominal wall.

Compliance in the abdomen is defined as “the change in volume per unit change in pressure and in the abdominal cavity, and it is expressed as the change in intra-abdominal volume (IAV) per change in intra-abdominal pressure”[39].

Normal abdominal compliance ranges between 250 to 450 mL (mm Hg).

Because the shape of the abdominal compartment alters during increasing IAV, unlike the cerebral compartment, which is housed within a hard bony structure, the relationship between abdominal volume and abdominal pressure is curvilinear. There is first a linear portion which is followed by an exponential rise the moment a critical volume is reached.

The factors that underlie this reshaping property of the abdominal wall and diaphragm are unclear[36] but, the anthropometric characteristics of the body including height, weight, and body mass index, and the distribution of visceral vs subcutaneous fat in the individual as well as well as age and gender, have an impact on the stretching capacity[40]. The physical properties of the abdominal wall muscles also aid in the resilience of the abdomen with the rectus abdominus being more compliant in the sagittal plan.

Individuals with comorbid conditions like emphysema which flattens the diaphragm circumferential burns, fluid overload amongst others have reduced elasticity of their abdominal walls[36].

The pressure-volume relationship between intra-abdominal pressure and intra-abdominal volume is illustrated in Figure 2.2 below.

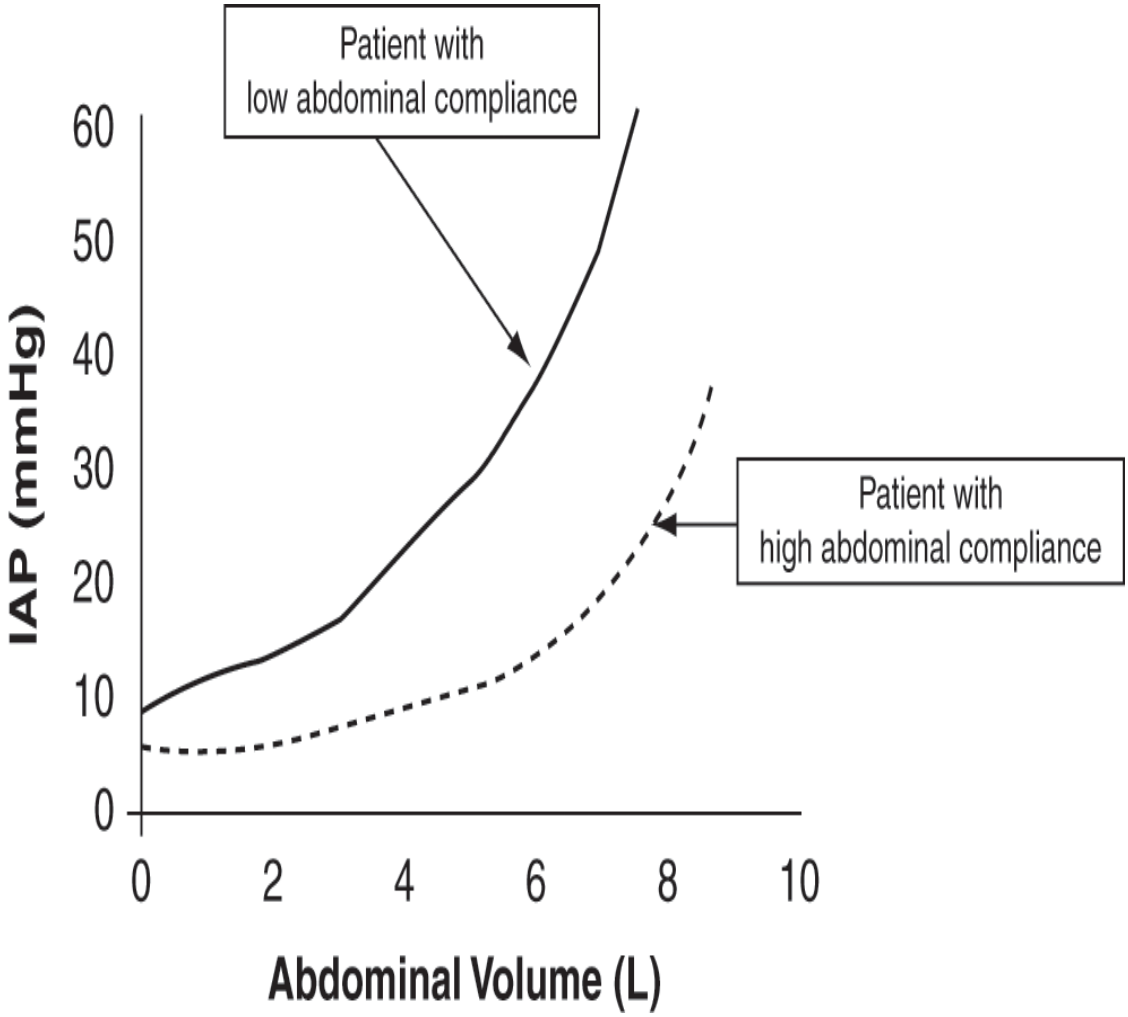


Figure 2.2: The relation between IAP and volume in the patient with low abdominal compliance compared with a person with high compliance (adapted from Malbrain et al[36]).

The pressure-volume curve shows that, at the baseline IAV of 4L, the same 2L rise in the intra-abdominal volume will result in only a small rise in IAP in a person with good compliance whereas it would result in a marked rise in cases of diaphragmatic and abdominal wall stiffness[36].

2.3.5 Abdominal perfusion pressure (APP)

Compared to other macro and microcirculatory parameters, Abdominal Perfusion Pressure (APP), defined as "Mean Arterial Pressure (MAP) minus Intra-Abdominal Pressure (IAP)," has demonstrated its effectiveness as a reliable predictor of visceral perfusion and serves as a precise endpoint for resuscitation. This concept aligns with the widely accepted principle of Cerebral Perfusion Pressure (CPP) [41].

APP considers the arterial supply (MAP) and any snags to venous blood flow (IAP). As a result, it stands out as a statistically superior outcome measure compared to either parameter in isolation, particularly in predicting the likelihood of survival in cases of IAH and ACS[42]. As a resuscitation endpoint, APP surpasses other indicators such as arterial pH, arterial lactate, and hourly urinary output. An APP measurement below 60mmHg is strongly associated with adverse outcomes in critically ill patients with intra-abdominal hypertension and abdominal compartment syndrome[42]. However, it is essential to note that studies on APP still need to be expanded in number, often taking a retrospective approach, and typically involving a relatively small patient population. Therefore, recommending APP as a standard resuscitation parameter may be challenging[43].

Target APP can be attained with judicious intravenous fluid resuscitation and the use of ionotropes and vasopressors.

2.3.6 Gastrointestinal Physiology

The physiology of the gastrointestinal system is diverse covering its endocrine, immunologic, exocrine and barrier functions and its role in food update, digestion and absorption. Adequate GI motility, local tissue perfusion and exocrine secretions are necessary to maintain GI functions, and these are controlled by intricate myogenic, neuronal, and humoral mechanisms[34]. The physiology of these is elaborated upon below.

2.3.6.1 Gastrointestinal Motility, Digestion and Absorption

GI motility is responsible for the mixing, propulsion, retropulsion and storage of food. This function appears to be profoundly disturbed in critically ill patient[34]. The gut's motility is regulated by the enteric, autonomic, and central neural systems; the modulators are hormones, neurotransmitters, and GI peptides[44].

The enteric nervous system which consists of the myenteric and submucosal plexuses is situated in the abdominal wall and can perform separately of the central nervous system[45].

The aetiology of gastrointestinal motility disturbances in the critically ill patient can be due to many factors like sepsis, trauma, shock, multiple organ dysfunction syndrome, brain injury, surgery, drugs, electrolyte disturbances, hyperglycaemia, ischemia, dysregulation of gut hormones, and IAH and ACS[44].

Disordered gut motility can result in bacterial overgrowth in the gut, increased mucosal permeability to microorganisms and bacterial translocation, and these can result in the onset of "systemic inflammatory response syndrome" (SIRS), sepsis, shock, and multiple organ dysfunction[34].

2.3.6.2 Immunological and Barrier Function

The non-immunological components of gut defence against pathogens include gastric acid, bile, intestinal mucus, and peristalsis, while an intact gut mucosa acts as a physical barrier[34]. The gastrointestinal-associated lymphoid tissue serves as a barrier to protect against pathogen entry and spread within the abdomen and beyond as part of the innate and adaptive immune responses[46]. Derangements in this gut immune system are GIT microbiome are associated with the general process of inflammation as occurs in critical illness, during allergic reactions and in metabolic diseases[46].

2.3.6.3 Blood supply to the intestines

The abdomen contains most of the internal organs in the body and is therefore supplied with numerous blood vessels. The arterial supply is through branches of the abdominal aorta while venous drainage is into tributaries of the inferior vena cava.

The small and large intestines get their blood supply from the superior and inferior mesenteric arteries, with connections between the arcading branches giving several collateral channels, while the stomach, pancreas, and spleen receive the majority of their blood supply from the coeliac artery[34]. The portal vein system is responsible for venous drainage from the spleen, pancreas, stomach, and intestines[45].

2.3.7 Gastrointestinal symptoms associated with intra-abdominal Hypertension

Most of the gastrointestinal symptoms associated with intra-abdominal hypertension were generally nonspecific. Some patients with mild IAH may have no gastrointestinal symptoms at all while the presence of symptoms leads to worse outcomes[47]. In a study at the University of Cape Town, the most common gastrointestinal symptoms identified were abdominal distension, absent bowel sounds, and high gastric residual volumes[48]. Other symptoms identified in that study included constipation, high nasogastric drainage volume and abdominal pain or tenderness.

2.4 CLASSIFICATION AND TYPES OF IAH/ACS

IAH/ACS can be categorised based on the IAP and the duration of symptoms. It can also be categorised based on the location of the aetiology causing the increased pressure.

Intra-abdominal hypertension can be classified as Hyper-acute, Acute, Subacute, or Chronic depending on the speed of onset and the duration of the increase in intra-abdominal pressure.

Hyper-acute intra-abdominal hypertension is characterized by a brief increase in intra-abdominal pressure brought on by laughing, sneezing, coughing, defecating, or engaging in physical exercise[4]. This brief elevation is usually subclinical with no deleterious effects as it is transient and not sustained long enough to cause harm to the individual.

However, acute intra-abdominal hypertension, which usually affects surgical patients, happens over several hours and is brought on by trauma or intra-abdominal hemorrhage[4]. Acute IAH is what commonly rapidly progresses to abdominal compartment syndrome as the body is unable to adapt to the sudden persistent increased pressure.

Subacute intra-abdominal hypertension on the other hand develops over a period of days and it is the type that is seen mostly in medical patients[21]. Intra-abdominal hypertension is said to be chronic if it develops over months or years.

Chronic IAH is the type that is seen in Pregnancy, in the presence of intra-abdominal tumours, morbid obesity, peritoneal dialysis, chronic ascites and cirrhosis. Although the body usually has time to adjust to the slow, steady increase in intra-abdominal pressure therefore making chronic IAH subclinical, it may predispose the patients to getting either acute or subacute IAH when they fall critically ill[4].

Based on the location of the aetiology causing the increased pressure, IAH and ACS can be categorised as primary or secondary.

Formerly referred to as surgical, post-operative, or abdominal ACS, primary ACS is characterized by the presence of acute or subacute IAH of a relatively short duration caused by an intra-abdominal pathology such as abdominal trauma, acute pancreatitis, haemoperitonium, retroperitoneal haemorrhage, or liver transplantation[20]. Primary ACS is defined as “a condition associated with injury or disease in the abdomino-pelvic region that frequently requires early surgical or interventional radiological intervention”[34]. It is the type of IAH that is encountered in trauma or post-operative patients.

Also known as medical or extra-abdominal ACS, secondary ACS manifests as subacute or chronic IAH, which arises due to various factors, including sepsis, significant haemorrhage shock, extensive burns, or any situation necessitating substantial fluid resuscitation[35].

When a patient has ACS symptoms again following the full recovery from a previous bout of abdominal compartment syndrome, the condition is said to be recurrent[20]. It can happen while having an open abdomen or as a new ACS episode after final closure of the abdominal wall, and it is most frequently linked to the development of acute IAH in a patient recovering from ACS[34]. The possibility of morbidity and death is higher when ACS recurs compared to primary ACS[34].

IAH is also classified by the WSACS into four (4) grades (Grade I-IV) depending on the measured IAP. The various grades with the corresponding intra-abdominal pressure are stated below.

"Grade I IAP 12-15 mmHg"

"Grade II IAP 16-20 mmHg"

"Grade III IAP 21-25 mmHg"

"Grade IV IAP > 25 mmHg"

Abdominal compartment syndrome is defined as sustained intra-abdominal pressure above 20mmHg that is associated with either new onset or worsening organ failure. In the paediatric population however, intra-abdominal hypertension is defined as IAP >10mmHg whiles abdominal compartment syndrome is defined as IAP>10mmHg with new onset organ failure. This implies that in adults, ACS is associated with either a grade III or a grade IV intra-abdominal hypertension whiles in children ACS can be defined with a grade I or less.

2.5 RISK FACTORS FOR IAH/ACS

Conditions that predispose an individual to developing intra-abdominal hypertension are enormous and may be due to factors that affect abdominal wall compliance and wall tension, factors that affect abdominal content or luminal content of intra-abdominal organs, sipping or leakage of fluid into the abdomen in the event of third spacing, amongst others.

Multiple risk factors can be present in an individual based on his/her pathology. These, when present, increase the chances of the individual developing intra-abdominal hypertension.

In their 2005 study, Malbrain et al. identified liver failure, ileus, abdominal surgery, and fluid resuscitation as independent predictors of intra-abdominal hypertension[7].

Holodinsky et al[49] identified 38 identified predisposing factors for IAH and 24 for ACS in their systematic review and meta-analysis. Notable amongst those predisposing factors were shock/hypotension, large-volume crystalloid resuscitation and the respiratory status of the patient[49]. Other notable predisposing factors identified in their study included obesity, sepsis, abdominal surgery, mechanical ventilation and ileus.

Again, Muturi et al identified large amounts of intravenous fluids administered in 24 hours, positive fluid balance and low haemoglobin and the transfusion of 3 or more pints of blood as important causes of intra-abdominal hypertension and abdominal compartment syndrome[50].

The WSACS IROI study provided a detailed insight into the vulnerability of patients in developing intra-abdominal hypertension on admission to the ICU as well as the evolving risk they encounter every day during the ICU stay[19]. Identified risk factors from the study included obesity, high disease severity score on admission, positive fluid balance, fluid resuscitation and abdominal distension. Contrary to other studies however, the study found no significant link between mechanical ventilation and intra-abdominal hypertension either on day one of ICU admission or during the ICU stay[19]. In other words, mechanical ventilation was not a strong predictor or risk factor of intra-abdominal hypertension according to that research. They also concluded that higher baseline intra-abdominal pressures present in obese patients, did not correlate with higher mortality. Another significant finding of the study was that positive fluid balance was an important predisposing factor for later ICU stay after aggressive fluid resuscitation and not on admission[19].

Massive fluid resuscitation is a significant predisposing factor for intra-abdominal hypertension. It increases the risk due to its combined effects on intra-abdominal volume (both intra and extra luminal due to ascites formation, gut oedema, and ileus), and the abdominal wall (tissue oedema from fluid administration decreases abdominal wall compliance)[1]. The IAH that develops further worsens intestinal swelling by decreasing venous return, creating a vicious cycle[17]. The risk of IAH/ACS is highly correlated with the volume of fluid given during resuscitation, with crystalloid resuscitation being identified as a major contributing factor[51].

Although the exact volume and duration of fluid resuscitation that can lead to IAH/ACS is unknown, fluid resuscitation greater than 5L of colloid or crystalloid in 24 hours has been suggested as a risk factor[4]. However, other evidence has suggested that the administration of fluid as little as 3.5L in 24 hours could lead to IAH[7]. It is therefore important that clinicians are more conservative, using goal-directed fluid therapy instead of administering fluids, especially crystalloids to patients liberally.

Risk factors due to reduced Abdominal Wall Compliance include prone positioning, abdominal surgery with tight fascial closure, major burns/trauma, central obesity and acute respiratory failure[14].

Risk factors which can be attributed to a rise in the intra-luminal contents include ileus, gastroparesis, faecal impaction and colonic pseudo-obstruction while increased abdominal content as occurs in haemo/pneumoperitoneum and ascites also increases intra-abdominal pressure.

Conditions that cause inflammation, capillary leak or third spacing can also predispose patients to developing intra-abdominal hypertension or in the worst-case scenario, ACS. Acute pancreatitis, sepsis, hypoalbuminemia, massive fluid resuscitation, acidosis (pH 7.2), hypotension, large transfusion (> 10 Units in 24 hours), coagulopathy, and damage control are a few of these conditions[14]. In patients with pancreatitis, frequent predisposing factors include age, gender, disease severity on admission (higher APACHE II), and large-volume crystalloid resuscitation[49].

The most common pre-ICU risk factors, defined as "pre-hospital and Emergency Department risk factors for ACS" include crystalloid fluid administration greater than 3L and hypotension of a systolic blood pressure <86 mmHg as well as a surgical procedure within the first 75 minutes of Emergency Department admission[52].

Intensive care unit ACS risk factors include high disease severity scores on admission, shock, hypotension, massive fluid resuscitation and positive fluid balance[49]. Sepsis, acidosis, Mechanical ventilation, the use of high PEEP and prone ventilation are other notable conditions or situations that predispose ICU to raised intra-abdominal pressure.

In the paediatric population, Thabet et al discovered that, the presence of a distended abdomen and a plateau pressure >30 cm H2O were important risk factors for intra-abdominal hypertension. They suggested that although the WSACS has come out with a wide range of

factors that predispose an individual to the development of IAH in children like, sepsis, gastroschisis, abdominal surgery with tight closure, faecal impaction, Hirschsprung disease and systemic inflammatory response syndrome, they were mainly speculative and had been generally coined from studies in adult populations[53]. This assumption was due to the fact that, to the best of their knowledge and based on a literature search, their study was the first of its kind in English to elucidate risk factors for intra-abdominal hypertension in paediatric critically ill patients.

The WSACS recommends screening of all patients for potential predisposing factors for raised IAP on admission to the ICU. Screening is also recommended if a patient develops a new organ failure or when there is progression in an existing organ failure. Once a risk factor is identified, it is recommended that the patient's IAP is measured on arrival and at frequent intervals for the first 24 hours, or till death or discharge in less than 24 hours[54]. The frequency of measurement is reduced in the ensuing 24 hours till risk factors resolve or till a decision is taken concerning monitoring based on the state of the patient.

Holodinsky et al suggested that there could be other risk which were not captured in their study[49]. This means that any list of risk factors at the bedside might not be exhaustive and this might lead to some false negatives. The question that arises then is whether intra-abdominal pressure should be monitored in all ICU patients regardless of whether they have risk factors or not on assessment. Indeed, measuring intra-abdominal pressure in all patients appears logical due to the fact that intra-abdominal hypertension has been associated with the general process of inflammation, third spacing or capillary leak, conditions that are frequent in ICU patients[11].

So, "Should we measure intra-abdominal pressures in every intensive care patient?" In their work, Starkopt et al[55] aimed to address this subject. They strongly suggested the monitoring of intra-abdominal pressure in all mechanically ventilated patients with severe burns, severe trauma, severe acute pancreatitis, liver failure or ruptured aortic aneurysm[55]. They made no recommendations for the monitoring of IAP in spontaneously breathing ICU patients. They also recommended the continuous evaluation of all ICU patients for signs of raised intra-abdominal pressure with the intension of initiating IAP measurement when a sign is picked. The study concluded that there were no clear guidelines as to which patient to select for intra-abdominal pressure measurements and which patient not to select[55]. In the end, they did not recommend measuring intra-abdominal pressure for every ICU patient. This is because they

thought it would be too expensive to do and also time-consuming as the widely accepted intravesical measurement has to be done at very frequent intervals.

Some identified risk factors for intra-abdominal hypertension and abdominal compartment syndrome are listed in Table 2.1 below.

Table 2.2- Risk Factors for IAH/ACS (Adapted from Kirkpatrick et al[14])

Risk Factors for Intra-abdominal Hypertension
• Diminished wall compliance -abdominal surgery -prone position -Burns -major trauma -morbid obesity • Increased intra-abdominal content -Acute Pancreatitis - Distended Abdomen - Haemoperitonium - Intra-abdominal infection/Abscess - Cirrhosis with ascites • Increased intra-luminal contents -Ileus - Gastroparesis - Volvulus • Capillary leak/ Fluid resuscitation -Acidosis -Massive fluid resuscitation -Hypothermia -Positive fluid balance -Massive blood transfusion • Others -Age -Bacteremia -Obesity -Coagulopathy - Mechanical Ventilation -PEEP -Sepsis

2.6 SYSTEMIC EFFECTS OF IAH/ACS

Elevated intraperitoneal pressure not only results in localised disruption of blood circulation and localised consequences within the peritoneal cavity, but it also has deleterious impacts on tissues and systems beyond the abdomen[17]. The harmful consequences of intra-abdominal hypertension on the body's various systems are enormous in literature and are said to be potentially deadly, especially when it leads to abdominal compartment syndrome.

The question of whether intra-abdominal hypertension in ICU patients increases mortality per se or merely serves as another indicator of the severity of the illness is still up for debate[34]. Malbrain et al stated that their study could not prove whether intra-abdominal hypertension could lead to death either directly or remotely but they could confirm that its presence predisposed patients to organ failure[7]. On the contrary, Ryu et al reported a significant association between intra-abdominal hypertension and mortality in the ICU as has been reported in some previous studies[56]. The differences in effects on outcomes found in the literature might probably be explained by the differences in duration and grades of IAH in the various study populations[34]. In other words, the degree of IAH, the duration of the elevated pressure and the speed of increase in the pressure are all critical variables to take into account when looking at the impact of intra-abdominal hypertension.

Chronic increases such as those that occur in obesity and pregnancy, for instance, are usually subclinical with no clinical importance because the body usually has time to adapt. It might also be the case that some individuals have baseline raised intra-abdominal pressure and therefore it would have been good to have baseline values to compare with when discussing the relevance of IAH concerning its effect on organ function.

Increased abdominal pressure primarily has negative consequences on the heart, lungs, and kidneys, but it can also have negative effects on the intestines, liver, and brain[57]. Just like any other compartment syndrome, ACS causes a reduced blood flow to the abdomen leading to ischaemia and hypoxia[58].

Although the exact pathophysiological process underlying intra-abdominal hypertension and abdominal compartment syndrome is unknown, it is believed that a cascade is set in motion and this cascade leads to a vicious cycle with subsequent multi-organ dysfunction[57]. The harmful sequelae of IAH/ACS on the organ systems are elaborated upon below.

2.6.1 Cardiovascular system

Patients with abdominal compartment syndrome or intra-abdominal hypertension may exhibit cardiovascular dysfunction and hemodynamic instability due to a variety of pathophysiological mechanisms.

First, the diaphragm is moved cephalad, or upward, by the increasing pressure. The diaphragm's upward movement raises the person's intrathoracic pressure (ITP) and intra-pleural pressure[43]. Experiments on animals and people have shown that 20% to 80%, or averagely 50%, of the IAP is passed to the thorax[59]. This elevated intrathoracic pressure greatly lowers venous return, lowering cardiac preload as a result[17]. Additionally, the diaphragm's upward movement compresses the heart directly leading to a decrease in the end-diastolic volumes of the right and left ventricles as well as compliance and contractility of the ventricles[43]. The reduced end-diastolic volumes will then lead to a decreased cardiac output which then further reduces cardiac preload setting in motion a vicious cycle which may be catastrophic to the patients. Meanwhile, there is a paradoxical increase in "intra-cardiac filling pressures" like the pulmonary artery occlusion pressure (PAOP) and central venous pressure (CVP) with IAH in spite of the decreased venous return and cardiac output[60]. For this reason, neither CVP nor PAOP is suitable for use a measure for assessing intravascular fluid status of patients with IAH/ACS.

Secondly, due to the elevated intraabdominal pressure, there is less venous outflow from the abdomen, resulting in a reduction in ventricular preload[43]. To make matters worse, the renin-angiotensin-aldosterone system is activated and the vascular beds are directly compressed, increasing the systemic afterload[61]. In patients who are hypovolaemic or on high PEEP, these cardiovascular implications can be exaggerated[62]. The impact of elevated IAP on mean arterial pressure (MAP) varies. Initially, there may be a rise in MAP because the body shunts blood away from the abdomen: a safety mechanism to auto transfuse blood to the body but this rise is transient and MAP usually normalises or even decreases thereafter[43]. There is significant increase in femoral venous pressure subsequent to an increase in inferior vena cava pressure secondary to the raised IAP. This reduces venous blood flow dramatically increasing extremity venous hydrostatic pressure which predisposes the patient to peripheral oedema and deep venous thrombosis[41]. When IAP is reduced under such circumstances, femoral venous blood flow is restored however, there is a risk of pulmonary embolism which can be fatal[17]. A summary of the cardiovascular effects of IAH is represented in Figure 2.3 below.

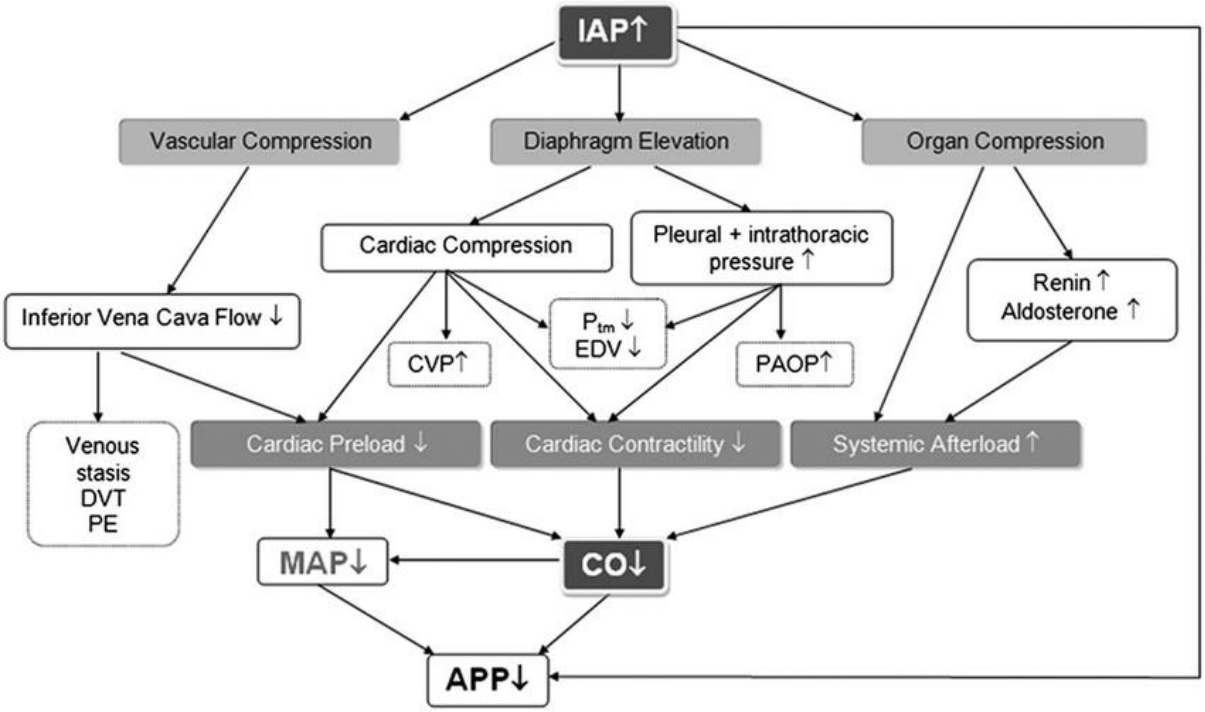


Figure 2.3: Cardiovascular effects of intraabdominal hypertension (Koen Ameloot; Carl Gillebert; Nele Desie; Manu L.N.G. Malbrain (2012). *Hypoperfusion, Shock States, and Abdominal Compartment Syndrome (ACS)., 92(2), 207–220.* doi: 10.1016/j.suc.2012.01.009)

All three crucial facets of cardiac function, namely preload, contractility, and afterload, are impacted by raised IAP.

2.6.1.1 The impact of intraabdominal hypertension on preload

The reduction in preload results from the increased IAP directly compressing vessels like the inferior vena cava, and the upward diaphragmatic displacement into the thoracic cavity. The elevated intrathoracic pressure (ITP) also causes compression of the heart[43]. Because of the changes that occur with IAH, preload assessment is often difficult in that patient cohort[17]. In this patient population, venous return and cardiac function are improved by lowering intrathoracic pressure by restricting peak and mean airway pressures using pressure-limiting ventilatory techniques or by giving neuromuscular blocking agents to enhance chest wall compliance[63].

There is also compression and narrowing of the inferior vena cava at the point of entry into the diaphragm due to the displacement of the diaphragm in the setting of the raised intraabdominal

pressure. This situation which may ensue at IAP as low as 10 mm Hg further lowers the heart's venous return effectively decreasing cardiac output through a reduction in stroke volume[17]. There is also a reduction in the central venous and mixed venous oxygen saturations.

Finally, in hypervolemic patients, in accordance with the analogy of the abdominal vascular zones described by West, IAH improves venous return when the transmural IVC pressure at the thoracic inlet, which is defined as IVC pressure minus IAP is higher than the critical closing transmural pressure[63]. In hypovolemic patients however, the transmural IVC pressure at the thoracic inlet is less than the critical closure transmural pressure and as a result, the venous outflow is drastically reduced[64]. The hydrostatic venous pressure in the lower extremity increases and this might lead to venous stasis, oedema and leg ulcers as seen on clinical examination in the case of chronic IAH, as seen with obesity[43].

2.6.1.2 The impact of intraabdominal hypertension on contractility

The upward movement of the diaphragm and the subsequent raised intrathoracic pressure leads to direct cardiac compression affecting cardiac contractility[43]. While concurrently lowering left ventricular preload, compression of the pulmonary parenchyma raises pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR)[41]. The increase in pulmonary pressures increases right ventricular afterload causing a dilatation of the right ventricle with a subsequent reduction in Right Ventricular Ejection Fraction. There is a rise in the myocardial oxygen demand and this coincides with an increased right ventricular work requirement, putting the heart in danger for subendocardial ischemia[63]. This subsequently leads to a worsening of right ventricular contractility[63]. The interventricular septum may protrude into the left ventricular chamber, obstructing its ability to function and causing yet another lowering in cardiac output[43].

Right ventricular contractility declines as a result of worsening right coronary artery blood flow, ischemia, and reduced left ventricular output. This reduced contractility causes a rightward and downward shift on the Frank-Starling curve, as shown in Figure 2.4.[63].

Huetteman et al. demonstrated that during laparoscopic herniorrhaphies in children, there was considerable reduction in the motion of the anteroseptal left ventricular wall as measured by transoesophageal echocardiography and this was seen at IAP as low as 12mmHg[65].

Patients in this scenario may initially respond to an initial fluid bolus and ionotropic support at lower grades if IAH but the biventricular decreased contractility caused by advanced IAH only improves when the IAP is reduced either medically or at worse, surgically through abdominal decompressive surgery[43].

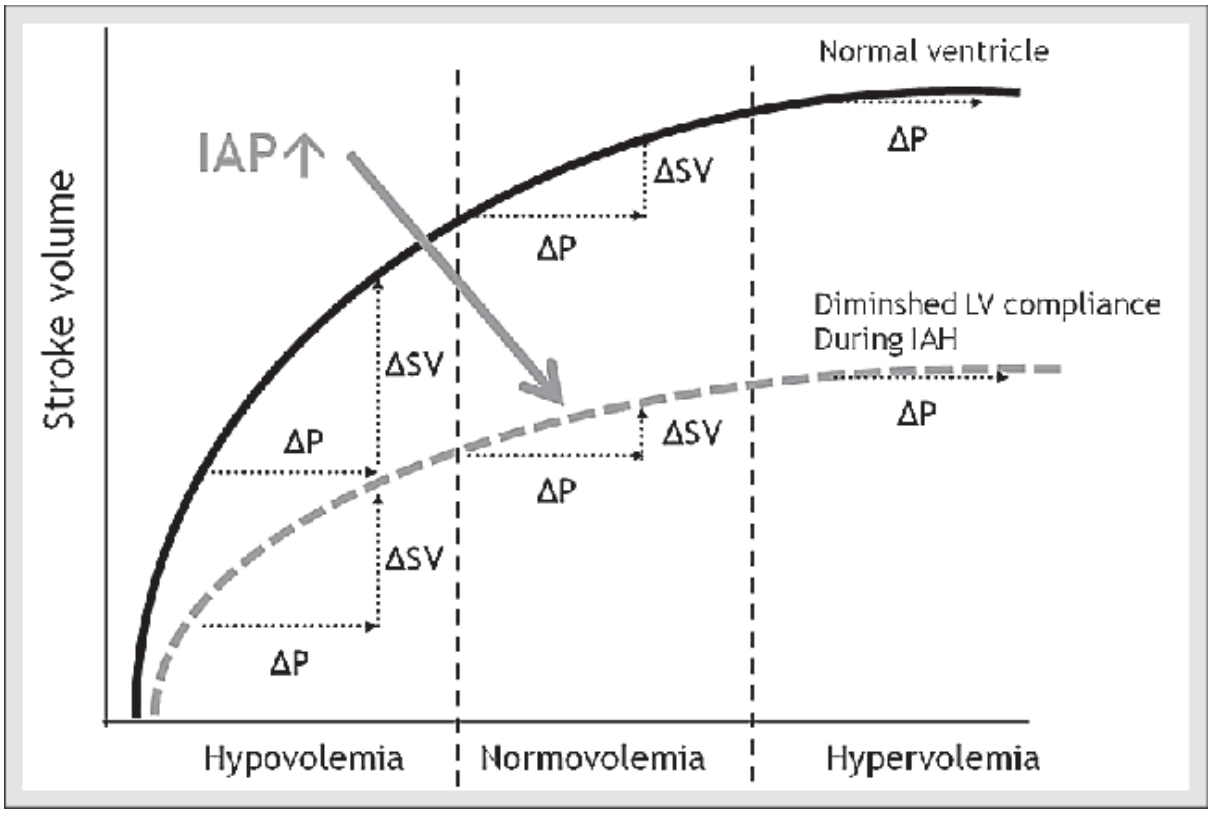


Figure 2.4: Frank-Starling curves and IAP (adapted from Malbrain et al[43])

2.6.1.3. Effect of intra-abdominal hypertension on afterload

Intra-abdominal hypertension and elevated intrathoracic pressure increase systemic vascular resistance (SVR) by causing directly compressing the aorta and systemic blood vessels and increasing the resistance in the pulmonary vessels via the compression of the pulmonary parenchyma[43]. The compression of the kidneys due to the increased pressure also causes changes in the RAAS system[61].

However, the response to the diminished venous return and declining stroke volume as a compensatory mechanism to maintain blood pressure is the most typical process that results in the increased SVR[43]. Even though venous return and cardiac output are decreased in the early stages of IAH/ACS, this compensatory mechanism maintains mean arterial pressure (MAP) largely steadily in a normal range[63]. This increase in afterload is particularly detrimental in

patients with baseline cardiovascular insufficiency as occurs in conditions like cardiogenic shock or heart failure and also in patients who have reduced intravascular volume[43].

Augmentation of Preload through volume administration and the using moderate PEEP leads to a decrease in the harmful effects of the increased afterload[63].

2.6.1.4 Clinical implications of the impact of IAH on the cardiovascular system

The Frank-Starling principle states that the length of the cardiac muscle fibres at the end of diastole is what determines ventricular preload. In other words, ventricular preload directly correlates with the length of the myocardial muscle fibre at the end of the diastolic phase[43].

The best clinical parameter to correspond with preload is left ventricular end-diastolic volume (LVEDV), but in clinical practice, it is challenging to measure this physiologic parameter serially and hence, the assumption is made that ventricular compliance is constant[42]. Measurements that are based on pressure like left ventricular end-diastolic pressure (LVEDP), left atrial pressure (LAP), and pulmonary artery occlusion pressure (PAOP), which are measured using a pulmonary artery catheter, have long been utilized in clinical settings as alternative estimations of intravascular volume, predicated on the previously mentioned steady ventricular compliance[63].

However, although these pressures, together with the CVP may be valid in normal healthy individuals, it is not same in IAH/ACS patients. This is because the assumption of a constant ventricular compliance does not apply in patient with IAH as the ventricular compliance has been shown to change constantly in the critically ill making the association between pressure and volume variable[43]. Due to these changes, the filling pressure do not correctly predict volume status of patients[43].

Furthermore, there is a risk of mitral regurgitation in patients with pulmonary hypertension or lung injury due to the raised pulmonary vascular resistance, and this makes the PAOP an inaccurate measure for calculating intravascular fluid status[43].

Based on these facts, it would be wrong to use these filling pressures are measures of intravascular volume in patients with raise intra-abdominal pressure. Therefore, it is advisable to refrain from using absolute PAOP or CVP measurements as doing so may result in poor therapeutic choices, inadequate resuscitation, and organ failure[43].

There have been suggestions by some authors to use of the transmural cardiac pressures, PAOP (PAOPtm) or CVP (CVPtm), which account for the pleural pressure, as a way of improving the reliability of PAOP and CVP as resuscitation endpoints[42].

2.6.1.5 Intra-abdominal pressure and fluid responsiveness

Stroke volume variation (SVV) and pulse pressure variation (PPV) will both rise in tandem with an increase in IAP. This is explicable by an alteration in aortic compliance and the rise in aortic transmural pressure brought on by an increase in IAP, either directly or indirectly through increased vasomotor tone[66]. Also, inaccuracies with regards to the measurement of dynamic indices with intra-abdominal hypertension, and again, the alterations in the chest wall compliance, extramural pressure and intrathoracic pressure increase PPV and SVV making the measurements higher than in normal subjects[43]. However, even at IAP values of 25 mm Hg, PPV (but not SVV) was still accurate at predictor of fluid responsiveness in some animal studies[43].

Jacques and colleagues have documented in their study on pigs with induced intra-abdominal hypertension (IAH) that respiratory variations in stroke volume (SVV) and arterial pulse pressure (PPV) continue to serve as reliable indicators of fluid responsiveness. However, it is noteworthy that the threshold values they observed were elevated compared to those within a normal intra-abdominal pressure (IAP) context. Consequently, higher-than-normal SVV or PPV values do not unequivocally signify fluid responsiveness in the context of IAH[67]. This is noteworthy because dynamic indices like PPV and SVV serve as exceptionally reliable indicators of fluid responsiveness in critically ill patients undergoing controlled positive pressure ventilation. Their accuracy surpasses that of traditional static indices assessing cardiac preload. Furthermore, in intra-abdominal hypertension (IAH) cases, static indices prove less precise due to the cardiopulmonary alterations. A recent systematic literature review determined mean threshold values for optimal differentiation between fluid responders and non-responders to be 12.5 ± 1.6% for PPV and 11.6 ± 1.9% for SVV[67]. The study which led to this finding however did not include spontaneously breathing patients and patients with cardiac arrhythmias or patients with other contraindications to the use of PPV and SVV as dynamic measures of fluid responsiveness.

A recent study by Biais and colleagues demonstrated that the predictive abilities of Stroke Volume Variation (SVV) and Pulse Pressure Variation (PPV) in determining fluid

responsiveness remained unaltered when patients were placed in a prone position during scoliosis surgery. However, it was noteworthy that the measured values were notably elevated compared to those observed in healthy subjects. This increase in values was attributable to a reduction in the static compliance of the respiratory system. As a result of this significant discovery, the study identified the 'optimal' threshold value for pulse pressure variation. In the supine position, a value of 11% was deemed optimal; in the prone position, an optimal threshold of 15% was established[68].

Using the passive leg raising (PLR) manoeuvre to assess fluid responsiveness can result in false negatives in this patient cohort as well[43]. The reason for this is that, the IAH reduced the venous drainage from the legs and mesenteric veins[66]. Performing the PLR test when the patient is sitting upright decreases the danger of aspiration and ventilator-associated pneumonia but the position will increase IAP reducing venous outflow[43]. When the manoeuvre is performed with the individual lying flat, there is no net effect on the IAP resulting in improved venous return from the legs. Performing the test in the Trendelenburg position leads to a more enhanced venous outflow from the legs and the mesenteric veins[43]. Figure 2.5 shows the compares what ensues when PLR is performed in the different positions.

TYPE	STARTING POSITION	POSITION DURING PLR	ADVANTAGES	DISADVANTAGES
HOB-elevated PLR	PPV↑↑ IAH	PPV↑↑ IAP↑	No risk for VAP	Labor intensive Increases IAP due to lung compression No endogenous transfusion
Supine PLR	PPV↑↑ IAH	PPV↑ IAP= 45°	No increase in IAP (no lung compression) Not labor intensive	Risk for VAP Risk for ICP increase Only small endogenous transfusion (from legs)
Trendelenburg PLR	PPV↑ IAH	PPV↘ IAP↓ 45°	Decrease in IAP (effects on lungs unclear) Not labor intensive Best endogenous transfusion in case of IAH	Biggest risk for VAP Biggest increase in ICP

Figure 2.5: Schematic overview comparing the possible effects and (dis)advantages of different PLR tests during increased IAP (adapted from Malbrain et al[69]).

2.6.2 Respiratory system

The abdomen and the thorax are linked through the diaphragm and as stated earlier on, 50% of intra-abdominal pressure on average, is transmitted to the intrathoracic compartment[45]. In the spontaneously breathing patient, lower opening pressures are required to overcome airway resistance and open the alveoli to enhance respiration. This is different from what happens in the presence of IAH where the decreased chest wall compliance following the elevation of the diaphragm, increases the elastic recoil of the chest wall and increases alveolar opening pressure[70].

The effort required to breathe is increased by the rise in alveolar opening pressure, and thereby causes a reduced gas supply to the dependent parts of the lungs like the lower lobes[71]. This limitation to gas flow eventually causes atelectasis, especially in the bases of the lungs[72]. Also, the increased work of breathing worsens further with sustained intra-abdominal pressure and that, coupled the an increase in respiratory rate, leads to a smaller proportion of the inspired gas reaching the areas of atelectasis and subsequently leading to even less lung compliance and subsequently lung collapse[70].

The trans-pulmonary pressure which is the pressure difference between the pleural pressure and the alveolar pressure, decreases making it harder for the patient to breathe as the lung's elastic recoil is affected by the lowered trans-pulmonary pressure[70]. This results in the need for greater opening forces to help in alveolar recruitment and opening[72].

Secondary acute respiratory distress syndrome (ARDS) occurs frequently in patients with IAH[72]. The pathogenesis of that is that intra-abdominal hypertension reduces the functional residual capacity (FRC) following the increase in chest wall elasticity. This then increases the plateau and peak airway pressures causing damage to the alveolar structures and triggering a neutrophil-activated inflammatory response[70]. Capillary permeability is enhanced promoting the exudation of a protein-rich fluid into the pulmonary intestitium, resulting in a non-cardiogenic pulmonary oedema[70].

Also, there is poor lymphatic drainage which increases the pulmonary interstitial fluid. The increase in pulmonary interstitial fluid is worsened by the obstruction to the flow through lymph channels, especially those that feed into the thoracic duct by the raised IAP[59]. Because the thoracic duct emerges from the abdominal cavity, there is direct compression on it due to the increased intraabdominal pressure. That together with the overall inflammatory process

affects splanchnic circulation further leading to engorgement of the abdominal viscera and the formation of ascites and these worsen the intra-abdominal hypertension[73].

In summary, the respiratory dysfunction caused by increased intra-abdominal pressure is characterised by reduced oxygen transport through the pulmonary capillary membrane, alveolar atelectasis, reduced capillary blood flow, intrapulmonary shunt, decreased carbon dioxide excretion and increased alveolar dead space as well as arterial hypoxemia and hypercarbia[17]. In addition, the mean and inspiratory airway pressures significantly rise, and the tidal volume and pulmonary compliance decrease[41]. Figure 2.6 summarises the implications of raised intra-abdominal pressure on the respiratory system.

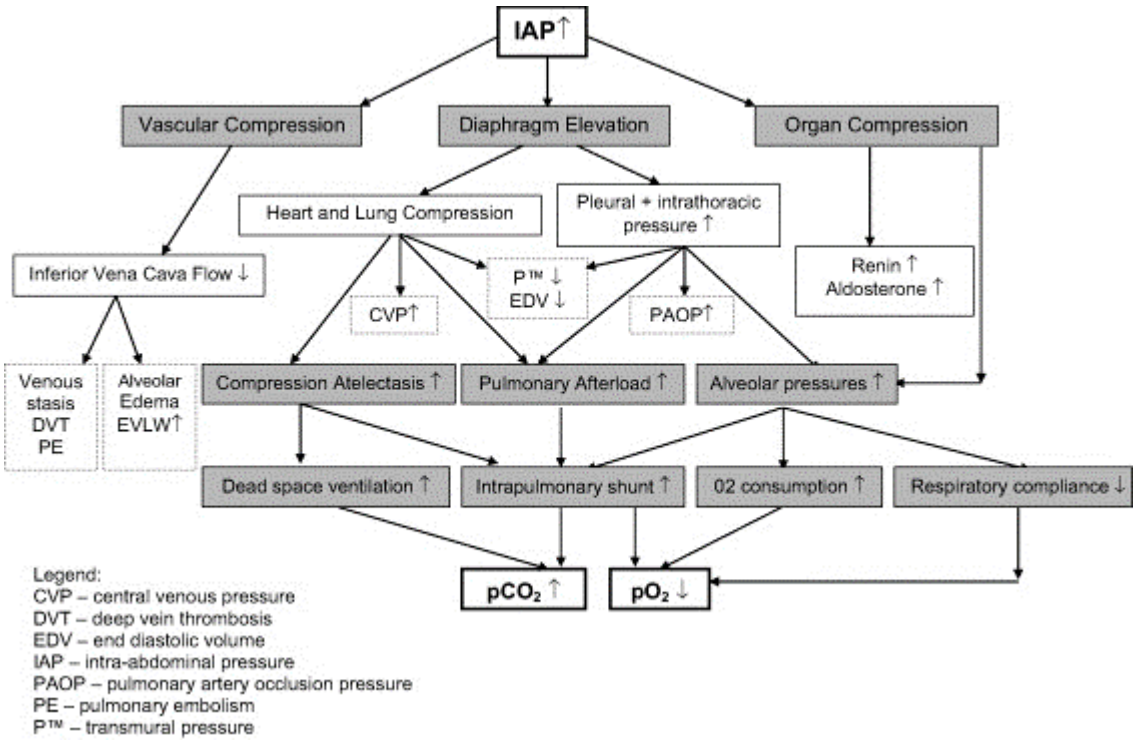


Figure 2.6: Respiratory effects of increased intra-abdominal pressure

2.6.3 Gastrointestinal system.

When the intra-abdominal volume increases and fills the abdominal compartment, IAH develops. One of the most vulnerable organ systems to intra-abdominal hypertension is the digestive system. IAP primarily affects gastrointestinal motility and the mucosal-barrier function, which affects bacterial translocation as well as intermucosal nutrient flow[17].

Due to venous outflow constriction, compromised arterial blood flow, and decreased microcirculatory flow, increased IAP causes organ dysfunction in all abdominal organs. Increased[2]. the mesenteric blood flow can reduce by up to 69% when IAP rises to about 40 mmHg and the reduction may appear with an IAP of only 10 mmHg[41]. The mucosa of the bowel appears to be particularly vulnerable to increased intra-abdominal pressure and the resultant intestinal oedema, increased permeability and loss of intestinal mucosal barrier results in bacterial translocation, sepsis and multi-organ failure[17]. Although IAH decreases intra and retroperitoneal organ perfusion, the adrenal glands are spared. This is thought to be due to the maintenance of adrenal blood flow secondary to the release of catecholamines subsequent to the ongoing shock[41].

Increased IAP decreases gastrointestinal motility by downregulating the electrical and mechanical motor function of the small intestine[17]. Below is a more detailed explanation of a few of the clinical aftereffects of intra-abdominal hypertension on the digestive tract.

2.6.3.1 IAH and gut permeability

Animal studies have shown that intra-abdominal hypertension increases levels of portal venous endotoxin and oxidative stress, as well as free radicals and oxidative stress in the splanchnic region. It also decreases the number and expression of intracellular tight junctions, increases gut permeability, and increases apoptosis activity in the gut[34]. Histological changes that occur in response to intra-abdominal hypertension include neutrophil infiltration, mucosal oedema, necrosis of the villi and mitochondrial swelling[74].

The hypoperfusion and ischaemic changes that occur secondary to increased IAP lead to bacterial translocation with its accompanying effects as stated previously[34] Translocation is said to occur as early as around 3 hours after exposure to intra-abdominal hypertension and persists for up to 24 hours after it resolves[75].

2.6.3.2 IAH and splanchnic organ perfusion

The abdominal compartment receives a significant amount of the cardiac output. The abdominal organs' both intra and retroperitoneal are highly vascularised making them highly sensitive to hypoperfusion and ischaemia

The pressure in the veins of the abdominal region increases linearly with increasing intra-abdominal pressure[76]. In the case of intra-abdominal hypertension, the increased pressure in the abdominal veins results in venous backflow pressure that is similar to the congestion seen in right heart failure patients, and this reduces the perfusion of the organs[34]. This decrease in blood flow and venous backflow affects the hepatic artery, mesenteric arteries, the portal veins and the renal artery causing hypoperfusion and organ dysfunction. Experimental and Doppler tests have demonstrated that the threshold IAP that results in the reductions in regional abdominal blood flow varies between 8mmHg and 20 mm Hg[34].

The University of Cape Town hospital conducted research that revealed a correlation between intra-abdominal hypertension and poor gastrointestinal function, enteral feed intolerance, prolonged hospital stays, and higher mortality rates[48].

2.6.4 Hepatic Function

2.6.4.1 The effect of IAH on liver histology.

Histological samples taken before and after intra-abdominal hypertension was induced through the insufflation of gas (pneumoperitoneum) showed minimal periportal and interlobular inflammation, mild to moderate dilatation of the portal venous branches with associated inflammation and focal detachment of endothelial cells[77]. Similar findings were seen in the hepatic venous branches and sinusoids. Nonetheless, the hepatocytes showed no signs of necrosis with very infrequent inflammatory infiltrates, appearing microscopically normal[75].

2.6.4.2 The effect of progressive IAH on liver blood flow

Malbrain et al studied the connection between hepatic perfusion and intra-abdominal pressure in 40 ICU patients by measuring the “plasma disappearance rate (PDR)” of indocyanine green (ICG). They discovered that while the dye's clearance and laboratory measures of liver illness did not significantly correlate, the dye's clearance and abdominal perfusion pressure did, and the two had an inverse relationship with IAP[77]. The conclusion of the study was that, there was a positive correlation between APP and the clearance of ICG while the clearance of the dye is inversely correlated to IAP meaning that, changes in IAP are associated with opposite changes in the clearance of the dye. Therefore, intra-abdominal hypertension could impair hepatosplanchnic perfusion[77].

IAH reduces blood flow through the hepatic vasculature, namely the hepatic artery, hepatic vein, and portal vein, which causes blood flow through the gastroesophageal collaterals to the Azygos vein as a compensatory mechanism[17]. However, the portal venous system only begins to show signs of compromise at an IAP of about 20 mmHg[17]. The reduction in Hepatic arterial blood flow is due directly to the decreased cardiac output while portal venous and hepatic venous flows are decreased due to both extrinsic compression of the liver and the narrowing of the hepatic veins as they go through the diaphragm[41]. Intra-abdominal hypertension also leads to increased death of the liver cells whiles enhancing the proliferation of the hepatocytes as well as causing alterations in mitochondrial function, glucose metabolism and lactate clearance[17].

The results of a recent study showed just a link between the grade of intra-abdominal hypertension and the degree of hyperbilirubinemia, and not a strict relationship between IAH and liver failure[78].

2.6.5 Renal system

IAH may cause organ dysfunction in the abdominal cavity and beyond[14]. Patients with IAH or ACS often develop Acute Kidney Injury (AKI) which exacerbates their outcomes furthur[79].

The main pathophysiological mechanisms underlying the onset of AKI during intra-abdominal hypertension are not completely understood, however, available evidence identifies a reduction in renal blood flow as the primary reason that accounts for the acute kidney injury[80]. There is a reduction in arterial supply and venous outflow with raised IAP leading to changes in the glomerular haemodynamics[79].

The decrease in the glomerular filtration gradient may be due to the intrarenal hemodynamic alteration and the activation of neuro-hormonal pathways (e.g., noradrenergic response and Renin-Angiotensin-Aldosterone system) that follows[80].

The glomerular filtration gradient (FG) "is the mechanical force across the glomerulus and equals the difference between the glomerular filtration pressure (GFP) and the proximal tubular pressure (PTP)"[41]. Mathematically, the FG is expressed as follows;

FG= GFP-PTP

When there is intra-abdominal hypertension, it is feasible to assume that the proximal tubular pressure is equal to the intra-abdominal pressure; this allows for the calculation of the

glomerular filtration pressure as MAP minus two times the intra-abdominal pressure[4]. Thus, alterations in intra-abdominal pressure will have a more significant effect on renal function and urine output than it would on MAP. It is for the reason that oliguria is one of the early signs of raised intra-abdominal pressure occuring at an IAP of about 15 mmHg while anuria, which is a complete lack of urine production, develops at 30mmHg[41]. The filtration gradient has an inverse association with the intra-abdominal pressure[81].

Again, the Filtration Gradient (FG) which depicts the balance between the hydrostatic and oncotic forces to support the ultrafiltration through the glomerular barrier is altered in IAH. When intra-abdominal hypertension occurs, there is a decrease of glomerular hydrostatic pressure due to hypoperfusion while that in the Bowman's space increases due to the intra-abdominal hypertension. These changes lead to an acute reduction in the filtration gradient[80].

Furthermore, a sudden spike in intra-abdominal hypertension narrows the renal veins and arteries, lowering renal blood flow and triggering auto regulatory processes[79]. These cause the afferent arterioles to vasodilate, ensuring glomerular filtration even in the early stages of an acute increase in IAP[82]. The activation of the auto regulatory mechanism and the initial vasodilation may lead to a sharp rise in glomerular filtration in times of stress, the degree of compensation however might be linked to the individual's renal functional reserves[79].

Furthermore, as demonstrated by Harman et al., the same level of intra-abdominal pressure may yield varying degrees of renal function reduction in different individuals. This discrepancy can be attributed, in part, to differing levels of myogenic response, which influence the effectiveness of auto regulatory mechanisms[82]. Their experimental data showed that a sudden rise in IAP is associated with only a mild reduction in renal function in patients with a robust myogenic response. Conversely, in patients with compromised myogenic response and lower renal functional reserve, an acute increase in IAP is linked to a significant reduction in renal function. This result is shown in Figure 2.7 below.

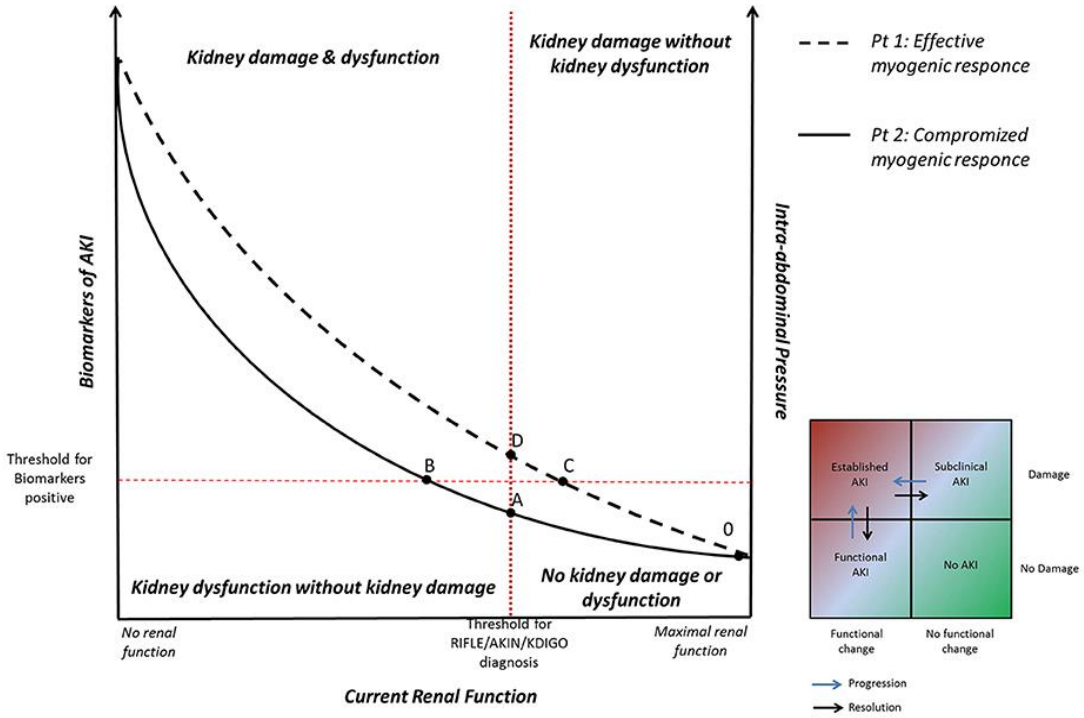


Figure 2.7: Correlation between current renal function, intra-abdominal pressure (IAP), and biomarkers of acute kidney injury (AKI). Adapted from Villa et al[79]

In patients exhibiting an effective myogenic response, a sudden elevation in intra-abdominal pressure results in a modest decline in renal function (Zone 0–C). A subsequent escalation in IAP can cause an elevation in biomarkers, indicating subclinical acute kidney injury (Zone C–D). Glomerular hypoperfusion becomes evident when IAP surpasses intrarenal autoregulation thresholds, culminating in a clinical presentation of acute kidney injury (beyond Point D). Conversely, in patients with a compromised myogenic response, an abrupt increase in IAP leads to a substantial reduction in renal function, progressing to clinical, functional acute kidney injury (Zone A–B). With further increases in IAP, the associated inflammatory and ischemic insults may result in discernible kidney parenchymal damage, which can be detected through biomarkers (above point B)[79].

In the pathological processes of Acute Kidney injury in patients with IAH, other mechanisms like the direct parenchymal compression, inflammation and myogenic response as well as renal reserves all play a role although the patient's hemodynamic state is certainly quintessential[83]. In addition to the underlying factors causing the sudden rise in IAP, the IAH itself has the potential to cause a systemic inflammatory response[84]. Apart from the systemic inflammatory

reactions, IAH also induces metabolic alterations locally in the kidney. Specifically, a multitude of genes are up- and down-regulated in the kidney with elevated IAP, resulting in a dynamic and ever-changing metabolic response[85]. In experimental models of IAH, evidence of high levels of locally-produced inflammatory mediators like TNF-a and IL-6, in the kidney has been reported during the increase in intra-abdominal pressure as well as their association with histopathological and cytoarchitectural alterations[79].

Theoretically, indicators of acute kidney injury could be used to identify individuals who are susceptible to kidney damage from hemodynamic or biological shocks during exposure to elevated and prolonged intra-abdominal pressure[79]. Several biomarkers like the kidney injury molecule-1 have been identified but recent literature has identified the biomarkers of cell-cycle arrest as the most sensitive and reliable biomarkers for AKI in most clinical settings[86]. Clinical AKI is strongly linked with increased risk of death and utilising biomarkers of kidney injury may provide details regarding the severity, prognosis, and recuperation from AKI[87].

In summary, despite the incomplete understanding of the pathophysiological mechanisms behind AKI during IAH, the reduction the blood flow to the kidneys is one of the most important causative factors[80]. IAH has been shown to affect renal artery blood flow more than celiac and superior mesenteric artery blood flow, which causes blood to be shunt away from the renal cortex and cause impaired glomerular and tubular function as well as significant decreases in urinary output[41]. The autoregulatory systems are activated by the decreased renal blood flow, acutely increasing glomerular filtration. The patient's capacity to uphold a sufficient glomerular filtration rate under the strain of the elevated IAP may be connected to the integrity of the person's myogenic response[81].

Other aetiological stimuli such as inflammatory mediators and/or exposure to toxins may also induce kidney impairment during intra-abdominal hypertension, leading to clinical or subclinical AKI[79].

2.6.6 Central Nervous System

Raised Intra-abdominal pressure may result in an increase in intracranial pressure. As stated earlier, the increased IAP is transmitted to the thorax through upward displacement of the diaphragm leading to increased intrathoracic pressure. The abdominothoracic pressure transmission increases jugular pressure which leads to a lowered venous return from the brain[88].

The Cerebrospinal fluid (CSF) is pushed towards the spine as a compensatory mechanism to try to maintain a constant intracranial pressure (ICP). However, this compensation is limited and when it is exhausted, such as occurs in patients with cerebral oedema or brain trauma, the intracranial volume increases and the ICP rises[88]. This relationship between acute increases in IAP and ICP has been demonstrated in many studies. It is therefore important to actively prevent the development of IAH in patients predisposed to developing intracranial hypertension. When intra-abdominal pressure rises acutely, it causes an increase in intracranial pressure (ICP) by augmenting the pleural pressure and impeding venous return which leads to elevated central venous pressure (CVP), increased intrajugular pressure, impaired venous outflow from the brain and increased intracranial pressure[2]. Chronic IAH, which develops slowly however increases intracranial pressure (ICP) slowly, allowing time for the body to compensate.[41]

Both cerebral function and perfusion are affected by increased intra-abdominal pressure. The aortic and atrial stretch receptors are triggered, causing vasoconstriction with an rise in catecholamine release as well as activation of the RAAS as the venous return is progressively compromised[41]. These compensatory adaptations help maintain cerebral blood flow, oxygen delivery, and consumption however, as the adaptation mechanisms become overwhelmed by the continuously decreasing stroke volume and cardiac output, disorders of consciousness and mentation like agitation, restlessness, and disorientation may ensue in patient who are not sedated[89]. Both intra-abdominal and intrathoracic pressure increase during episodes of coughing, defecation, vomiting etc and this may increase in the pressure in the cranium directly causing transient increases in ICP[41].

2.6.6.1 Importance of the Impact of IAH on ICP

The intracranial pressure stays stable over a relatively wide range of intracranial volumes through compensatory mechanisms mainly, the drainage of cerebrospinal fluid through the foramen magnum[88]. Any modest increase in intra-abdominal pressure results in a significant increase in intracranial pressure (ICP) when these compensatory mechanisms are depleted. If IAH occurs when ICP is already high for example, after a head trauma, any variation in IAP will impact on ICP[88].

The pressure within the spinal canal as well as that within the intra-dural compartment are regulated by an important system of venous structures that belong to the extradural neural axis

compartment[90]. The ventricular venous system (VVS) is part of this pivotal system and it is connected, through a number of networks to both the superior and the inferior vena cava mainly through the intrathoracic (hemi)azygos venous system and the intra-abdominal lumbar veins. Being valveless, the VVS depends on pressure gradients between the IAP, intrathoracic pressure (ITP), and the pressure in the spinal canal, which is primarily controlled by the ICP, to determine flow and the direction of flow[91]. The flow and its direction are also dependent on the gravitational forces and the hydrostatic factors that may result from the changes in posture or position (lying, sitting, standing)[92].

Abdominal decompression has been used successfully to treat refractory intracranial hypertension in trauma patients[88]. This attests to the impact that the intra-abdominal pressure has on the intracranial pressure. Intra-abdominal hypertension must be treated in patients diagnosed with, or at risk of, developing intracranial hypertension[88]

2.6.6.2 Conditions related to IAH and ICP

Intra-abdominal hypertension has been shown to cause ventriculoperitoneal (VP) shunt dysfunction and in some cases recurrent hydrocephalus[90]

Chronic increased IAP is thought to be an important contributor to the onset of idiopathic intracranial hypertension or pseudotumour cerebri in obese patients[88]

Intracranial pressure also increases secondary to the increase in IAP that occurs during laparoscopic surgeries. This has been demonstrated to increase the likelihood of postoperative nausea and vomiting[88].

2.6.6.3 Implications for clinical management

It is highly recommended to monitor the IAP in all patients who are predisposed to increased ICP. Neurological assessment should also be monitored frequently in patients with IAH[88]. Even in the absence of overt central nervous system symptoms or lesions, increased IAP should be treated as a possible cause of intracranial hypertension in patients with abdominal trauma[93]. Preventive treatments should be implemented in all patients with intracranial hypertension to avoid the onset of intra-abdominal hypertension. Also, measures to reduce ICP should be employed in all individuals with IAH to prevent intracranial hypertension.

2.6.6.4 Prevention of IAH-induced raised ICP

Measures that limit increases in the intra-abdominal volume should be instituted early in all patients at risk of IAH including head-injured patients. These measures include gastric suctioning, nasogastric tube insertion, use of prokinectics, frequent bedside ultrasounds to detect intraperitoneal fluids and the avoidance of restrictive abdominal bandages in all patients and constipation [88].

Medical procedures that increase intra-abdominal pressure like, laparoscopy, colonoscopy and gastroscopy should be avoided, if possible, in patients with identifiable predisposing factors for raised ICP or those with intracranial hypertension[90].

Again, there should be judicious use of intravenous fluids to present massive fluid resuscitation at all costs and this is a major predisposing factor for the development of intra-abdominal hypertension. The avoidance of massive fluid resuscitation is not always straightforward. It may be complicated in patients with intracranial hypertension as fluid resuscitation is required to ensure adequate cerebral perfusion, especially in patients at risk of vasospasm like patients with subarachnoid bleeding[88]. IAP monitoring should be mandatory in all patients with intracranial hypertension requiring massive fluid resuscitation to optimise perfusion and once IAH develops, fluids should be restricted and treatment regimen should be instituted promptly[90]. One option is to use fluid administration to optimize cerebral perfusion in patients while monitoring IAP. A restrictive fluid regimen should be instituted when IAH develops.

2.6.7 Summary of Clinical Recommendations

Intra-abdominal pressure should be measured in all patients with head injury, either traumatic or nontraumatic, who are at risk of intracranial hypertension or intra-abdominal hypertension[4]. Also, preventive measures should be instituted in all IAH patients to avoid an increase in intra-abdominal pressure[94].

Again, in all patients with intra-abdominal hypertension, measures to prevent intracranial hypertension like head of bed elevation, avoiding hypervolemia, hypernatremia and hyperthermia, maintenance of hypo/hyperglycaemia and nursing the patient in a neutral position should be instituted to prevent intracranial hypertension.

Additionally, neurologic assessment should be frequently done in all patients with intra-abdominal hypertension and hypervolemia should be avoided in patients with IAH to prevent any increase in intracranial pressure.

Monitoring of fluid status might be difficult to do in the clinical setting because the routinely used cardiac filling pressures of haemodynamic assessment are not reliable in the presence of intra-abdominal hypertension[90]. This might be challenging to accomplish in a clinical context, as the absence of trustworthy hemodynamic monitoring data makes volume status monitoring for these patients more challenging. The use of transmural filling pressures or by using volumetric hemodynamic monitoring parameters has been recommended as measures of intravascular volume[42].

Abdominal perfusion pressure can be used as a resuscitation endpoint in head-injured patients in centres where intracranial pressure measurement techniques are not available[90].

2.7 Measurement of intra-abdominal pressure

Pressure is the force per unit area of an object, and is expressed in N/m2 or pascal (pa) in the SI system. It is also the continuous physical force exerted on or against an object by something in contact with it. Jean Léonard Marie Poiseuille, a French physicist and physiologist was the first to measure pressures with mathematical accuracy in confined body regions[25]. Within confined cavities or spaces, the total pressure within the cavity can be set to the sum of the pressures each of the contents of the cavity exerts in it. In the abdomen for instance, the total pressure would be contributed to by the viscera, the hollow viscus and their content, the fluid content as well as the component of the abdominal wall itself.

The concept of IAP measurement became necessary when it was realised from evidence that neither clinical judgement nor physical examination was accurate enough in predicting IAP[41]. According to research by Sugrue et al, ICU doctors had a less than 50% chance of properly diagnosing increased IAP using clinical judgment, and they occasionally exaggerated IAP, which resulted in a false diagnosis of intra-abdominal hypertension[95].

IAP can be monitored directly through a hole made in the abdomen using a needle as occurs during laparoscopy or peritoneal dialysis or indirectly through transduction of bladder, stomach, colon or uterine pressure using a balloon catheter[4]. Indirect measurements date back to the 1800s when Braune and Schatz of Germany measured IAP through the rectum in 1865

and through the gravid uterus in 1872 respectively[19]. Kron and colleagues measured the IAP through the bladder[96] and their study in 1984 is seen as the benchmark in the clinical perception of IAH/ACS[19]. To reliably diagnose IAH or ACS, the technique used for measurement must be accurate. The various ways and routes of indirect measurement are stated below.

2.7.1 Intravesicular method

The original measurement technique used by Kron et al, was the open system single measurement technique. When using this technique, the patient's Foley catheter is disconnected, and 50 to 100 ml of saline are infused into the bladder after which a pressure manometer is connected to a clamped system with a needle for each measurement[20]. Every time an IAP measurement is performed using this method, the typically sterile urine drainage system is disrupted, increasing the patient's risk of urinary tract infection. This original Kron technique has subsequently been modified by other researchers to allow for measurements to be done without compromising the sterility of the urine drainage system[89]. In the modified Kron method, a pressure transducer is connected to the Foleys catheter and connected to the patients monitor. The transducer is zeroed and the symphysis pubis or iliac crest is used as the phlebostatic axis. In accordance with the WSACS guidelines, 25ml of saline is infused into a previously emptied urinary bladder and the IAP measurement is recorded at end-expiration with the patient completely supine, with a relaxed abdominal wall[6]. It is important for the patient to be completely supine as even minimal head end of bed elevations have been shown to impact significantly on the measured IAP[97]. According the WSACS, the recommended direct method of measurement is laparoscopic whiles the intravesical method is the recommended indirect method of measurement of choice[6].

How much saline infused into the bladder has been shown to be important in some studies as volumes greater than 55mls overestimated the IAP[6]. The recommendation is not to use more than 25mls of saline. In fact, De Waele et al. found from their study that, volumes as low as 10ml were enough for IAP measurement using the modified Kron's technique to avoid overestimation and they also recommended that due to the differences in the speed of instillation and temperature of saline infused, researcher should wait at least 30-60 seconds after instillation of saline into the bladder to allow the detrusor muscles to relax before taking measurements[98].

The bladder method of IAP measurement is recommended and widely used because it is simple to do, reliable, user-friendly, economical and reproducible as well as minimally invasive and low risks of complication especially if done in a closed system[6].

There are however concerns with this technology in that, it is thought not to be aseptic enough as it is a potential source of urinary tract infection. Also, measurement can be time-consuming.

2.7.2 Intragastric method

The stomach can also be used for measurement through either a nasogastric tube or a gastrostomy tube. This method is particularly useful in patients with a contraindication to urethral catheterization or in patients whom intravesicular monitoring is not possible such as in case of pelvic haematomas or fractures, bladder trauma or a neurogenic bladder[99].

The benefits of this method include its low cost, lower risk of sepsis, and minimal interference with urine output measurement. The disadvantages however are the issues of gastric wall compliances and the fact that fluid easily moves out of the gastric mucosa via the pylorus[89]. Measurement can also interfere with normal gastrointestinal motor function and with the administration of intragastric nutrition. Although this method compares well with bladder pressure measurements in the non-critically ill, in critically ill patient with certain clinical conditions like, ileus or bowel obstruction with large volume gastric aspirate, and in patients who had had gastrectomy, either partial or total, this method is less useful[89]. Again, the air in the stomach needs to be aspirated before measurements can be done and this is usually difficult to verify[19].

2.7.3 Rectal pressure

Measurement through the rectum is expensive as it requires a special fluid-filled balloon catheter. The major problem with the use of the rectum is the fact that residual faecal matter may occlude the opening of the catheter-tip and that can lead to an overestimation of IAP[99]. Also, the technique is difficult requiring frequent manipulation and is contraindicated in patients with lower gastrointestinal bleeding or patients with diarrhoeal episodes[102].

2.7.4 Uterine pressure

The catheter used for this method is the same to that used for the rectal pressure measurement making it an expensive method as well. This type of monitoring is used usually in pregnancy and labour by gynaecologists.

Measurement is done using a, fluid-filled intrauterine pressure catheter (IUPC) via an open-end attached to an external strain gauge transducer[100]. The transducer-monitor unit then displays the intrauterine pressure in graphic form. Insertion of the catheter requires time, skill and assistance

2.7.5 Inferior vena cava

The intra-abdominal pressure can be estimated using the Inferior Vena Cava pressure (IVC) as a surrogate. The IVC is accessed through a standard 30-cm central venous catheter inserted into the femoral vein and advanced into the IVC. The major advantages of this technique include a continuous trend of IAP measurements much like that for usual central venous pressure (CVP) measurements. Its disadvantage is the fact that it is invasive and there is the risk of IVC thrombosis, bacteraemia and sepsis.

No matter the technique that is used, however, it must be accurate and reproducible when measured on different patients. The position of the patient during measurement as well as the relaxation of the abdominal muscles and bladder detrusor muscles are all important to improve the accuracy of IAP measurements[4].

Other methods that are used to estimate intra-abdominal pressure include abdominal CT, abdominal perimeter measurement and abdominal ultrasound[21]

2.8 Management of IAH/ACS

Like every other condition, prevention is key. It is vital to identify patients who are at risk of developing IAH/ACS and take steps to reduce that risk.

When determining the best course of action for a given patient with IAH/ACS, it is crucial to consider three key factors: (1) the measured IAP value (or the degree/magnitude of IAP increase); (2) the characteristics of organ dysfunction (or the impact of increased IAP); and (3) the course and type of the underlying disease[1]. Following a diagnosis of IAH, the objective is

to monitor IAP serially, institute strategies to improve systemic perfusion and organ function, implement targeted therapy to lower both IAP and organ dysfunction, and, if necessary, perform emergency decompressive surgery for refractory IAH and ACS[96]. Similar to the standard management of compartment syndrome in other compartments like the limbs and thoracic, definitive management depends on surgical decompression of the peritoneal cavity[89]. However, before surgical intervention, less invasive medical interventions can be tried[21]. To prevent the consequences of ACS, vigorous non-operative intensive care support is essential. This entails vigilant monitoring of the cardiorespiratory system, renal function, and aggressive intravascular fluid replacement[17]. Definitive, non-operative management is chosen based on the underlying condition. For example, patients with large-volume ascites may benefit from large-volume paracentesis, although the benefits are only transient if the underlying cause of ascites is not addressed[89].

The management of IAH or ACS is based on four important principles namely: general supportive therapy, specific medical therapy to reduce IAP and the effects of ACS, surgical decompression, and the optimisation after surgery to maintain organ function and prevent post-operative complications[2].

2.8.1 Medical management

As stated earlier, medical management can be tried as the first line in certain patients especially those with secondary intra-abdominal hypertension or ACS before surgical intervention[21]. The principles of management of IAH include lowering intra-abdominal volume, increasing, abdominal wall compliance or both. These principles are based on the pathophysiology of IAH[2]. The medical management is grouped into 5 major categories by the WSACS namely: "improvement of abdominal wall compliance, evacuation of intraluminal contents, evacuation of abdominal free fluid collection, correction of capillary leak and positive fluid balance and specific treatment to support end-organ function"[101]. The algorithm is shown in Figures 2.9 and 2.10 below.

Some medical interventions include gastric suctioning, rectal lavage, and suction decompression, as well as gastro- and colono-prokinetics like erythromycin and metoclopramide, diuresis (with or without concomitant colloid administration), aggressive ultrafiltration, heavy sedation or neuromuscular blockade to eliminate the contribution of muscular tension across the abdominal wall[89].

2.8.2 Surgical management

Surgical decompression also known as decompressive laparotomy is the current "gold standard" for the management of the ACS and is coupled with an open abdomen management technique where the fascia and skin are left widely separated to augment the size of the peritoneal envelope and diminish the pressure exerted by the peritoneal contents[89]. Surgery however leads to an open abdomen making patients care and nursing very challenging for clinicians and nurses alike[21]. Regardless though, decompressive surgery should be performed in the setting to ACS that is refractory to conservative surgery to improve patient outcomes[17].

The abdominal wall can be temporarily closed using towel clips or moist gauze, the Bogota bag, zippers and the Wittmann patch as well as vacuum-assisted fascial closure systems[21]. It is important to recognize that decompressive laparotomy arose as the gold standard out of the crucible of damage-control laparotomy where the primary aetiology of the ACS was haemorrhage. Thus, the gold standard for primary ACS may not be directly applicable to secondary ACS as their aetiologies may be quite distinct[89]. Figure 5 shows suggested surgical management of Primary ACS

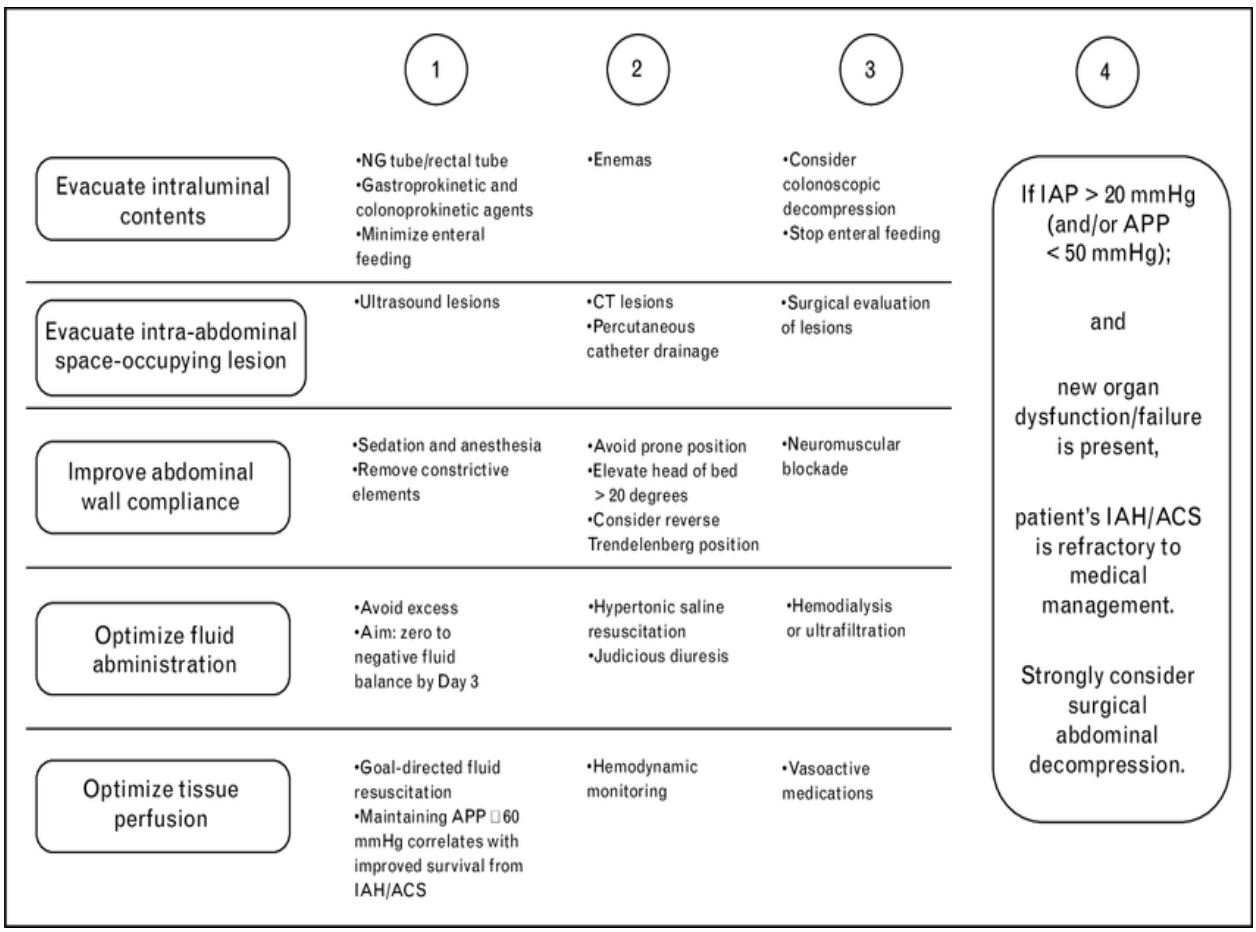


Figure 2.9- medical management of IAH/ACS(G C, Kirkpatrick W, States U. Intra-abdominal Hypertension and the abdominal Compartment syndrome. 2007;197–204.)

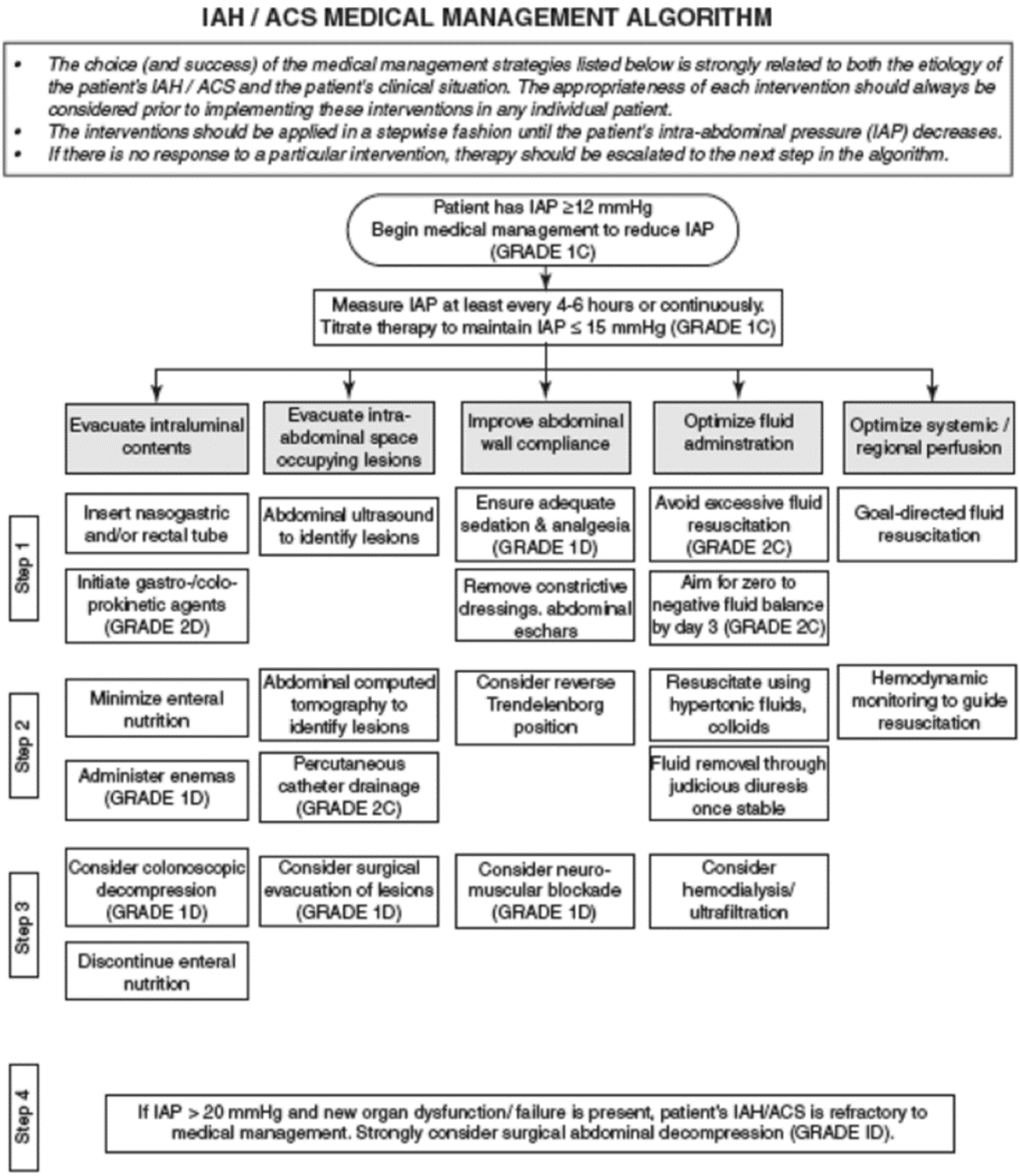


Figure 2.10("De Laet IE, Malbrain MLNG, De Waele JJ. A Clinician's Guide to Management of Intra-Abdominal Hypertension and Abdominal Compartment Syndrome in Critically Ill Patients". Crit Care. 2020;24(1):1–9)

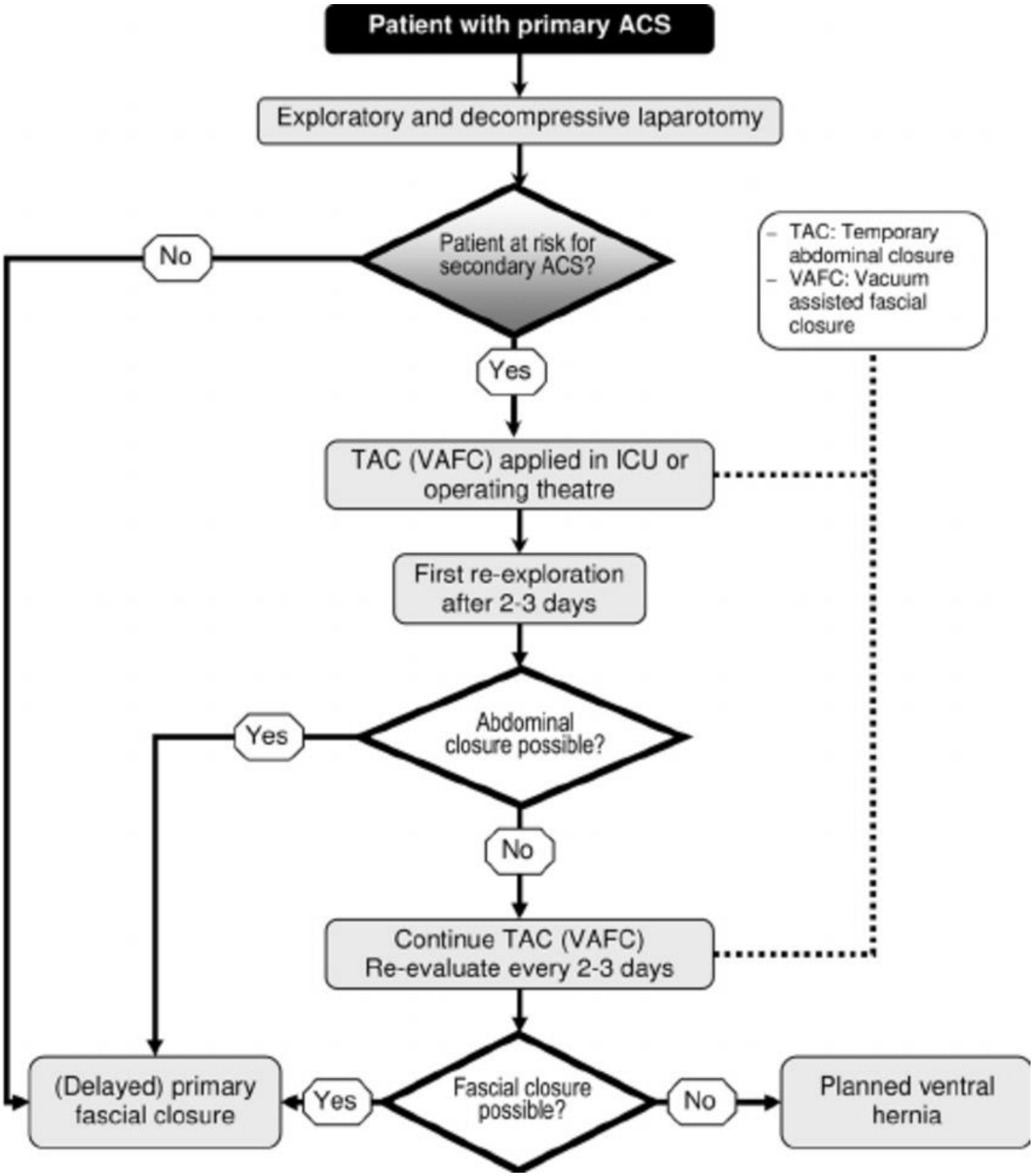
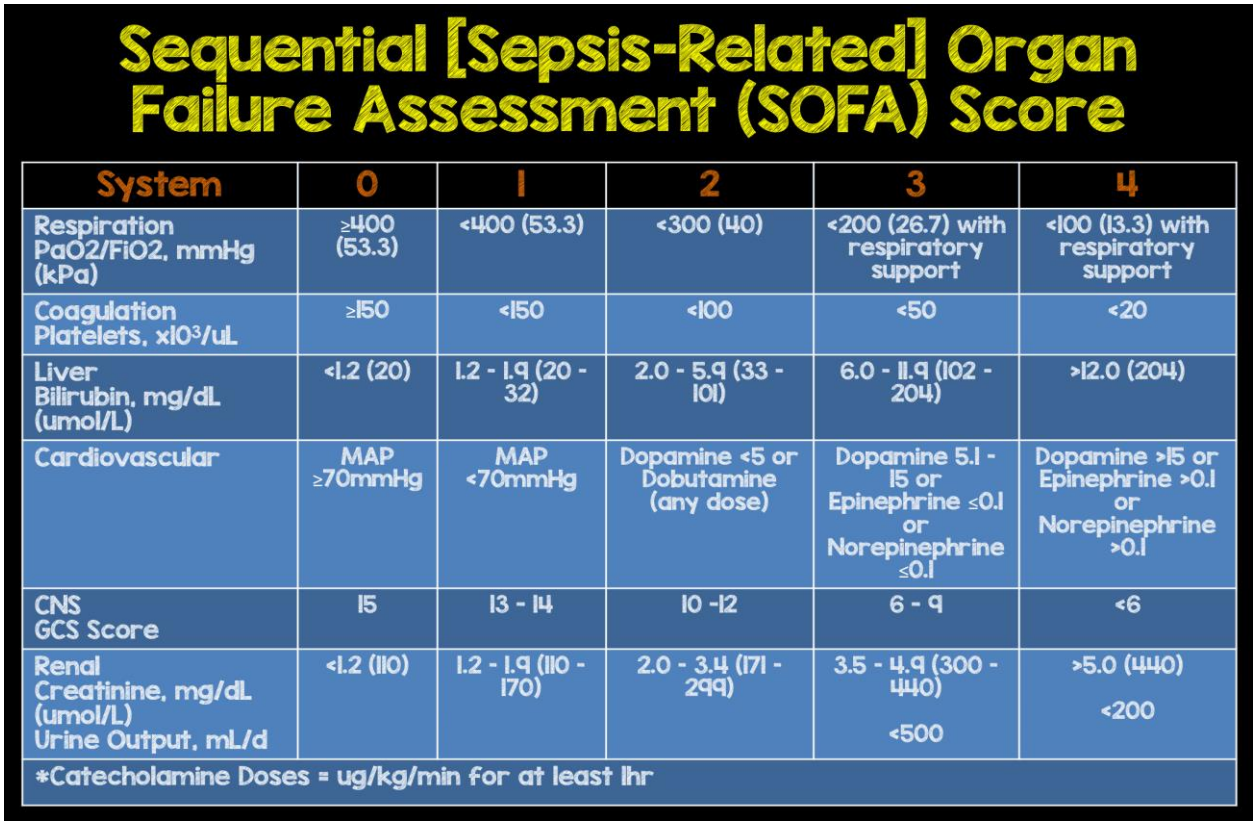


Figure 2.11("Cheatham ML. Abdominal Compartment Syndrome: pathophysiology and definitions. 2009; 11:1–11")

2.9 THE SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE (SOFA SCORE)

The sepsis-related organ failure assessment (SOFA) score was created by the European Society of Intensive Care Medicine in October 1994 to objectively explain and quantify the extent of organ dysfunction/failure in critically ill patients over time[102]. The scoring system is unlike other disease severity scoring systems like the Acute Physiology and Chronic Health Evaluation (APACHE) II and the Simplified Acute Physiology Score (SAPS) II scoring systems in that it quantifies disease severity serially over time and not just within the first 24 hours of ICU admission. The SOFA score provides a more comprehensive outlook by considering the course of a patient's condition and noting all changes in organ function during the entire period of ICU stay[103]. The SOFA score aids in enhancing our understanding of the course of organ failure and the interaction between the various organ systems and it also helps us assess new treatments in the course of the organ failure[102]. The name was later changed to Sequential Organ Failure Assessment Score when it was realised that it could equally be used in non-septic patients. The SOFA score evaluates six organ systems of the body and scores each from 0, being normal function to 4, being the worst form of dysfunction for every organ system. The worst score for the day is used as the score for the day. Table 2.12 below shows the SOFA score and its interpretation.

Table 2.3- "Sequential Organ Failure Assessment (SOFA) scoring". Crit Care Med. 2005; 33(9):1988–93



2.10 ICU LENGTH OF STAY (LOS)

There's no consensus on what defines a protracted stay in the intensive care unit, despite the fact that length of stay is routinely employed as a metric of ICU resource consumption[104]. Length of stay is crudely defined as “the time that each patient spent in the unit before death or discharge which does not include day-case patients”. Patients who pass away the day they are admitted have a length of stay of 1[105]. The term "prolonged ICU stay" has also been used to refer to a stay of more than 10 days, 14 days, 21 days, or 30 days depending on local practice[104]. Prolonged ICU admission is also commonly defined by lengths of ICU stay 2 to 3 weeks[106]. Regardless of the definition used, increased LOC worsens outcomes in ICU patients as it is associated with increased risk for infectious complications, malnutrition and ICU acquired weakness amongst others. It also puts a considerable strain on the limited ICU resources. Hence, it is important to identify patient who are at risk of increased LOS in the ICU early to enable planning to improve the unit’s efficiency. In the setting of medical futility, exploration of alternative care like palliative care consultation, physiotherapy, transfer to an in-hospital chronic ventilator unit or discharge to a long-term acute care facility can be done[104].

There are two reasons why length of stay matters as a performance metric. Firstly, it pertains to the efficiency of the intensive care process, impacting both the costs within the ICU and the overall expenses of the institution. Secondly, it indirectly indicates the quality of care; more effective therapy leads to quicker recovery, while complications and errors can prolong the patient's stay[107].

2.11 VENTILATOR FREE DAYS (VFDs)

VFD score is defined as "one point [for] each day during the measurement period that [patients] are both alive and free of mechanical ventilation"[108]. Ventilator-free days at 28 days is one of the outcome measures used in critical care. Originally designed for patients with ARDS, it combines both duration of invasive Mechanical ventilation and mortality in a unique quantitative score making a very useful tracker of Patients' outcomes[108].

VFDs are defined as zero (0) if the patient expires within 28 days whiles still on the mechanical ventilator. It is calculated as 28-x, where x is the number of days patient was off the ventilator and it is zero (0) if the patient stayed on the ventilator for all 28 days[109].

Mechanical ventilation has been shown to predispose patients to intra-abdominal hypertension by increasing intrathoracic pressure which is then transmitted to the abdomen[110]. So far, there is no prospective data available on the effect of IAH on Ventilator days as searches on Pubmed Advance search and Google Scholar using the keywords intra-abdominal hypertension or intra-abdominal hypertension and ventilator-free days or ventilator-free days yielded no related results.

2.12 REVIEW OF LITERATURE

Malbrain et al studied the prevalence of IAH and ACS in what is referred to as the first comprehensive multicentre study on the subject. They enrolled 97 patients from 13 ICUs from six (6) countries and reported a prevalence of 50.5% and 8.2% respectively for intra-abdominal hypertension and abdominal compartment syndrome[5]. The same author and colleagues studied the incidence and prognosis of IAH and ACS in another multicentre study the following year involving 14 ICUs and 265 participants and found out that 32.1% had IAH on admission while 4.2% had ACS on admission. Predisposing factors for IAH were identified as liver dysfunction, intra-abdominal surgery, fluid resuscitation and ileus[7]. The mean SOFA scores were also

observed to be considerably higher on admission in patients with IAH than those with without the condition.

In the study by Holodinsky et al that identified risk factors for both IAH and ACS in adult ICU patients, the main risk factors identified were shock, hypotension, large volume crystalloid resuscitation, sepsis, obesity, ileus and abdominal surgery[49].

In another research that was done at the ICU of Victoria Hospital in London in 2015 involving 285 patients, the incidence of IAH on admission was 30%, whilst another 15% developed IAH in the course of their ICU stay bringing the total prevalence to 45%[22]. There was a higher mortality rate and longer length of stay in the ICU and general worse outcome in the participants who had intra-abdominal hypertension. Again, they identified obesity, sepsis, mechanical ventilation and a positive fluid balance as the main contributors to the development of IAH[22].

The more recent WSACS-approved multicentre "Incidence, Risk Factors, and Outcomes of Intra-abdominal (IROI)" study involving 15 ICUs around the world found an IAH incidence of 34% on the day of admission and a total incidence of 48.9%[19]. The study involved 491 participants and identified positive fluid balance, high PEEP≥7cmH20, Body mass index, APACHE II score ≥18, presence of abdominal distension and paralytic ileus as independent predictors of intra-abdominal hypertension[111]. It was also observed that IAH was twice as prevalent in participants who were on mechanical ventilation compared to those who were breathing spontaneously and having intra-abdominal hypertension increased both 28-day and 90-day mortality.

Mbiine et al studied Intra-abdominal hypertension in severe burns patients in the Mulago National Referral Hospital (MNRH) involving 64 patients in Uganda and documented that the prevalence of IAH was 57.8%. On admission day one, 21.9% of patients had IAH and the total mortality was over 80% in the group that developed IAH[112]. The most affected systems were the respiratory system and the renal system while the least affected system was the neurological system. Overall, patient with intra-abdominal hypertension were particularly prone to developing organ dysfunction[115].

Taurai Zimunhu studied the prevalence and clinical significance of abdominal compartment syndrome in surgical patients who were admitted to the two ICUs of the two Harare Teaching Hospitals and found a 74% prevalence of intra-abdominal hypertension. There was a worsening

of organ function observed with worsened SOFA scores and increased 30-day Mortality (21%). However, IAH did not significantly affect ICU length of stay[12].

In a sample of 113 mixed surgical and medical patients in the critical care units of the Kenyatta National Hospital, Muturi et al. discovered a 67.3% prevalence of IAH and a 4.4% prevalence of ACS[50]. The prevalence of IAH they found, was remarkably higher in their study than the other rates quoted in the literature[50].

A literature search in Google Scholar and Pubmed Advanced Search reviewed no published data currently from the West African Sub-region and Ghana

CHAPTER 3: MATERIALS AND METHODS

3.1 Setting

The setting for the study was the Main intensive care unit (ICU) of the Komfo Anokye Teaching Hospital (KATH). The hospital, which is a tertiary health care centre is the second largest referral centre in Ghana with a 1250 bed capacity. It has four ICUs namely, the main ICU which is a mixed surgical and medical intensive care unit; the setting for the study, the Paediatric ICU, the Burns ICU and the Obstetric ICU. The main ICU is an 8-bed ICU with 6 regular beds and two isolation beds with about 70-30% surgical-medical patient ratio on average. Patients are managed by ICU-trained intensivists and Anaesthesiologists in collaboration with primary speciality teams for the patients.

3.2 Study design

The study was an observational, prospective single-centre cross-sectional study of patients who were admitted to a mixed medical and surgical ICU in a Teaching Hospital.

3.3 Study population

The study population included patients admitted to the main ICU of the Komfo Anokye Teaching Hospital.

3.4 Inclusion criteria

All patients of at least 16 years of age who were admitted to the ICU during the period of the study and consented to the study were enrolled.

3.5 Exclusion criteria

- Patient or next of kin's refusal to consent
- Age < 16 years
- Pregnancy

- Contraindication for insertion of urethral catheter for example patients with pelvic fracture, haematuria, or neurogenic bladder.
- Bladder surgery

3.6 Sample size

The number of admissions to our intensive care unit has averagely been 100-150 per annum for the past 5 years. The sample size for the study was calculated using Cochran's correction formula for finite population given as:

n = S / 1+ ((S−1) / Pop)

$$S = \frac{z^2 * p\,(1-p)}{d^2}$$

Where:

S = initial sample size

z^2 = the table value of chi-square for 1 degree of freedom at the desired confidence level 0.05(3.8416)

p = the population proportion (assumed to be 0.50 since this would provide the maximum sample size)

d = margin of error set at 5%, thus 0.05

n = sample size required

Pop = target population **(**100 patients admitted annually at the Main ICU at KATH)

Hence,

$$S = \frac{3.8416*0.5*(1-0.5)}{(0.05)^2}$$

$$S = \frac{0.9604}{0.0025}$$

S=384.16 ~384

Therefore, n= 384/1+ ((384-1)/100) = 79.5 ~ 80. Adding a 10% margin for error, the sample size for the study will be 88 participants.

3.7 Sampling

Convenience Sampling was done to consecutively recruit all patients who were admitted to the ICU and met the inclusion criteria.

3.8 Study procedure

The data collection for the study commenced after obtaining approval and ethical clearance from the Komfo Anokye Teaching Hospital Institutional Review Board.

The patients were screened on admission into the ICU and enrolled for the study once they met the inclusion criteria. The study procedure as well as the nature and purpose of the study was explained to the conscious patient, herein defined as a patient with a Glasgow coma score of 15/15 and the next of kin for the semi-conscious/unconscious patient and a written and signed informed consent was obtained from participants. A patient became a participant in the study after informed consent was signed. The consent form is attached in Appendix ii below. Once recruited, participants' basic data and characteristics were taken. These included age, sex, date of admission, and category of patient: whether surgical or medical as well as participant's admission number. The participant's current diagnosis together with previous medical and surgical history was also recorded. Participants were then screened for risk factors of IAH/ACS using the list of risk factors attached in the data collection sheet in Appendix I below. The vital signs of Participants which included their respiratory rate, oxygen saturation (SPO_2) and blood pressure were also recorded.

The procedure was explained to the awake participants as non-invasive with minimal participant participation. The same was explained to the next of kin of unconscious or sedated patients during the consenting process. Intravesical measurement of IAP was done using a latex Foley's urethral catheter, and in accordance with the modified Kron's technique. Almost all participants had a Foley's urethral catheter already in place on admission to the ICU and for those that did not have, a Foley's catheter was passed into the urethra under sterile conditions and connected to a urine drainage bag for continuous drainage of the bladder. A pressure system was set up using a pressure transducer connected to a 500ml normal saline drip and the

set-up was then connected to the Patient's monitor. The transducer was connected to a 3-way stopcock on the urethral catheter through a sample line. The setup is similar to the invasive blood pressure and central venous pressure setups, the difference being that the 500ml saline bag is not pressurised and the infusion is also not heparinised. A 20ml syringe was then connected to the side port of the 3-way stopcock on the catheter to be used to instil saline into the bladder during measurements. Before measurement, the transducer was levelled at the mid-axillary line of the patient at the level of the iliac crest with the patient lying supine and zeroing was done to ensure accuracy of measurements. After that, the urine drainage system was clamped before 25mls of saline was instilled into the bladder using the 20ml syringe. After the saline was injected, the intra-abdominal pressure reading was measured 30 to 60 seconds later to give the detrusor muscles time to relax. The pressure was also taken at the end of expiration with the participant in a completely supine position. The possibility of some discomfort was explained to participants to ensure maximum cooperation. An average of two (2) measurements were taken per time after which an average was taken as the intra-abdominal pressure for that time. After the measurement was completed, the drainage clamp was removed to allow the free flow of urine. At the next measurement of the participant's urine output, 25mls being the volume of the saline that was instilled for the measurement was deducted. The intra-abdominal pressure measurements were done every 6 hours for the first 48 hours of ICU admission or till the diagnosis of intra-abdominal hypertension or till discharge or death of the participant within 48 hours. The transducer was zeroed twice a day while the level was confirmed before every measurement.

The Participant's mean arterial pressure, heart rate, ionotropic requirement and mode of ventilation were also recorded 6 hourly.

Intra-abdominal hypertension was defined with reference to the standard definition by the WSACS as "IAP≥ 12mmHg" whereas abdominal compartment syndrome was defined as "an IAP ≥20mmHg with at least one organ failure". Participants were studied for 30 days to determine their ICU length of stay, Ventilator free days and overall outcomes in terms of mortality.

Prognostication was done using the SOFA score. The admission SOFA score served as a baseline for comparing daily SOFA scores over the first 7 days in the study participants. The relationship between the intra-abdominal pressure and SOFA score has been extrapolated. The SOFA measurements ceased after the 7th day of the participant's hospital admission or sooner

if the participant was discharged from the ICU before day 7. However, participants were followed up until 30 days from the day of enrolment into the study, death or discharge from the hospital, whichever came first.

The total fluid output was subtracted from the total input to obtain the daily fluid balance. During the 48-hour period of IAP readings, exposure to any other known risk factors that was not present at the time of admission was investigated.

Following a diagnosis of intra-abdominal hypertension, patients were managed in accordance with international and WSACS guidelines, which called for regular intra-abdominal pressure monitoring, optimising systemic perfusion and organ function, and implementing targeted therapies to reduce both IAP and organ dysfunction. Some non-operative management strategies that were employed included withholding enteral feeding, passage of Nasogastric tube, heavy sedation and neuromuscular paralyses.

3.9 Study period

The study was undertaken in a period of five (5) months from May 2023 to September 2023. The Gantt chart summarising the timelines for the study has been attached in Appendix 2.3.

3.10 Data management and Analysis

3.10.1 Data collection

The data for the study was collected using a data collection sheet designed for the study. The data from the sheet was entered onto an Excel sheet. The data collection sheet has been attached in Appendix 1.

3.10.2 Data handling

Data collected has been entered into a password- protected Microsoft Excel sheets for storage. Only the researcher who is the primary investigator and the supervisors have primary access to the data collected. This is to ensure maximum confidentiality of the study's participants. However, the Ethics committee would be given access to the data upon request.

3.10.3 Data analysis

Data from the 90 participants recruited for the study was cleaned and exported to STATA version 13.0 for analysis to achieve the specific objectives of the study. All univariate data analysed have been presented in graphs and tables with their frequencies and percentages determined as well as their means and standard deviations. The prevalence of intra-abdominal hypertension within the first 48 hours of admission to the ICU was also obtained through measurement. To determine the effects of Intra-abdominal hypertension on SOFA scores, ICU length of stay and ventilator-free days, a further analysis was performed using regression analysis. All statistically significant results of p-values obtained have been reported and compared with a standard p-value set to 0.05 (taking into consideration a 95 % confidence interval and a margin of error rate at 0.05).

3.11 Ethical and legal considerations

3.11.1 Approval for Study

Permission to carry out the research was sought and the same was granted by the Research and Development Unit of the Komfo Anokye Teaching Hospital (KATH) and ethical approval was granted by the KATH Institutional Review Board (IRB). The IRB was responsible for ensuring that the study protocol and study procedure followed ethical proceedings. The Directorate of Anaesthesia and Intensive Care, the primary location of the study also granted approval for the study. The Approval for the study is attached in Appendix 4.

3.11.2 Ethical Considerations

The study procedure did not expose participants to any added clinical risks. Loss of privacy and inconvenience, which were the main other risks participants were exposed to, were minimised as much as possible. Although the study was not an interventional study, all patients who developed intra-abdominal hypertension were managed using approved treatment WSACS protocols. The study did not cause harm to any participant.

3.11.4 Informed Consent

The study procedure, expected benefits and risks of the study were explained clearly to all participants using a participant information leaflet. The details of the study were explained in detail to the conscious and alert patient, defined as someone with a Glasgow coma score of 15/15 or the next of kin of the unconscious patient. The participant information leaflet for participants and that of the next of kin is attached in Appendix 2.1 and 2.2 respectively. The process of consent was done using the language the participant understood and so, was in Twi and English.

3.11.5 Confidentiality and Voluntariness

The initial letters of the Participants were used as code names for their name. However, since confidentiality could not be fully guaranteed because participant's hospital identification numbers were on the data collection sheet, only my supervisor and I had access to the completed forms.

Electronic records were encrypted and password-secured. Only the investigator, supervisors, and the Ethics Board had access to this information when needed. Participants or their next of kin were made aware that they could withdraw freely from the study at any time without any consequence to them or their relatives.

3.12 Logistics and Time-schedule

The study spanned 5 months and commenced as soon as ethical clearance was obtained from the KATH IRB. The logistics for the study included pressure transducers and monitoring systems, syringes, sample lines and infusions which were already available in the intensive care unit. Almost all of the study's participants already had Foley's urethral catheters inserted and that was used for the measurements. For the few that did not have urethral catheters in situ, catheters were readily available in the ICU to be used.

3.13 Budget/resources

The study was funded out of pocket with no external funding on a three thousand and five hundred Ghana cedi budget. Table 3.2 below shows the breakdown of the budget.

TABLE 3.2: BUDGET

ITEM/ACTIVITY	**AMOUNT (Ghana cedi)**
Payment for registration	250
Stationary	250
Mobile data	200
Research Assistant	1,500
Printing and binding	800
Miscellaneous	500
Total	3,500

CHAPTER 4 RESULTS

4.0 Introduction

The findings on the prevalence and outcomes of intra-abdominal hypertension in critically ill patients at the main intensive care unit of the Komfo Anokye Teaching Hospital which is a mixed intensive care unit are presented in this chapter. A total of 90 participants were recruited for the study and their information has been analysed. The results are presented in figures and tables followed by narrations explaining the data.

4.1 Patient Characteristics

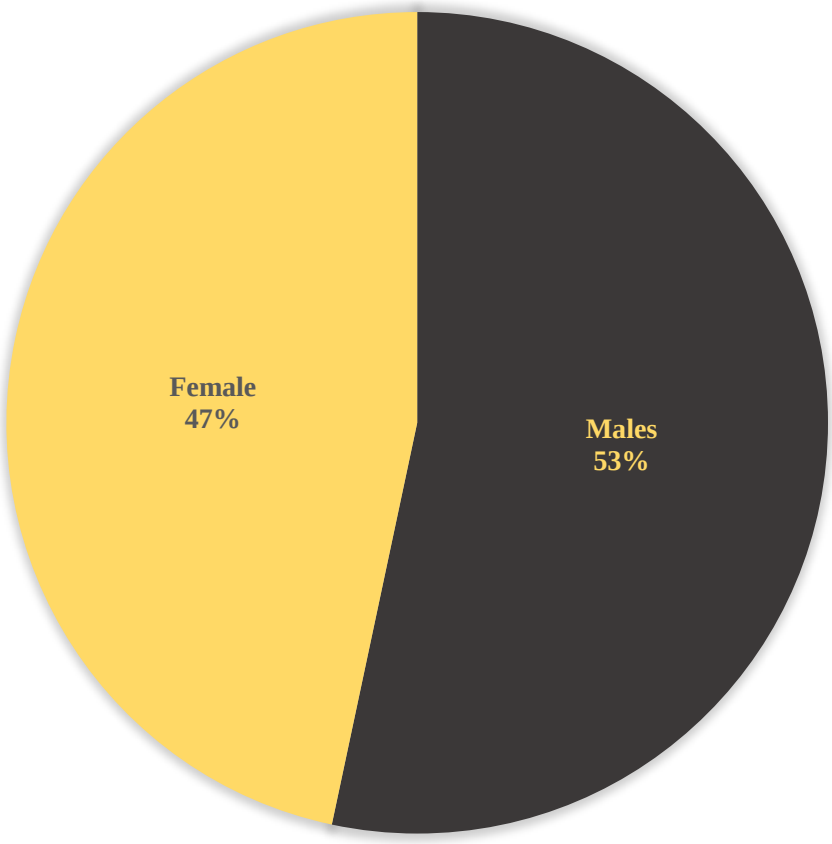


Figure 4.1 Total distribution of participants based on sex.

From the figure, the males constituted the simple majority, representing 53.3% of participants while the females represented 46.6% of participants.

Table 4.1: Participants' age distribution

Age (years)	Frequency	Percentage	Cumulative percentage
16 – 20	8	8.89	8.89
21 – 30	18	20.00	28.89
31 – 40	16	17.78	46.67
41 – 50	14	15.56	62.22
51 – 60	16	17.78	80.00
> 60	18	20.00	100.00
Total	90	100.00	

Table 4.1 shows the frequencies of the age categories as stated. The age range of 21-30 and > 60 constituted the majority with 20% apiece. The least was those between 15-20years who formed 8.89% of the study participants.

Table 4.1.1: Average Age of study participants

Average Age		Age(yrs.)	95% conf. interval
		44.3(S.D= 17.9)	40.5-48.03

The table shows the average age of the study participants which was 43.3 years.

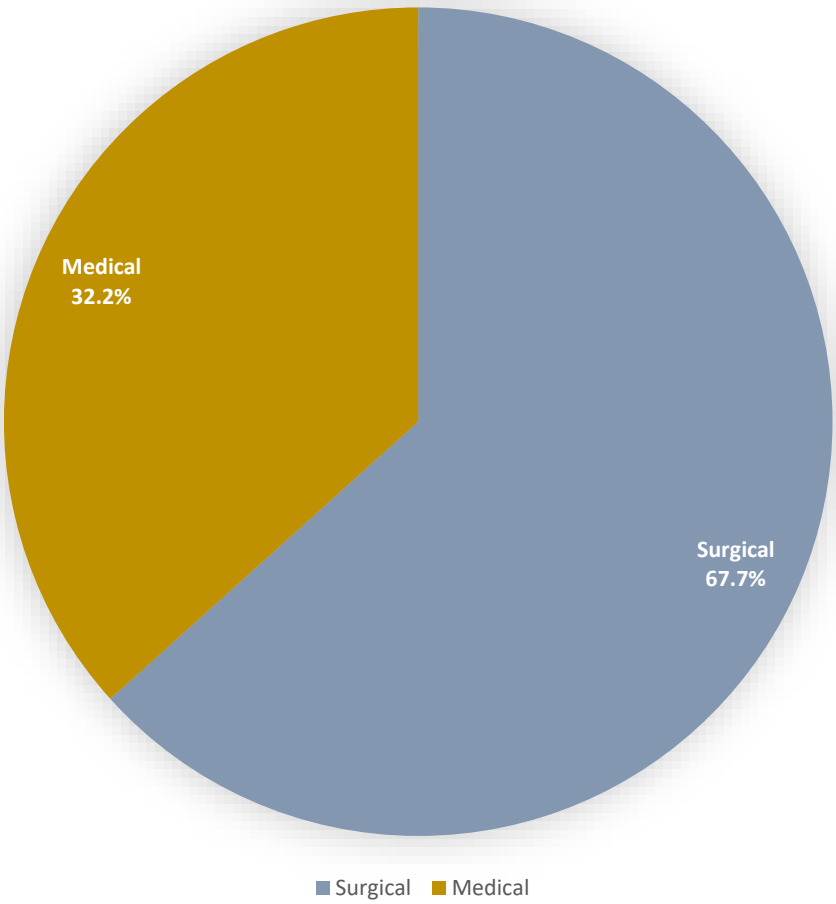


Figure 4.2 Distribution by medical specialty.

This figure shows the percentages of the study population who were medical patients and those who were surgical patients. It can be seen from the table that majority of our study participants, 67.7% were surgical patients whiles 32.2% were medical patients.

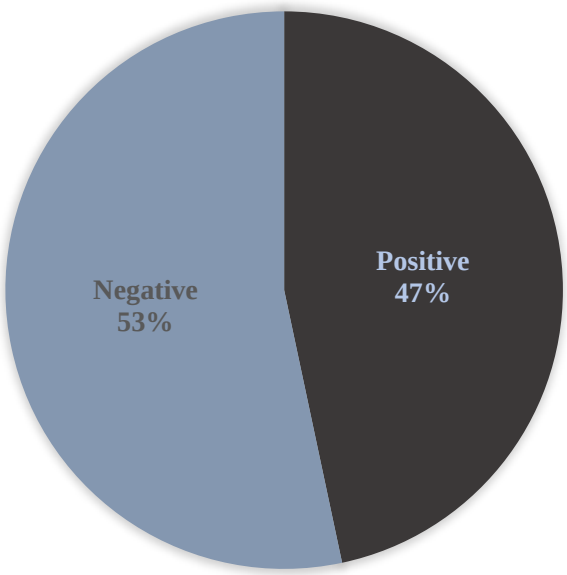


Figure 4.3: Prevalence of intraabdominal hypertension.

The prevalence of intra-abdominal hypertension in this patient cohort was approximately 47%.

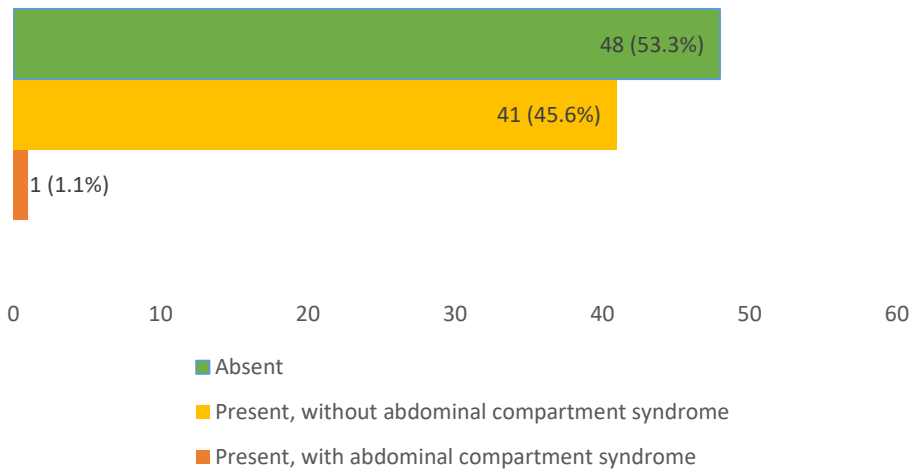


Figure 4.4: prevalence of abdominal compartment syndrome

The prevalence of abdominal compartment syndrome is shown in Figure 4.4 above. Out of the 47% that developed the condition, one (1) person developed abdominal compartment syndrome representing 1.1% of the general population and 2.38% of the population that developed intra-abdominal hypertension

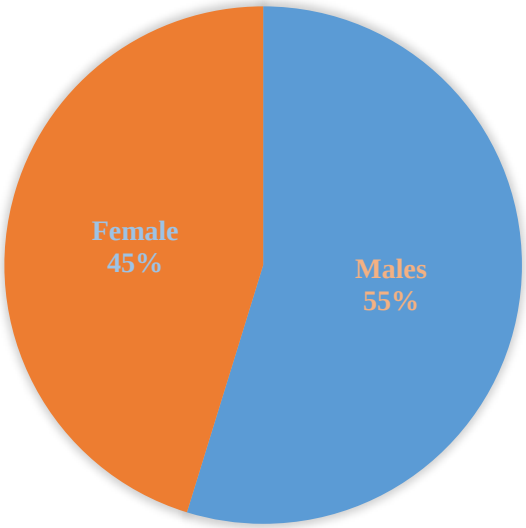


Figure 4.4 Sex distribution of patients with raised intraabdominal pressure. Of the participants who developed intra-abdominal hypertension, 55% were males while 45% were Females.

Tables 4.3.1 Mean SOFA scores.

Mean Sofa Scores		n/%	95% conf. interval
	Day 1	7.3±3.9	[6.4-8.1]
	Day 2	6.9±5.2	[5.8-8.0]
	Day 3	6.3±5.6	[5.1-7.5]
	Day 4	6.1±5.5	[4.8-7.3]
	Day 5	5.7± 5.5	[4.4-7.1]
	Day 6	5.0±5.3	[3.7- 6.3]
	Day 7	4.6± 5.3	[3.3-6.0]

Table 4.3.1 shows the mean SOFA scores of all study participants over 7 days. Means SOFA scores were high in this patient cohort. A SOFA score of 5 or more is associated with high mortality whiles a score of 2 or less is associated with mild to moderate disease[113]. On day 1, mean score was 7.3±3.9 as shown in the table. The scores generally trended downwards from

the second day with days 2 to 4 ranging between which 6.1± 5.5 to 6.9±5.2. The trend continued with 5.7±5.5 and 5.0±5.3 on days 5 and 6 till scores finally went below 5 on day 7 with 4.6±5.3.

Table 4.3.2 Comparison of Mean SOFA scores between the two groups

	Intra-abdominal Hypertension		Pr (|T| > |t|)
Sofa Scores	**Positive**	**Negative**	
Day 1	8.4±3.7	6.4±3.9	0.012
Day 2	8.8±4.8	5.3±5.1	<0.001
Day 3	8.6±5.6	4.3±4.8	<0.001
Day 4	8.0±5.8	4.2±4.4	<0.001
Day 5	7.4±6.1	3.9±4.1	<0.001
Day 6	6.7±5.8	3.1±3.9	<0.001
Day 7	6.0±5.9	3.1±4.2	0.02

Table 4.3.2 shows the comparison of mean SOFA scores between IAH (positive) and normal IAP (negative) groups.

The means Sofa score of 8.4±3.7 in the intra-abdominal hypertension group on day 1, was significantly higher than that of the normal abdominal pressure group (6.4±3.9, p- value 0.012) as well as the Mean SOFA score of the entire cohort which was 7.3±3.9.

On day 2, the Mean SOFA score in the Positive group increased to 8.8±4.8 signalling worsening disease severity within the group parallel to the trend of that of the entire cohort. In the Negative group however, SOFA scores trended downwards from the second day with a mean score of 5.3±5.1. Again, this difference in SOFA scores was statistically significant (p-value<0.001).

After, the initial increase on day 2, the Mean score of the intra-abdominal hypertension group dropped to 8.6±5.6 on day 3 which was still higher than that of the first day in the same group which was 8.4±3.7. It was also significantly higher than that of the negative group (4.3±4.8). The downward trend continued in both groups from the fourth day till the seventh day but the SOFA scores in the Positive group were significantly higher than those of the Negative group. From day 4 onwards, SOFA scores in the negative (normal intra-abdominal pressure) group were below 5 whiles the scores stayed above 5 in the Positive (intra-abdominal hypertension)

group for all the 7 days with a score of 6.0±5.9 on day 7. The Mean SOFA scores of the group with normal intraabdominal pressure were lower than the scores of the entire participant cohort. This difference in Mean SOFA scores between the IAH and normal IAP group were statistically significant (p-value of <0.001- 0.02).

Table 4.4 Risk factors for intra-abdominal Hypertension

Risk factors	Coefficient	Std Err.	P>|z|
Mechanical Ventilation	1.13	0.39	0.004
Massive fluid resuscitation.	1.22	0.48	0.012
Abdominal Surgery	0 .24	0.45	0.585
Sepsis	0.12	0.45	0.780
Obesity	1.00	0.56	0.073
Major trauma	0.16	0.52	0.762
Positive fluid balance	0 .77	0.35	0.028
Acidosis	-0.35	0.72	0.624

Table 4.4 shows the identified risk factors for intra-abdominal Hypertension from the study and how significant they were as possible enabling conditions for intra-abdominal hypertension. The main risk factors identified in the study were Mechanical Ventilation, positive fluid balance, obesity and massive fluid resuscitation. Others included abdominal surgery, Sepsis, and Major trauma.

Table 4.5.1: Average length of stay in the ICU

Average Length of Stay	In Days	n/%	95% conf. interval
		8.1±7.2	[6.6-9.6]

Table 4.5.1 shows the average length of stay in the ICU for all participants over the study period. This was 8.1±7.2 days on average.

Table 4.5.2 ICU Length of stay in the IAH and normal IAP groups

Length of stay (Days)	Intra-abdominal Hypertension		Pr (|T| > |t|)
	Positive	Negative	
	9.1±7.7	7.1±6.5	0.189

Table 4.5.2 shows the effect of intra-abdominal hypertension on the average length of stay in the ICU. The table compares the length of stay of patients in the positive (intra-abdominal hypertension) group with those in the negative (normal intra-abdominal pressure) group. The average ICU length of stay in the cohort was 9.1±7.7 in the intra-abdominal hypertension group compared to the 7.1±6.5. Statistically, there was no significant difference between the lengths of stay of both groups.

Table 4.6.1 Mean ventilator-free days

Mean Ventilator Free Days		n/%	95% conf. interval
		17.7±11.1	[15.3-20.0]

Table 4.6.1 shows the mean ventilator-free days of the study participants. The average ventilator-free days, calculated as 28 days minus the number of days a patient was on the ventilator was 17.7±11.1. It ranged from 0 days, in the case of a patient dying while being mechanically ventilated within the 28 days, to 28 days for patients who maintained their airways.

Table 4.6.2: Ventilator-free days and effect on intra-abdominal pressure

Ventilator Free Days	Intra-abdominal Hypertension		Pr (|T| > |t|)
	Positive	Negative	
	13.5±12.2	21.3±8.6	<0.001

Table 4.6.2 shows the comparison between the ventilator-free days in the intra-abdominal hypertension group and the normal intra-abdominal pressure group. The ventilator-free days in the normal intra-abdominal pressure group were 21.3±8.6 days whiles that of the intra-abdominal hypertension group was 13.5±12.2 days. This means that those who developed

intra-abdominal hypertension spent about 8 days more on the ventilator averagely than those who did not and this difference, was statistically significant (p-value <0.001).

Table 4.7 Mortality

Mortality Rate		n/%	95% conf. interval
		18[20.00]	[0.12-0.29]

Table 4.7 shows the overall the overall mortality rate of the study group was 20%.

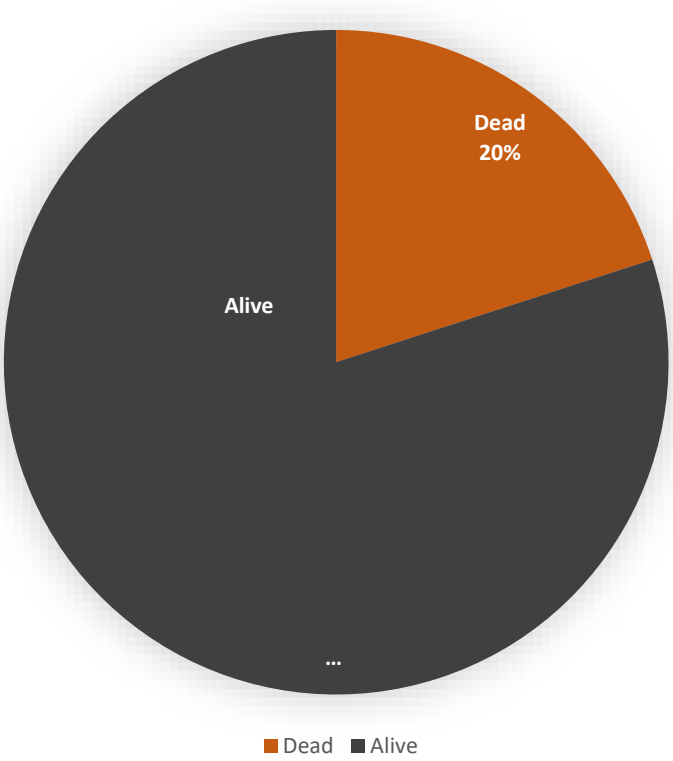


Figure 4.6 ICU Mortality in the study population.

The figure shows that the mortality rate was 20%.

Table 4.7.1 comparison of mortality between the IAH group and normal pressure group

Dead?	Intra-abdominal Hypertension No n/%	 Yes n/%	Total n/%
No **Yes**	44(91.6%) 4(8.3%)	28(66%) 14(33%)	72(80%) 18(20%)
Total	48(100%)	42(100%)	90(100%)

Pearson chi2 (1) = 8.7500 Pr= 0.003

The table above compares the mortalities between the intra-abdominal hypertension group and the normal intra-abdominal pressure groups. It can be seen from the table that, of the 42 participants who developed intra-abdominal hypertension, 14 participants representing 33% of those who developed IAH died whiles 4 participants out of the 48 who did not have intra-abdominal hypertension giving a mortality rate of 8.3% within the normal group. It can be deduced from the table that, people who had intra-abdominal hypertension had an increased risk of mortality than those who did not and the difference was statistically significant (p-value 0.003). Intra-abdominal hypertension increased one's risk of mortality by about 4 folds.

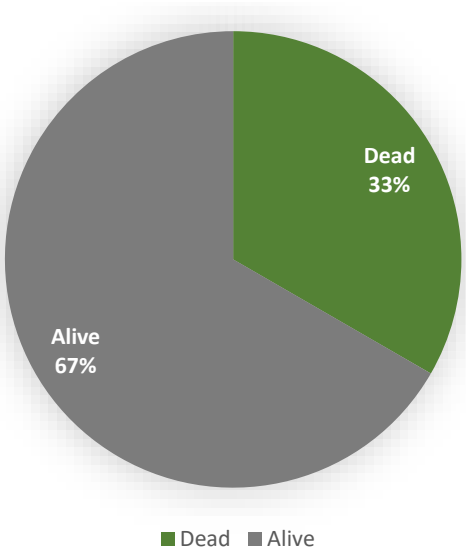


Figure 4.7 Mortality rate within the IAH group

The figure shows the mortality rate within the IAH group was 33% which was high

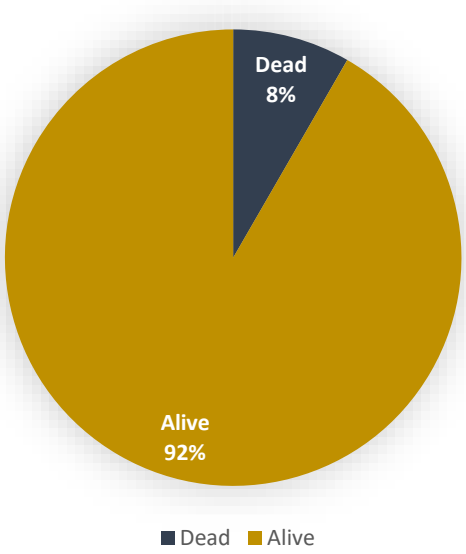


Figure 4.8 Mortality in the normal IAP group

The figure shows a mortality rate of 8%.

CHAPTER FIVE: DISCUSSION

5.1 Introduction

This section discusses the results of the study as seen in Chapter 4 and also compares the findings from the study with findings from other studies. The chapter reveals the prevalence of intra-abdominal hypertension in the main ICU at the Komfo Anokye Teaching Hospital and compares the findings to other studies.

It also elucidates the risk factors that were identified in the study, as well as the effect of intra-abdominal hypertension on mean SOFA scores as a function of organ dysfunction, Ventilator-free days and ICU length of stay, as markers of good outcome in the intensive care unit.

5.2 Patients' Characteristics

The study included both males and females with either medical or surgical conditions. A total of 90 participants were included in the study. Out of the participants, 48 representing 53.3% were males while 46.6% were females. Similarly in the study by Nansubuga et al[114] and Murtaza et al[115], there were male preponderance of 59.5% and 66% respectively. Again, Smit et al[8] and Muturi et al[50] had more male participants in their respective studies.

The ages of the study participants in this current study ranged from 18 to 84 years with the mean age being 44.3 years (S. D= 17.9, CI=40.5-48.03). In the study by Muturi et al, the average age of participation was 37.2 years[50]. The ages of the study participants ranged from 15-90 years old, this might have accounted for the difference in the mean age between the two groups. In the study by Taurai Zimunhu in Harare, participants included patients who were 12 years of age and older. The mean age of participation in that study was 37.29±16.18 years[12].

5.3 Prevalence of intra-abdominal hypertension

Out of the 90 study participants in this study, 42 participants representing 47% had intra-abdominal hypertension while 48 participants, representing 53% had normal intra-abdominal pressure (95% conf. interval: 0.36-0 .57). This prevalence is much lower than others reported from studies from other mixed ICUs in Africa. Nansubuga et al[114] reported a prevalence of 62.7%[114] while Muturi et al reported a prevalence of 67.3% and 71.7% respectively using mean

IAP and maximum IAP respectively[50]. In a burns ICU in Uganda, the overall prevalence of IAH was 57.8% while the prevalence in children and adults was 54.5% and 61.3% respectively[112]. In the study by Taurai Zumunhu in Zimbabwe, the prevalence was 74% and as high as 92% when the maximum IAP was used.

In the study by Nansubuga et al[114], intravesical measurements were done using a manometer held at 30 cm above the symphysis pubis. This was different from the described modified Kron's method which was employed in the current study. The volume of saline used was 20mls in that study instead of the recommended 25mls. Perhaps, the difference in prevalence between the index study and that study is attributable to the different methodologies used for the intra-abdominal pressure measurements.

The study by Muturi et al[50] in the Kenyatta Hospital involved surgical ICU patients from various surgical ICUs. Perhaps, the study being conducted in an all-surgical ICU population accounted for the higher prevalence of 67.3% compared to the 47% in our mixed ICU population. Abdominal surgery is an identified risk factor for intra-abdominal hypertension according to Holodinsky et al[49] and Malbrain et al[7]. In that study, 39.5% of the participants had Abdominopelvic conditions leading to the development of IAH. In the study population of the index patients, most surgical patients did not have Abdominopelvic conditions and that perhaps is the reason why surgery was not a risk factor in the index study. The measurement technique used by Muturi et al was the same as the one used by Nansubuga et al, the only differences being that the volume of normal saline that was instilled in the bladder was 25mls, as recommended by the WSACS and the figures recorded where stated as being in centimetres of water, needing a conversion factor of 1.36 to convert figures to millimetres of mercury (mmHg). This difference in measurement techniques could have accounted for the difference in prevalence between the index study and that study.

Again, in the study by Murtaza et al[115], the measurements were done similarly to the current study, using Kron's method. The differences in the methodology were the volume of saline instilled and the frequency of measurement. 50mls of normal saline was instilled instead of 25mls and the measurements were done within the first 12 hours of admission and twice daily thereafter until discharge, death or diagnosis of intra-abdominal hypertension. The reduced frequency of measurement could account for the difference in prevalence in the two studies. Indeed, the frequency of measurement is known to improve the accuracy and reliability of intra-abdominal pressure measurements. Measuring 4-6 hourly or more frequently when IAH

is diagnosed, or even measuring continuously is recommended[50]. In that study under review, once intra-abdominal pressure was ≥12, the measurements were done at 6-hour intervals and intra-abdominal hypertension was diagnosed if pressure measurements on two consecutive readings 6 hours apart were ≥12 mm Hg.

The prevalence of intra-abdominal hypertension was 50.5% according to the multicentre research that was conducted by Malbrain et al. This research involved 97 participants from 13 intensive care units in six countries and is said to be the biggest multicentre research on the subject of intra-abdominal hypertension. It was a one-day point-prevalence epidemiological study and intra-abdominal pressure was measured 6 hourly making 4 measurements. Again, 50mls of normal saline was used instead of 25mls. Using 50mls of normal saline overestimates the IAP values. This was a stated shortfall of their study[115]. Therefore, it could be that the difference in the methodologies between the two studies accounted for the difference in the prevalence rates.

Murphy et al found a 45% prevalence in their study cohort in a mixed medical-surgical ICU[22]. This finding was very similar to the 47% prevalence realised in the index study. Indeed, the methodology was similar save from the fact that IAP monitoring was done 12 hourly instead of 6 hourly in the index study. Perhaps the reduced frequency of measurement by Murphy et al, resulted in the lower prevalence they found.

The prevalence of abdominal compartment syndrome in the current study was 1.1% of the general patient cohort and 2.38% of the group that developed intra-abdominal hypertension. This was also much lower than the prevalence of ACS in other studies appraised. The reasons for the difference in prevalence could be due to the different participant populations used, the difference in the methodology and/or the difference in the ages of the participants.

5.4 Effect of Intra-abdominal hypertension on mean SOFA scores as a measure of organ dysfunction.

The “Sequential Organ Failure Assessment Score” (SOFA score) was employed as a measure of organ dysfunction in this study. The SOFA score was chosen out of the other disease severity scores like the APACHE II score based on simplicity and ease of usage and how comprehensive it is as it covers six major systems.

The mean Sofa scores were computed for all study participants from day 1 to day 7, allowing for comparison between the positive (intra-abdominal hypertension) group and the negative (normal intra-abdominal pressure) group. The mean SOFA scores for days 1 to day 7 were 7.3±3.9, 6.9±5.2, 6.3±5.6, 6.1±5.5, 5.7± 5.5, 5.0±5.3, and 4.6± 5.3. A SOFA score of 2 or less is a marker of mild or moderate disease and is associated with 100% survival SOFA score ≥5 is linked with high mortality with a score of 11 and above being associated with almost 100% mortality[113].

Participants with intra-abdominal hypertension had a higher SOFA score on day one of participation than those who did not have increased intra-abdominal pressure; 8.4±3.7 compared to 6.4±3.9. That could imply that people with high disease severity scores had a risk of developing intra-abdominal hypertension or intra-abdominal hypertension led to organ dysfunction such that, SOFA scores were high on day one. Indeed, Smit et al identified high disease severity score on admission was a risk factor for developing intra-abdominal hypertension[8]. The disease severity score used in that study however, was the Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II Scoring System.

The mean SOFA scores worsened on day 2 in the positive group while the scores in the negative group declined. The difference in SOFA scores was significant statistically. Mbiine et al demonstrated an association between organ dysfunction and intra-abdominal function with the renal system being more affected[112]. Again, Santa-Teresa et al found a similar relation between intra-abdominal hypertension and SOFA scores as a measure of organ dysfunction[10]

From the third day, however, mean SOFA scores started to decline in the positive group as well signifying improvement in participants' conditions, but the scores remained higher in the positive group compared to the negative group.

Similarly, Zimunhu found a similar positive association between SOFA scores and intra-abdominal hypertension[12].

5.5 Risk factors for intra-abdominal hypertension

The risk factors identified in this study are stated in Table 4.3. The main risk factors were Mechanical Ventilation, obesity, positive fluid balance and massive fluid resuscitation. Others included abdominal surgery, Sepsis and Major trauma. Holodinsky et al. identified shock/hypotension, large-volume crystalloid resuscitation, and the patient's respiratory

condition as common risk factors for IAH and ACS that cut across nearly all of the studies that were appraised in their systematic review and meta-analysis covered 14 studies[49]. Other risk factors included sepsis and obesity as well as abdominal surgery and ileus.

Intra-abdominal hypertension appears to have a strong correlation with massive fluid resuscitation. The increase in intra-abdominal pressure results from an increased intra-abdominal volume (both intra and extra luminal due to ascites formation, gut oedema, and ileus) and a decrease in abdominal wall compliance that results from the tissue oedema of the abdominal wall[1]. In the study by Muturi et al, large-volume crystalloid resuscitation in 24 hours was strongly associated with intra-abdominal hypertension. Also, defining massive fluid resuscitation as the administration of more than 3.5 litres of colloids or crystalloids in the 24 hours before the study, Malbrain et al found fluid resuscitation as a significant risk factor for IAH[5].

There are conflicting results on the importance of Mechanical ventilation, which was an important risk factor in this study, as a contributor to the development of intra-abdominal hypertension. The artificial ventilation is said to exert a direct influence on the intra-abdominal pressure by increasing intrathoracic pressures which is then transmitted to the abdomen.

The WSACS IROI study found a weak relationship between mechanical ventilation and the development of IAH[19]. Nansubuga et al found that neither Mechanical Ventilation nor positive 24-hour and cumulative fluid balance had any significant impact on intra-abdominal pressure[114]. Also, Malbrain et al found no significant association between mechanical ventilation and intra-abdominal hypertension. In fact, in their study, which was conducted in mixed ICU populations like ours, the only variable that was significantly associated with intra-abdominal hypertension was Body mass index (BMI). Transfusion rate and fluid resuscitation (and probably the associated positive net balance) were not statistically significant. Mechanical ventilation was defined in that study as “the use of invasive positive pressure ventilation with or without positive end-expiratory pressure (PEEP)”. The patients in KATH ICU are always ventilated with a PEEP of at least 5 and for this patient cohort, almost all ventilated patients were ventilated with the Synchronised Intermittent mandatory Ventilation (SIMV) in volume-controlled mode. It could be that just as Muturi and colleagues reported, the association is between SIMV and intra-abdominal hypertension and not mechanical ventilation generally. Indeed, Rafiei et al found an association between increase abdominal pressure and SIMV mode of ventilation. They realised from their study that patients on SIMV had a significant risk for

developing IAH than patients on BIPAP and CPAP modes (P = 0.01)[116]. This could be explained by the fact that volume-controlled modes like the SIMV used in the study lead to a progressive increase in intrathoracic pressure as was reported by Guldager et al[117] whiles the intrathoracic pressure in pressure modes stay relatively stable in pressure control modes. Also, the Peak inspiratory pressure is significantly higher in volume modes than in pressure modes. The close linkage between the thoracic cavity and the abdominal cavity presupposes that, that intrathoracic pressure is transmitted to the abdominal cavity leading to the added risk of developing Intra-abdominal hypertension.

Morejon et al also found a link between controlled mechanical ventilation (CMV) and pressure support ventilation (PSV) and intra-abdominal hypertension[118]. In their study however, SIMV was not one of the modes used. Since the CMV used in that and SIMV used in the current study were both volume-controlled, could the link between IAP and mechanical ventilation be assumed to be between volume-controlled modes and IAP? The confounder there though would be the fact that they found a link between pressure support ventilation, which is not a volume-controlled mode and raised IAP. The four modes of ventilation used were CMV, assisted/controlled ventilation (ACV), pressure support ventilation (PSV), and continuous positive airway pressure (CPAP)[119].

5.6 The effect of intra-abdominal hypertension on ICU length of stay.

The mean length of stay in the ICU amongst the study participants of this current study was 8.1±7.2 days. The average in the intra-abdominal hypertension group was 9.1±7.7 days while the length of stay in the negative group was 7.1±6.5 days. No significant difference was found between those with intra-abdominal hypertension and those who did not develop the condition. Similarly, Nansubuga et al realised that the average ICU length of stay of was nine days and there was no significant difference between those who had intra-abdominal hypertension and those who did not develop the condition[114].

In the study by Santa-Teresa et al, however, the participants who developed intra-abdominal hypertension had significantly longer than those without the condition[10]. Additionally, Smit et al. discovered that, compared to patients with normal intra-abdominal pressure, individuals with intra-abdominal hypertension had a mean length of critical care stay that rose by a factor of 4 and abdominal compartment syndrome by a factor of 9[8]. Again, in the study by De Waele

et al, the length of stay in the ICU was considerably longer in the intra-abdominal hypertension group[120]. The same conclusion was reached after the study by Kyoung and Hong. Their study also found that the duration of intra-abdominal hypertension was more significant in terms of prognosis than the development of intra-abdominal hypertension[121].

5.7 Effect of Intra-abdominal hypertension on ventilator-free days

Ventilator-free days (VFDs) is one of the organ failure–free outcome measures used in critical care to ascertain the effectiveness of therapies and interventions[109]. Although it is usually used in acute respiratory distress syndrome, it is a useful measure of overall outcomes in the ICU.

The ventilator-free days of a patient was calculated as 28- the number of days the patient stayed on the ventilator. VFDs is 0 if a patient dies within 28 days of mechanical ventilation or, spends more than 28 days on the mechanical ventilator. The mean ventilator-free days for this study was 17.7±11.1 meaning, participants stayed on the ventilator for at least 11 days on average. The mean in the intra-abdominal hypertension group was 13.5±12.2 days while that of the normal intra-abdominal pressure group was 21.3±8.6 days (p-value <0.001). This means that patients with intra-abdominal hypertension spent relatively more days on the ventilator than those without the condition and this finding, was statistically significant.

The studies appraised did not look at ventilator-free days as an entity but assessed the time the participant stayed on the ventilator as a measure of outcome. In the studies by Nansubuga et al and Mbiine et al which are other African studies on the topic, intra-abdominal hypertension was linked to prolonged ventilation. Also, the study by Murtaza et al found that it was difficult to liberate patients with IAH from the mechanical ventilator; 37.9% vs. 25.9% (p-value 0.008) failure rate between the IAH and normal IAP groups respectively[115].

This requirement of prolonged ventilation may be explained by the fact that Intra-abdominal hypertension has been demonstrated to cause secondary acute lung injury and adult respiratory distress syndrome[122]. Also, IAH causes an increase in chest wall elasticity and it also reduces the functional residual capacity. Additionally, there is an increase in peak airway and plateau pressures, which can lead to barotrauma and aggravate the ARDS by encouraging a neutrophil-activated inflammatory response[70]. Non-cardiogenic pulmonary oedema can be brought on by increased capillary permeability and exudation of protein-rich fluid into the pulmonary interstitial space as a result of the pulmonary congestion brought on by the elevated diaphragm

caused by the IAH and the inflammatory processes[122]. All these processes make liberation from mechanical ventilation difficult.

5.8 Effect of Intra-abdominal hypertension on overall outcomes

The mortality rate in this participant cohort was 20%. Of those who had intra-abdominal hypertension, mortality rate was 33% whiles 8% of those who did not develop intra-abdominal hypertension died. It can be seen that, IAH increased the chances of a patient dying in this patient cohort. Similar outcomes have been found in other studies.

ICU mortality was considerably higher in the IAH and ACS group than in the normal IAP group, according to Smit et al. (4.8% and 16.7% vs. 1.2%) ($p < 0.01$)[8]. In the burns ICU patient cohort in Uganda, the one-week mortality of patients with IAH was 82.6% with the risk of dying being 3.34 ($p=0.0035$) and seven-day survival was less than 50%[112]. Again, Nansuguba et al found that more patients died in the IAH group compared to the normal IAP group (p-value 0.003)[114].

5.9 Limitations to the study

The main limitation to this study was with the computing of SOFA scores:

Firstly, due to the lack of biochemistry laboratory services on some of the days during the study, liver function and renal function were assumed as normal in computing SOFA scores in patients who did not have the laboratory results. Also, anytime daily laboratory results were not available, the previous day's results were used to compute the SOFA scores. This could have affected the use of the SOFA scores measured as a means of organ dysfunction.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. The prevalence of intra-abdominal hypertension within the first 48 hours of admission at the main ICU of the Komfo Anokye Teaching Hospital is 47%.
2. The common risk factors for intra-abdominal hypertension at the Komfo Anokye Teaching Hospital main ICU are Massive fluid resuscitation, defined as intravenous fluid volumes of ≥3.5.L in 24 hours, positive fluid balance, obesity and mechanical ventilation.
3. Intra-abdominal hypertension is associated with a high SOFA score.
4. There is no effect of intra-abdominal pressure within the first 48 hours of ICU admission on the ICU length of stay.
5. Intra-abdominal hypertension reduces the ventilator-free days.
6. ICU mortality is increased by intra-abdominal hypertension.

6.2 Recommendations

1. Routine IAP monitoring should be performed for all patients with risk factors of intra-abdominal hypertension to enable prompt diagnosis and management.
2. Protocol-driven care should be instituted to address the diagnosis and management of the condition holistically.
3. Goal-directed fluid resuscitation is encouraged, especially in patients in the ICU, to lower the incidence of intra-abdominal hypertension given the positive connection between positive fluid balance and intra-abdominal hypertension. Given the positive association of positive fluid balance and intra-abdominal hypertension, Goal-directed fluid resuscitation is advocated especially in patients in the ICU to reduce the incidence of intra-abdominal hypertension.
4. To lower the risk of intra-abdominal hypertension, protocols for prompt liberation of patients from mechanical ventilation should be implemented.

References

1. De Laet IE, Malbrain MLNG, De Waele JJ. A Clinician's Guide to Management of Intra-Abdominal Hypertension and Abdominal Compartment Syndrome in Critically Ill Patients. Crit Care. 2020;24(1):1–9.
2. Malbrain MLNG, De Laet IE, De Waele JJ, Kirkpatrick AW. Intra-abdominal hypertension: Definitions, monitoring, interpretation and management. Best Pract Res Clin Anaesthesiol. 2013;27(2):249–70.
3. Chiumello D. Intra-abdominal pressure in critically ill patients: It is worthwhile to measure? Minerva Anestesiol. 2007;73(9):445–6.
4. Malbrain MLNG, Cheatham ML, Kirkpatrick A, Sugrue M, Parr M, De Waele J, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. Intensive Care Med. 2006;32(11):1722–32.
5. Malbrain MLNG, Chiumello D, Pelosi P, Wilmer A, Brienza N, Malcangi V, et al. Prevalence of intra-abdominal hypertension in critically ill patients: A multicentre epidemiological study. Intensive Care Med. 2004;30(5):822–9.
6. Milanesi R, Caregnato RCA. Intra-abdominal pressure: an integrative review. Einstein (Sao Paulo). 2016;14(3):423–30.
7. Malbrain MLNG, Chiumello D, Pelosi P, Bihari D, Innes R, Ranieri VM, et al. Incidence and prognosis of intraabdominal hypertension in a mixed population of critically ill patients: A multiple-center epidemiological study. Crit Care Med. 2005;33(2):315–22.
8. Smit M, Koopman B, Dieperink W, Hulscher JBF, Hofker HS, van Meurs M, et al. Intra-abdominal hypertension and abdominal compartment syndrome in patients admitted to the ICU. Ann Intensive Care. 2020;10(1).
9. Smit M, Koopman B, Dieperink W, Hulscher JBF, Hofker HS, van Meurs M, et al. Intra-abdominal hypertension and abdominal compartment syndrome in patients admitted to the ICU. Vol. 10, Annals of Intensive Care. 2020.
10. Santa-Teresa P, Muñoz J, Montero I, Zurita M, Tomey M, Álvarez-Sala L, et al. Incidence and prognosis of intra-abdominal hypertension in critically ill medical patients: A prospective epidemiological study. Ann Intensive Care. 2012;2012(Suppl 1):1–13.
11. McNelis J, Marini CP, Simms HH. Abdominal compartment syndrome: Clinical manifestations and predictive factors. Curr Opin Crit Care. 2003;9(2):133–6.
12. Zimunhu T. ABDOMINAL COMPARTMENT SYNDROME IN ABDOMINAL SURGICAL PATIENTS ADMITTED TO INTENSIVE CARE UNITS OF HARARE TEACHING HOSPITALS Prevalence and clinical significance. University of Zimbabwe Theses and Dissertations Collection. 2013;

13. Cullen DJ, Coyle JP, Teplick R, Long MC. Cardiovascular, pulmonary, and renal effects of massively increased intra-abdominal pressure in critically ill patients. Crit Care Med. 1989;17(2):118–21.

14. Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain MLNG, De Keulenaer B, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: Updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. Intensive Care Med. 2013;39(7):1190–206.

15. Luiz Carlos Von B, Lange PAL, Alves RFF, Soares HMN, de Souza TM, Aline Cadena Von B. Abdominal compartment syndrome: Knowledge of the medical staff of a university hospital in curitiba. Rev Col Bras Cir. 2018;45(3):1–8.

16. Wise R, Rodseth R, Blaser AR, Roberts DJ, De Waele JJ, Kirkpatrick AW, et al. Awareness and knowledge of intra-abdominal hypertension and abdominal compartment syndrome: Results of a repeat, international, cross-sectional survey. Anaesthesiol Intensive Ther. 2019;51(3):186–99.

17. Theodossis S Papavramidis1, Athanasios D Marinis2, Ioannis Pliakos1, Isaak Kesisoglou1 NP. Abdominal compartment syndrome - Intra-abdominal hypertension: Defining, diagnosing, and managing. J Emerg Trauma Shock 2011; 4:279-91; 2011. p.: 279-291.

18. Harrahill M. Intra-abdominal pressure monitoring. Journal of emergency nursing: JEN: official publication of the Emergency Department Nurses Association. 1998;24(5):465–6.

19. Reintam Blaser A, Regli A, De Keulenaer B, Kimball EJ, Starkopf L, Davis WA, et al. Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients - A Prospective Multicenter Study (IROI Study). Crit Care Med. 2019;47(4):535–42.

20. Kimball EJ, Kim W, Cheatham ML, Malbrain MLNG. CLINICAL AWARENESS OF INTRA-ABDOMINAL HYPERTENSION AND ABDOMINAL COMPARTMENT SYNDROME IN 2007 CLINICAL AWARENESS OF INTRA-ABDOMINAL HYPERTENSION AND ABDOMINAL COMPARTMENT SYNDROME IN 2007. 2016;3286(March).

21. Fernández Meré LA, Alvarez Blanco M. Abdominal compartment syndrome. Rev Esp Anestesiol Reanim. 2007;54(6):359–70.

22. Murphy PB, Parry NG, Sela N, Leslie K, Vogt K, Ball I. Intra-abdominal hypertension is more common than previously thought: A prospective study in a mixed medical-surgical ICU. Crit Care Med. 2018;46(6):958–64.

23. Van Hee R. Historical highlights in concept and treatment of abdominal compartment syndrome. Acta Clin Belg. 2007;62(SUPPL. 1):9–15.

24. Denlinger LC, Proctor RA. Potential risk factors for developing apoptosis during septic shock. Crit Care Med. 2000;28(6):2133–4.

25. Malbrain M, Waele J De. What is intra-abdominal pressure? In: Cambridge University Press. Cambridge University Press; 2013. p. 3–13.

26. Bradley SE, Bradley GP. the Effect of Increased Intra-Abdominal Pressure on Renal Function in Man. J Clin Invest. 1947;26(5):1010–22.

27. Richardson JD, Trinkle JK. Hemodynamic and respiratory alterations with increased intra-abdominal pressure. Journal of Surgical Research. 1976;20(5):401–4.

28. Diaz FJ, Fernandez Sein A, Gotay F. Identification and management of Abdominal Compartment Syndrome in the Pediatric Intensive Care Unit. P R Health Sci J. 2006;25(1):17–22.

29. Pereira BM. Abdominal compartment syndrome and intra-abdominal hypertension. Curr Opin Crit Care. 2019;25(6):688–96.

30. Õiglane-Šlik E. Dissertationes Medicinae Universitatis Tartuensis 134. 2007;

31. Rezeni N, Thabet F. Awareness and management of intra-abdominal hypertension and abdominal compartment syndrome by paediatric intensive care physicians: a national survey. Anaesthesiol Intensive Ther. 2022;54(4):315–9.

32. Wiegandt P, Jack T, von Gise A, Seidemann K, Boehne M, Koeditz H, et al. Awareness and diagnosis for intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) in neonatal (NICU) and pediatric intensive care units (PICU) – a follow-up multicenter survey. BMC Pediatr. 2023;23(1):1–10.

33. Khot Z, Murphy PB, Sela N, Parry NG, Vogt K, Ball IM. Incidence of Intra-Abdominal Hypertension and Abdominal Compartment Syndrome: A Systematic Review. J Intensive Care Med. 2021;36(2):197–202.

34. Reintam Blaser A, Malbrain MLNG, Regli A. Abdominal pressure and gastrointestinal function: an inseparable couple? Anaesthesiol Intensive Ther. 2017;49(2):146-158. doi: 10.5603/AIT.a2017.0026. Epub 2017 May 17. PMID: 28513822.

35. Carriquiry CE. Anatomy and physiology of the abdominal wall. Operative Techniques in Plastic and Reconstructive Surgery. 1996;3(1):2–6.

36. Malbrain MLNG, De Laet I, De Waele JJ, Sugrue M, Schachtrupp A, Duchesne J, et al. The role of abdominal compliance, the neglected parameter in critically ill patients - A consensus review of 16. Part 2: Measurement techniques and management recommendations. Anaesthesiol Intensive Ther. 2014;46(5):406–32.

37. Förstemann T, Trzewik J, Holste J, Batke B, Konerding MA, Wolloscheck T, et al. Forces and deformations of the abdominal wall-A mechanical and geometrical approach to the linea alba. J Biomech. 2011;44(4):600–6.

38. Accarino A, Perez F, Azpiroz F, Quiroga S, Malagelada JR. Abdominal Distention Results from Caudo-ventral Redistribution of Contents. Gastroenterology. 2009;136(5):1544–51.

39. Malbrain MLNG, Roberts DJ, De Laet I, De Waele JJ, Sugrue M, Schachtrupp A, et al. The role of abdominal compliance, the neglected parameter in critically ill patients - A

consensus review of 16. Part 1: Definitions and pathophysiology. Anaesthesiol Intensive Ther. 2014;46(5):392–405.

40. Mulier J, Coenegrachts K, Van De Moortele K. CT analysis of the elastic deformation and elongation of the abdominal wall during colon inflation for virtual coloscopy. Eur J Anaesthesiol. 2008;25(Sup 44):42.

41. Cheatham ML. Abdominal Compartment Syndrome: pathophysiology and definitions. 2009; 11:1–11.

42. Cheatham ML, Malbrain MLNG. Cardiovascular implications of abdominal compartment syndrome. Acta Clin Belg. 2007;62(SUPPL. 1):98–112.

43. Malbrain MLNG, Waele JJ De, Keulenaer BL De. What every ICU clinician needs to know about the cardiovascular effects caused by abdominal hypertension. Anestezjol Intens Ter. 2015;47(4):402–13.

44. Grajecki D, Tacke F. Gastrointestinal motility disorders in critically ill patients. Deutsche Medizinische Wochenschrift. 2022;147(11):696–704.

45. Barrett KE. Gastrointestinal (GI) Physiology. Third Edit. Reference Module in Biomedical Sciences. Elsevier; 2014. 1–14 p.

46. Walker WA. Immunology of the GI Tract Physiology Education Series.

47. Reintam Blaser A, Parm P, Kitus R, Starkopf J. Intra-Abdominal Hypertension and Gastrointestinal Symptoms in Mechanically Ventilated Patients. Crit Care Res Pract. 2011; 2011:1–5.

48. Nutrition H, Town C, Hill B, Nutrition MH, Miller M, Care FCAC, et al. The effect of intra-abdominal hypertension on gastro- intestinal function. 2011;27(1).

49. Holodinsky JK, Roberts DJ, Ball CG, Blaser AR, Starkopf J, Zygun DA, et al. Risk factors for intra-abdominal hypertension and abdominal compartment syndrome among adult intensive care unit patients: a systematic review and meta-analysis. 2013.

50. Muturi A, Ndaguatha P, Ojuka D, Kibet A. Prevalence and predictors of intra-abdominal hypertension and compartment syndrome in surgical patients in critical care units at Kenyatta National Hospital. BMC Emerg Med. 2017 Mar 23;17(1).

51. Vatankhah S, Sheikhi RA, Heidari M, Moradimajd P. The relationship between fluid resuscitation and intra-abdominal hypertension in patients with blunt abdominal trauma. Vol. 8, International Journal of Critical Illness and Injury Science. 2018. p. 149–53.

52. Balogh Z, McKinley BA, Holcomb JB, Miller CC, Cocanour CS, Kozar RA, et al. Both primary and secondary abdominal compartment syndrome can be predicted early and are harbingers of multiple organ failure. Journal of Trauma. 2003;52(5):848–61.

53. Thabet FC, Bougmiza IM, Chehab MS, Bafaqih HA, Almohaimeed SA, Malbrain MLNG. Incidence, Risk Factors, and Prognosis of Intra-Abdominal Hypertension in Critically Ill Children: A Prospective Epidemiological Study. J Intensive Care Med. 2016;31(6):403–8.

54. Luckianow GM, Ellis M, Governale D, Kaplan LJ. Abdominal compartment syndrome: Risk factors, diagnosis, and current therapy. Crit Care Res Pract. 2012;2012.

55. Starkopf J, Tamme K, Blaser AR. Should we measure intra-abdominal pressures in every intensive care patient? Ann Intensive Care. 2012;2012(Suppl 1):1–7.

56. Ryu DY, Kim H, Seok JP, Lee CK, Yeo KH, Choi SU, et al. Clinical Effects of Intra-Abdominal Pressure in Critically Ill Trauma Patients. Journal of Trauma and Injury. 2019;32(2):86–92.

57. Smit M, van Meurs M, Zijlstra JG. Intra-abdominal hypertension and abdominal compartment syndrome in critically ill patients: A narrative review of past, present, and future steps. Scandinavian Journal of Surgery. 2021.

58. Maluso P, Olson J, Sarani B. Abdominal Compartment Hypertension and Abdominal Compartment Syndrome. Crit Care Clin. 2016;32(2):213–22.

59. Wauters J, Claus P, Brosens N, McLaughlin M, Hermans G, Malbrain M, et al. Relationship between abdominal pressure, pulmonary compliance, and cardiac preload in a porcine model. Crit Care Res Pract. 2012;2012.

60. Cullen, David J. Coyle, Joseph P. Teplick, Richard. Long M. Cardiovascular, Pulmonary and Renal effects of massively increased intra-abdominal pressure in critically ill patients. Crit Care Med. 1989;17(2).

61. Gudmundsson FF, Gislason HG, Myking OL, Viste A, Grong K, Svanes K. Hormonal changes related to reduced renal blood flow and low urine output under prolonged increased intra-abdominal pressure in pigs. European Journal of Surgery. 2002;168(3):178–86.

62. Simon, Ronald J. MD, FACS; Friedlander, M. H. MD; Ivatury, R. R. MD, FACS; DiRaimo, R. MS; Machiedo, G. W. MD F. Hemorrhage_Lowers_the_Threshold_for_Intra-abdominal_Hypertension-induced_. The Journal of Trauma: Injury, Infection, and Critical Care. 1997;42(3):398–405.

63. Ameloot K, Gillebert C, Desie N, Malbrain MLNG. Hypoperfusion, Shock States, and Abdominal Compartment Syndrome (ACS). Surgical Clinics of North America. 2012;92(2):207–20.

64. Takata M, Wise RA, Robotham JL. Effects of abdominal pressure on venous return: Abdominal vascular zone conditions. J Appl Physiol. 1990;69(6):1961–72.

65. Huettemann E, Sakka SG, Petrat G, Schier F, Reinhart K. Left ventricular regional wall motion abnormalities during pneumoperitoneum in children. Br J Anaesth. 2003;90(6):733–6.

66. Overall P. Chapter 15 : Cardiovascular system - The heart.

67. Tavernier B, Robin E. Assessment of fl uid responsiveness during increased intra-abdominal pressure : keep the indices , but change the thresholds. 2011;i:7–8.

68. Biais M, Bernard O, Ha JC, Degryse C, Sztark F. Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery. Br J Anaesth. 2010;104(4):407–13.

69. Malbrain MLNG, Ameloot K, Gillebert C, Cheatham ML. Cardiopulmonary monitoring in intra-abdominal hypertension. Am Surg. 2011;77 Suppl 1(July).

70. Christensen M, Craft J. The cardio-respiratory effects of intra-abdominal hypertension: Considerations for critical care nursing practice. Intensive Crit Care Nurs. 2018;44:53–8.

71. Regli A, Pelosi P, Malbrain MLNG. Ventilation in patients with intra-abdominal hypertension: what every critical care physician needs to know. Ann Intensive Care. 2019;9(1).

72. Regli A, Pelosi P, Malbrain MLNG, de Cleva R, de Assumpção MS, Sasaya F, et al. Correlation between intra-abdominal pressure and pulmonary volumes after superior and inferior abdominal surgery. Clinics. 2014;69(7):483–6.

73. Malbrain MLNG, Pelosi P, De Laet I, Lattuada M, Hedenstierna G. Lymphatic drainage between thorax and abdomen: Please take good care of this well-performing machinery... Acta Clin Belg. 2007;62(SUPPL. 1):152–61.

74. Cheng J, Wei Z, Liu X, Li X, Yuan Z, Zheng J, et al. The role of intestinal mucosa injury induced by intra-abdominal hypertension in the development of abdominal compartment syndrome and multiple organ dysfunction syndrome. Crit Care. 2013;17(6).

75. Eleftheriadis E, Kotzampassi K, Papanotas K, Heliadis N, Sarris K. Gut ischemia, oxidative stress, and bacterial translocation in elevated abdominal pressure in rats. World J Surg. 1996;20(1):11–6.

76. De Keulenaer BL, Regli A, Dabrowski W, Kaloiani V, Bodnar Z, Cea JI, et al. Does femoral venous pressure measurement correlate well with intrabladder pressure measurement? A multicenter observational trial. Intensive Care Med. 2011;37(10):1620–7.

77. Malbrain MLNG, Viaene D, Kortgen A, De laet I, Dits H, Van Regenmortel N, et al. Relationship between intra-abdominal pressure and indocyanine green plasma disappearance rate: Hepatic perfusion may be impaired in critically ill patients with intra-abdominal hypertension. Ann Intensive Care. 2012;2012(Suppl 1):1–11.

78. Dupont S, Schiffer ERC, White MJ, Diaper JRA, Licker MJ, Masouyé PC. Changes in hepatic blood flow and liver function during closed abdominal hyperthermic intraperitoneal chemotherapy following cytoreduction surgery. Gastroenterol Res Pract. 2018;2018.

79. Villa G, Samoni S, De Rosa S, Ronco C. The pathophysiological hypothesis of kidney damage during intra-abdominal hypertension. Front Physiol. 2016;7(FEB):1–4.

80. De Waele JJ, De Laet I, Kirkpatrick AW, Hoste E. Intra-abdominal hypertension and abdominal compartment syndrome. American Journal of Kidney Diseases. 2011;57(1):159–69.

81. Harman PK, Kron IL, McLachlan HD, Freedlender AE, Nolan SP. Elevated intra-abdominal pressure and renal function. Ann Surg. 1982;196(5):594–7.

82. Just A. Mechanisms of renal blood flow autoregulation: Dynamics and contributions. Am J Physiol Regul Integr Comp Physiol. 2007;292(1).

83. Doty JM, Saggi BH, Blocher CR, Fakhry I, Gehr T, Sica D, et al. Effects of increased renal parenchymal pressure on renal function. Vol. 48, Journal of Trauma - Injury, Infection and Critical Care. 2000. p. 874–7.

84. Rezende-Neto JB, Moore EE, De Andrade MVM, Teixeira MM, Assis Lisboa F, Esteves Arantes RM, et al. Systemic inflammatory response secondary to abdominal compartment syndrome: Stage for multiple organ failure. Journal of Trauma - Injury, Infection and Critical Care. 2002;53(6):1121–8.

85. Edil BH, Tuggle DW, Puffinbarger NK, Mantor PC, Palmer BW, Knutson ZA. The impact of intra-abdominal hypertension on gene expression in the kidney. Journal of Trauma. 2003;55(5):857–9.

86. Kashani K, Al-Khafaji A, Ardiles T, Artigas A, Bagshaw SM, Bell M, et al. Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury. Crit Care. 2013;17(1):R25.

87. Endre ZH, Pickering JW, Walker RJ, Devarajan P, Charles L, Bonventre J V, et al. Baseline Renal Function. Kidney Int. 2011;79(10):1–25.

88. Malbrain, Manu; De Waele J. Chapter 18 Central nervous system and IAH. i:153–8.

89. Lui F, Sangosanya A, Kaplan LJ. Abdominal Compartment Syndrome: Clinical Aspects and Monitoring. Crit Care Clin. 2007;23(3):415–33.

90. Depauw PRAM, Groen RJM, Van Loon J, Peul WC, Malbrain MLNG, De Waele JJ. The significance of intra-abdominal pressure in neurosurgery and neurological diseases: a narrative review and a conceptual proposal. Acta Neurochir (Wien). 2019;855–64.

91. Akinci IO, Tunali U, Kyzy AA, Guresti E, Sencer A, Karasu A, et al. Effects of prone and jackknife positioning on lumbar disc herniation surgery. J Neurosurg Anesthesiol. 2011;23(4):318–22.

92. Al-Abassi AA, Al Saadi AS, Ahmed F. Is intra-bladder pressure measurement a reliable indicator for raised intra-abdominal pressure? A prospective comparative study. BMC Anesthesiol. 2018;18(1):1–9.

93. De Laet I, Citerio G, Malbrain MLNG. The influence of intra-abdominal hypertension on the central nervous system: Current insights and clinical recommendations, is it all in the head? Acta Clin Belg. 2007;62(SUPPL. 1):89–97.

94. Rosenthal RJ, Friedman RL, Phillips EH. Intra-abdominal Pressure, Intracranial Pressure, and Hemodynamics: A Central Nervous System-Regulated Response. The Pathophysiology of Pneumoperitoneum. 1998;85–98.

95. Sugrue M, Bauman A, Jones F, Bishop G, Flabouris A, Parr M, et al. Clinical examination is an inaccurate predictor of intraabdominal pressure. World J Surg. 2002 Dec;26(12):1428–31.

96. G C, Kirkpatrick W, States U. Intra-abdomInal HypertensIon and tHe abdomInal Compartment syndrome. 2007;197–204.

97. Cheatham ML, De Waele JJ, De Laet I, De Keulenaer B, Widder S, Kirkpatrick AW, et al. The impact of body position on intra-abdominal pressure measurement: A multicenter analysis. Crit Care Med. 2009;37(7):2187–90.

98. De Waele JJ, Cheatham ML, Malbrain MLNG, Kirkpatrick AW, Sugrue M, Balogh Z, et al. Recommendations for research from the international conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. Acta Clin Belg. 2009;64(3):203–9.

99. Malbrain MLNG. Different techniques to measure intra-abdominal pressura (IAP): Time for a critical re-appraisal. Vol. 30, Intensive Care Medicine. 2004. p. 357–71.

100. Dowdle M. Evaluating a New Intrauterine Pressure Catheter. 1997;506–13.

101. Cheatham ML, Safcsak K. Is the evolving management of intra-abdominal hypertension and abdominal compartment syndrome improving survival? Crit Care Med. 2010;38(2):402–7.

102. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med. 1996;22(7):707–10.

103. Arts DGT, De Keizer NF, Vroom MB, De Jonge E. Reliability and accuracy of Sequential Organ Failure Assessment (SOFA) scoring. Crit Care Med. 2005;33(9):1988–93.

104. Kramer AA, Zimmerman JE. A predictive model for the early identification of patients at risk for a prolonged intensive care unit length of stay. BMC Med Inform Decis Mak. 2010;10(1).

105. Finkielman JD, Morales IJ, Peters SG, Keegan MT, Ensminger SA, Lymp JF, et al. Mortality rate and length of stay of patients admitted to the intensive care unit in July. Crit Care Med. 2004;32(5):1161–5.

106. Laupland KB, Kirkpatrick AW, Kortbeek JB, Zuege DJ. Long-term mortality outcome associated with prolonged admission to the ICU. Chest. 2006;129(4):954–9.

107. Straney LD, Udy AA, Burrell A, Bergmeir C, Huckson S, Cooper DJ, et al. Modelling risk-adjusted variation in length of stay among Australian and New Zealand ICUs. PLoS One. 2017;12(5).

108. Bodet-Contentin L, Frasca D, Tavernier E, Feuillet F, Foucher Y, Giraudeau B. Ventilator-free day outcomes can be misleading. Crit Care Med. 2018;46(3):425–9.

109. Yehya N, Harhay MO, Curley MAQ, Schoenfeld DA, Reeder RW. Reappraisal of ventilator-free days in critical care research. Vol. 200, American Journal of Respiratory and Critical Care Medicine. 2019. p. 828–36.

110. De Dios Caridad, Morejón S, Osmin Teddy BT. Effect of mechanical ventilation on intra-abdominal pressure in critically ill patients without other risk factors for abdominal hypertension: an observational multicenter epidemiological study. Soler Morejón and Tamargo BarbeitoAnnals of?Intensive Care2012,2(Suppl 1):S22; 2012.

111. Reintam Blaser A, Regli A, De Keulenaer B, Kimball EJ, Starkopf L, Davis WA, et al. Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients - A Prospective Multicenter Study (IROI Study). Crit Care Med. 2019;47(4):535–42.

112. Mbiine R, Alenyo R, Kobusingye O, Kuteesa J, Nakanwagi C, Lekuya HM, et al. Intra-abdominal hypertension in severe burns: prevalence, incidence and mortality in a sub-Saharan African hospital. Int J Burns Trauma. 2017;7(6):80–7.

113. Fayed M, Patel N, Angappan S, Nowak K, Vasconcelos Torres F, Penning DH, et al. Sequential Organ Failure Assessment (SOFA) Score and Mortality Prediction in Patients with Severe Respiratory Distress Secondary to COVID-19. Cureus. 2022;14(7).

114. Nansubuga P, Kavuma Mwanje A, Kizito S et al. The prevalence, incidence and mortality associated with intra-abdominal hypertension among patients in intensive care units of a low-income country: a cohort study [version 1; peer review: 4 approved with reservations]. AAS Open Res 2020, 3:53 (https://doi.org/10.12688/aasopenres.13101.1)

115. Murtaza G, Pal KMI, Jajja MRN, Nawaz Z, Koondhar R, Nasim S. Intra-abdominal hypertension; incidence, prevalence and outcomes ina mixed intensive care unit: Prospective cohort study. International Journal of Surgery. 2015; 19:67–71.

116. Rafiei MR, Aghadavoudi O, Shekarchi B, Sajjadi SS, Masoudifar M. Can selection of mechanical ventilation mode prevent increased intra-abdominal pressure in patients admitted to the intensive care unit? Int J Prev Med. 2013;4(5):552–6.

117. Guldager, Nielsen, Carl, Soerensen. A comparison of volume control and pressure-regulated volume control ventilation in acute respiratory failure. Crit Care. 1997;1(2):75–7.

118. Morejón C de DS, Barbeito TOT. Effect of mechanical ventilation on intraabdominal pressure in critically ill patients without other risk factors for abdominal hypertension: An observational multicenter epidemiological study. Ann Intensive Care. 2012;2012(Suppl 1): S22.

119. De Dios C, Morejón S, Osmin T, Barbeito T. Effect of mechanical ventilation on intra-abdominal pressure in critically ill patients without other risk factors for abdominal hypertension: an observational multicenter epidemiological study. 2012.

120. De Waele JJ, Leppäniemi AK. Intra-abdominal hypertension in acute pancreatitis. Vol. 33, World Journal of Surgery. 2009. p. 1128–33.

121. Kyoung KH, Hong SK. The duration of intra-abdominal hypertension strongly predicts outcomes for the critically ill surgical patients: A prospective observational study. World Journal of Emergency Surgery. 2015;10(1):1–6.

122. Pelosi P, Quintel M, Malbrain MLNG. Effect of intra-abdominal pressure on respiratory mechanics. Vol. 62, Acta Clinica Belgica. 2007. p. 78–88.

Appendix 1: Data Collection sheet

PREVALENCE AND OUTCOMES OF INTRA-ABDOMINAL HYPERTENSION IN CRITICALLY ILL PATIENTS IN A MIXED INTENSIVE CARE POPULATION

Date:

Patient's Initials:

Hospital number:

Next of Kin:

Age:

Sex:

Admission date:

Discharge date:

Primary Diagnosis:

Reason for ICU admission:

Admission SOFA score:

Identified risk factors (see Appendix iii):

DAILY SOFA SCORES

Respiratory system (Pa02/Fi02) ----------score

Nervous System (GCS) ----------score

Cardiovascular system (MAP or Ionotropes) ----------score

Liver (Bilirubin, mg/dl) ----------score

Coagulation (platelet count) ----------score

Renal system (creatinine or urine output) ----------score

Total score ----------

Length of stay ----------

Ventilator-free days ----------

Outcome at 30 days Died Discharged

MONITORING CHART

Time	6hrs post admission	12hours post admission	18hours post admission	24hours post admission	30hours post admission	36hours post admission	42 hours post admission	48hours post admission
Heart rate								
Mean arterial pressure								
Ionotropes								
Vent mode								
IAP monitoring								
Urine output								
Fluid balance								

RISK FACTORS

Does the patient have any of the risk factors listed below? Please check on admission and daily.

- Diminished wall compliance

-abdominal surgery

-prone position

-major trauma

-morbid obesity

- Increased intra-abdominal content

-Acute Pancreatitis

- Distended Abdomen

- Haemoperitonium

- Intra-abdominal infection/Abscess

- Cirrhosis with ascites

- Increased intra-luminal contents

-Ileus

- Gastroparesis

- Capillary leak/ Fluid resuscitation

-Acidosis

-Massive fluid resuscitation

-Hypothermia

-Positive fluid balance

-Massive blood transfusion

- Others

-Coagulopathy

- Mechanical Ventilation

-PEEP

-Sepsis

-Obestiy

Appendix 2.1: consent form

CONSENT FORM

Statement of person obtaining informed consent:
I have fully explained this research to _____ and have given sufficient information about the study, including that on procedures, risks and benefits, to make an informed decision.

DATE: _____ SIGNATURE: _____

NAME: _____

Statement of person giving consent:
I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction.

I have read the description of the research or have had it translated into language I understand. I have also talked it over with the interviewer to my satisfaction. I understand that my participation is voluntary. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I may freely stop being part of this study at any time. I have received a copy of this consent form and additional information sheet to keep for myself.

DATE: _____ SIGNATURE/THUMB PRINT: _____

Appendix 2.2: next of kin consent

CONSENT FORM FOR PARTICIPANT'S NEXT OF KIN

Statement of person obtaining informed consent:

I have fully explained this research to _____ who is the next of Kin of_____ and have given sufficient information about the study, including that on procedures, risks and benefits, to make an informed decision.

DATE: _____ SIGNATURE: _____

NAME: _____

Statement of person giving consent:

I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction.

I have read the description of the research or have had it translated into language I understand. I have also talked it over with the interviewer to my satisfaction. I understand that my Relative's participation is voluntary. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want my relative to take part in it. I understand that I may freely ask that my relative be withdrawn from this study at any time. I have received a copy of this consent form and additional information sheet to keep for myself on behalf of my relative.

DATE: _____ SIGNATURE/THUMB PRINT: _____

WITNESS' SIGNATURE (if applicable): _____

WITNESS' NAME (if applicable): _____

Appendix 2.3: Gantt chart- Study Timelines

ACTIVITY/TIMELINE	15th -25th May	26th May– 30thAugust	1st September – 15th September	16th – 30th September
Proposal Writing				
Ethical Clearance				
Data Collection				
Data Analysis				
Final write-up and submission				

Appendix 3: Ethical Clearance

KOMFO ANOKYE
TEACHING HOSPITAL

P. O. Box 1934
Kumasi - Ghana
Tel: +233 - 3200-22301 - 4
Fax: +233 - 3220-24654 / 24621
Website: www.kathhsp.org

Our Ref. No: KATH IRB/AP/064/23

Your Ref... No:.....

Komfo Anokye Teaching Hospital Institutional Review Board

26th May 2023

Dr Irene Bandoh
Directorate of Anaesthesia and Intensive Care
Komfo Anokye Teaching Hospital
P. O. Box KS 1934
Kumasi.

Dear Dr. Bandoh,

Ethics Approval

Protocol title:	Prevalence and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients in A Mixed Intensive Care Population.
Study site:	Directorate of Anaesthesia and Intensive Care Unit of the Komfo Anokye Teaching Hospital, Kumasi
Sponsor:	Self-funded

We write in response to the clarifications and revised documents following review by the Komfo Anokye Teaching Hospital Institutional Review Board (KATH IRB) in respect of the research study referenced above.

We are pleased to inform you that KATH IRB, per your correspondence of 22nd May 2023, has given approval for the following study documents:

- *Protocol version 1.1 last updated 20th May 2023*
- *Informed consent form (adult), version 1.1 last updated 20th May 2023*
- *Informed consent form (next of kin), version 1.1 last updated 20th May 2023*
- *Case report form version 1.0 last updated 3rd April 2023*

Approval for the study is in effect until **25th May 2024** and it is the responsibility of the Principal Investigator to maintain the study in good standing at the Komfo Anokye Teaching Hospital. The Board anticipates to be notified of the actual start date of your project.

Prior to the expiration of the study approval, you must submit to the KATH IRB an "Application for Continuing Review" along with provision of "Annual Report" when the study is ongoing, or a "Termination Report" if the research has been completed.
You must hastily report to the KATH IRB should a modification to the research be proposed, and without delay if an unanticipated development occurs before the next required review. Regulations do not permit you to modify conduct of the study in its present form prior to ethics approval; except where urgent action is required to eliminate an apparent immediate hazard to a study subject or other person. It is of utmost importance data generated from this study must be used for the intended purposes only.

Thank you.

Sincerely,

Prof. Kwabena Antwi Danso, BSc, MB ChB, FWACS, FGCS, FACOG
Chairman, KATH IRB

Appendix 4: Site Approval

Gmail

Renéé Rendoh <bandohirene@gmail.com>

RE:Prevalence and outcomes of Intra-abdominal Hypertension in Critically I'll patients in a mixed critical care population

3 messages

Research and Development Unit <kathrdu@kath.gov.gh> 16 February 2023 at 15:08
To: bandohirene@gmail.com
Cc: Deputy Director Research <ddr@kath.gov.gh>

Dear **Dr Bandoh Irene**,

Reference is made to your application on the above subject.

This is to inform you that your protocol titled
" :Prevalence and outcomes of Intra-abdominal Hypertension in Critically I'll patients in a mixed critical care population"

has been reviewed by the Anaesthesia and ICU **Directorate** of this hospital.

Your protocol was found to be **feasible** for its conduct at the above-mentioned directorate,
subject to ethical clearance from the Komfo Anokye Teaching Hospital Institutional Review Board (KATH IRB).

Kindly submit your documents to KATH IRB for ethical clearance
(Attached are the forms/templates required for your IRB submission (select as applicable).
KINDLY USE THE VERSIONS OF THE FORMS ATTACHED TO THIS EMAIL.
Kindly also add a printed copy of this email as part of the required documents for your ethics submission).

PLEASE NOTE:

- **This email does not constitute site approval or ethical clearance for the conduct of the study.**
- **Ethical clearance from the KATH IRB is required to conduct the study at the hospital.**
- **Approval from KATH IRB is mandatory for every research to be conducted at KATH even if the work has been approved by other IRBs.**

PLEASE RESPOND TO THIS EMAIL WHEN RECEIVED.

Further information can be accessed at www.kathhsp.org
or from R&D unit-0322498697/0322000617.

Research and Development Unit

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