THE MORTALITY RATE OF PATIENTS WITH OPEN ABDOMEN AND CONTRIBUTING FACTORS: THREE YEAR AUDIT IN A MAJOR ACADEMIC TRAUMA UNIT.

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine
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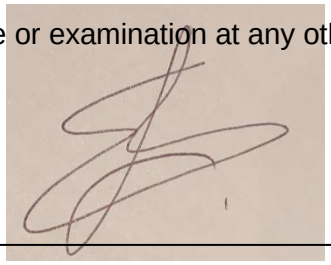
Declaration

I, Estelle van der Merwe, declare that this research is my own, unaided work. It is being submitted for the Degree in Master of Medicine in Surgery at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any other degree or examination at any other University.



23rd day of June 2022 in Johannesburg

Dedication

I would like to dedicate this work to my husband, father, mother, brother, and cousin. Without your ongoing love and support I will not be who I am today.

Abstract

Background

Damage control surgery is a well-known and widely used approach in trauma. (1) An essential element of damage control surgery is the need to leave the abdomen open with a temporary closure device in place. An open abdomen carries complications, such as infections, enteric fistula and ventral hernia formation. These patients also have increased length of hospital and ICU stay, with increased morbidity and mortality. (2) This study aims to quantify the mortality rate of patients with an open abdomen and determine possible contributory factors to mortality. Secondary objectives were to determine factors influencing the decision to perform DCS and assess morbidity in the open abdomen patient: surgical site infection, hernia rate and entero-atmospheric fistula.

Materials and Methods

A retrospective review was conducted on 205 patients submitted to damage control surgery in the Charlotte Maxeke Johannesburg Academic Hospital Trauma Unit. Mortality rates were evaluated over a 24-hour, 7-day and 28-day period. Data were collected by filling a data collection sheet, including patients over a three-year period: 01 January 2016 to 31 December 2018.

Results

The study found a mortality rate of 26.8% for open abdomen patients, 34.5% within the first 24-hours, 40% in the 24-hours to 7-day, and 25.4% in the 8-day to 28-day periods. Statistically significant factors found to contribute to mortality were haemodynamic instability (p-value 0.003), hypothermia (p-value 0.047), coagulopathy (p-value 0.004), massive transfusion (p-value 0.003), vasopressor usage (p-value 0.008), and significant associated injuries (0.008). For survival analysis, pH, lactate, injury severity score (ISS), and systolic blood pressure BP reading, were found to correlate with the increased risk of mortality in patients with an open abdomen. Open abdomen patients were found to have multiple morbidities, of which entero-atmospheric fistula (EAF) was found in 7.3%, surgical site infection in 45.3% and ventral hernia in 10.24%.

Conclusions

Our data demonstrated that patients undergoing damage control surgery are at risk of mortality due to multiple contributing factors. The majority of patients demised within 24-hours to 7-days (40%). The most common morbidity associated with an open abdomen was surgical site infection (45,46%). Open abdomen management remains an appropriate management in critically ill patients but does carry a high risk of mortality and morbidity.

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LIST OF ABBREVIATIONS

ICU	Intensive Care Unit
ISS	Injury severity score
EAF	Entero-atmospheric Fistula
DCS	Damage control surgery
PTT	Partial thromboplastin time
DCR	Damage control resuscitation
WSACS	World Society of Abdominal Compartment Syndrome
BP	Blood pressure
GSW	Gunshot wound
MVC	Motor vehicle crash
PRBC	Packed Red Blood cells
MTF	Massive transfusion

1. Introduction

1.1 Background

South Africa is a country with a high level of trauma caused by blunt and penetrating mechanisms. In the context of abdominal trauma, a laparotomy remains one of the effective ways of assessing and treating an intra-abdominal injury. (1)

Damage control surgery (DCS) is a well-known and widely used approach in trauma. (1) Open abdomen has become one of the cornerstones in severe trauma, compartment syndrome and severe contamination. (2)

The concept of DCS was introduced to civilian trauma care by Burch *et al.* and Rotondo *et al.* in the early ’90s, aiming to reduce mortality in severe trauma by performing abbreviated surgery to control bleeding and contamination, followed by active resuscitation in intensive care and return to theatre for definitive repair once the physiological and metabolic insults have reversed. A key element of DCS is the need to leave the abdomen open with a temporary closure device in place. (3)

1.2 Rationale behind the open abdomen

-The need to prevent the development of abdominal hypertension and abdominal compartment syndrome
-The need to re-examine the abdominal cavity when intestinal viability is questionable or potential residual contamination is present
-The need to shorten the surgical time during DCS by using temporary closure techniques
-The need to return to the peritoneal cavity to remove packs and vascular shunts and perform complex gastrointestinal anastomoses and vascular repairs. (3)

Factors used to decide the need for an open abdomen include:

Clinical

- Haemodynamic status: sustained hypotension, need for inotropic support
- Intra-operative thrombocytopaenia and increased PTT and INR.
- Severe hypothermia < 35 Celsius

Metabolic

- Metabolic status: severe metabolic acidosis (pH <7.2, Base Excess (BE) <-8)

- The volume of crystalloids infused during initial resuscitation
- The volume of blood infused during initial resuscitation: massive transfusion defined as the use of 50% of blood volume in 6-hours, 100% of blood volume in 24-hours or ongoing transfusions needed.

Anatomical/Surgical

- Multiple injuries: lengthy operations
- Bowel oedema at the end of surgery (4)

1.3 Morbidities

An open abdomen carries complications, of which the most common are secondary and tertiary infections and enteric fistula formation. In addition, an open abdomen carries problems such as failure to perform anatomical fascial closure with a residual ventral hernia and the presence of stomas. These issues prolong ICU and hospital stay, delay recovery, and return to a normal quality of life and impose the need for further surgeries, which add an array of new complications. (2)

A feared complication as mentioned above is entero-atmospheric fistulae which develop due to the manipulation of the viscera, as well as failed anastomosis. (3) There is controversy in literature regarding the exact etiology of fistulae, as multiple local and systemic factors may contribute to the formation. These factors include infection, breakdown of an anastomosis due to ischaemia, tension, or distal obstruction. Technical problems include inadvertent bowel- or mesenteric vessel injury, suture-line defects, peri-suture haematoma, and tight suture causing ischaemic necrosis. (3)

Defined as an abnormal communication between the intestinal tract and the atmosphere, it is described in 2 - 43% of trauma patients. The number of re-looks performed, and a delayed period, increases the risk of these patients developing fistulae. These patients experience an ongoing cycle of repeated surgeries, continuous loss of intestinal fluid with essential electrolytes, re-infection, septic wounds, and malnutrition leading to mortality. (5)

1.4 Damage control resuscitation

Recent developments leading to a deeper understanding of the pathophysiology of traumatic bleeding and acute coagulopathy associated with trauma have changed the approach to the resuscitation of severely injured patients. Damage control resuscitation (DCR) was first described in 2007 in a warzone, with the emphasis on using lower volumes of crystalloids, early use of blood and blood products, permissive hypotension leading to decreased clot disruption, and the use of point of care coagulation testing to guide product resuscitation, allowing for a “better” resuscitated patient at the end of surgery. (6)

Damage control resuscitation is aimed at allowing volume re-expansion along with increased oxygen-carrying capacity. This period of resuscitation is described as starting in the emergency department, to be continued in theatre, and in ICU. These new strategies may play a significant role in changing the need to leave an open abdomen following a trauma laparotomy. (7)

There is currently no specific time cut-off for the end of the resuscitative period after initial damage control laparotomy. It was shown that lactate clearance to normal levels within 24 hours correlate with improved survival rates. Mostly patients will be taken to theatre for definitive surgery once physiologically improved within 24 – 48 hours, but a subgroup will require re-exploration before physiology has been corrected. This group will require ongoing transfusions and/or show no improvement in lactate or base excess, despite resuscitation. Commonly these patients will have a missed visceral or vascular injury. (6)

A second group requiring early relook surgery are the patients developing intra-abdominal hypertension. Abdominal compartment syndrome is defined by the World Society of Abdominal Compartment Syndrome [WSACS] as pressures >20 mmHg with new single or multi-organ dysfunction (Normal pressures 2 – 7 mmHg). (5) Abdominal compartment syndrome is subdivided into primary, with an abdomino-pelvic pathology, and secondary, with pathology not involving the abdomino-pelvic regions. Clinically these patients can present with abdominal distention, impaired ventilation, hypoxia, hypercarbia and/or decreased urine output. (8) Abdominal wall compliance can be improved by good sedation and neuromuscular blockade. (3)

Current options for abdominal wall closure include mesh, vacuum dressings, grafting and abdominal wall reconstruction. (2) The ideal vacuum dressing or temporary abdominal wall closure should absorb fluid, prevent evisceration, and allow expansion. There is a high risk of ventral hernia formation if a mesh is used; however, not all will require repair in the long term. (3)

In our unit, laparotomy patients are frequently left with open abdomens post DCS. The factors influencing the surgeon's choice of an open abdomen and the role of an open abdomen in the outcome of these patients has not been investigated.

The primary objective of the study was to (i) quantify the mortality rate of patients with an open abdomen over a 24-hour, 7-day and 28-day period in the major trauma unit of the Charlotte Maxeke Johannesburg Academic Hospital, (ii) determine possible contributory factors to mortality.

Secondary objectives were to (i) determine factors influencing the decision to perform DCS, (ii) assess morbidity in the open abdomen patient: surgical site infection, hernia rate and entero-atmospheric fistula.

2. Materials and Methods

2.1 Patient selection and data collection

A retrospective review of patients (18 years and older) undergoing DCS and having an open abdomen post-surgery was performed. The mortality rates of these patients were assessed over a 24-hour, 7-day and 28-day period. The study was conducted at Charlotte Maxeke Johannesburg Academic Hospital Trauma ICU. Patient data were reviewed over a 3-year period from 01 January 2016 to 31 December 2018.

This research received ethical clearance from the University of Witwatersrand Human Research Ethics Committee with clearance number M190982. Permission to perform the study was granted by the CEO of Charlotte Maxeke Johannesburg Academic Hospital.

Retrospective data were collected from prospectively completed MediBank forms, RedCap trauma database and patient ICU files. Inclusion criteria were all patients above the age of 18 years who underwent DCS as decided by the surgeon, were transferred to ICU post-operatively for physiological optimisation, and subsequently underwent definitive surgery if they were suitable candidates. This included all patient's that underwent DCS, whether they demised pre-relook, or had subsequent relooks. Exclusion criteria were patients transferred to the Trauma Unit with an open abdomen following a laparotomy performed at another institution.

A data collection sheet (Annexure 1) was completed for all patients included in this study. The data collection sheet included sex, age, mechanism of injury (GSW, MVA, Stab and other (Fall from Heights, Motor-Bike accidents, Pedestrian-vehicle accidents), cause of injury, ISS (>16), BP, fluids (Crystalloids vs Colloids) and blood given during resuscitation, factors used to decide on an open abdomen, number of laparotomies prior to definitive closure, length of ICU stay, whether the patient demised and when, and if any morbidities occurred. For this study, 24 hours post damage control surgery was used as day one. Superficial site infection was defined as any infective changes of the skin or subcutaneous tissue, requiring management.

Factors assessed to play a part in decision making for open abdomen were abnormal haemodynamics (shock defined as Systolic Blood Pressure < 90 mmHg, on arrival at emergency department), hypothermia (Temperature < 35 degrees Celsius), acidosis

(pH < 7,2, BE < -2, Lac >2), coagulopathy, contamination, vasopressors, bowel oedema, severe associated injuries, massive transfusion (receiving 4 Packed red blood cells, 4 Fresh Frozen Plasma, 1 Mega Unit of Platelets in Emergency Department or during surgery), complex bowel repair, packs in the abdomen, temporary vascular shunt.

2.2. Statistical analyses

Statistical analysis and management were conducted using STATA version 14. The Mann-Whitney U test was used to assess not normally distributed variables. Chi-Square and Fisher's Exact tests were conducted for analysis of categorical variables. Kaplan Meier analysis was performed to assess how time to death varied among study participants according to different characteristics (demographic, clinical). The Cox regression model was used to relate risk factors/variables which were significant in the Kaplan Meier analysis to survival time. A p-Value of <0.05 was considered statistically significant.

3. Results

During the study period, a total of 205 patients that underwent DCS at Charlotte Maxeke Johannesburg Academic Hospital, Trauma Unit were identified. For each patient, records were reviewed from initial presentation and resuscitation to intra-operative notes, followed by ICU notes.

The mortality rate was quantified in patients with an open abdomen. The study found that fifty-five (26.8%) patients with an open abdomen demised within 28 days. Nineteen patients (34.5%) at <24-hours, 22 (40%) between 24-hours and 7-days, and 14 (25.46%) between 8 and 28-days. The median mortality day was found to be five days.

One hundred and ninety-three patients who underwent DCS were male (94.15%). Penetrating trauma accounted for 162 patients (79.02%), of which 130 (63.41%) were gunshot wound-related. Eighty-eight patients presented in shock. One hundred and eighty-one patients (88.3%) received more than one litre of crystalloids during resuscitation, and 35 patients (17%) received enough transfusion to meet the criteria for massive transfusion. Table 3.1 shows the demographics and initial resuscitation presentation and actions.

Table 3.1: Demographics and initial resuscitation presentation and actions

Factors	Subtypes	Percentage
Sex	Male Female	193 (94.15%) 12 (5.85%)
Mechanism of injury	Blunt Penetrating	43 (20.98%) 162 (79.02%)
Cause	Stab GSW MVC Other	32 (15.61%) 130 (63.41%) 22 (10.73%) 21 (10.24%)
Haemodynamics	Shock No shock	88 (42.93%) 117 (57.07%)

Fluids	Crystalloids > 1L Crystalloids and Colloids: >1L < 500 ml	181 (88.3%) 4 (1.96%) 20 (9.27%)
Blood products	1 PRBC 2 PRBC MTF None	26 (12.6%) 30 (14.14%) 35 (17.07%) 114 (56%)

Abbreviations: GSW, Gunshot wound; MVC, Motor vehicle crash; PRBC, Packed Red Blood Cells; MTF, Massive transfusion.

The following factors shown in Table 3.2 were found to play a role in the decision to do DCS and leave the abdomen open. Our study found that the most common reasons for the surgeon to perform DCS was metabolic acidosis (168; 82.43%), contamination (136; 66.34%), abnormal haemodynamics (180; 88.29%), coagulopathy (129; 62.29%) and vasopressor usage (140; 68.29%).

Table 3.2: Factors used to decide on damage control surgery

Metabolic acidosis	168 (82.43%)
Hypothermia	83 (40.48%)
Contamination	136 (66.34%)
Abnormal haemodynamics	180 (88.29%)
Packs in abdomen	93 (45.36%)
Coagulopathy	129 (62.92%)
Massive transfusion	71 (34.63%)
Complex repair	79 (38.53%)
Vasopressors	140 (68.29%)
Associated injuries	21 (10.24%)

Viable bowel	2 (0.97%)
Bowel oedema	11 (5.8%)
Other	4 (1.9%)

Table 3.3 lists multiple factors found to be associated with increased mortality that were statistically significant. They were compared using the Chi-Square and the Fisher's Exact Tests. These factors were shock (p-value 0.003), amount of relooks (p-value 0.008), hypothermia (p-value 0.047), coagulopathy (p-value 0.004), MTF (p-value 0.003), vasopressor usage (p-value 0.008) and associated injuries (p-value 0.008).

Table 3.3: Statistically significant factors associated with increased mortality rate

Factors	**Alive**	**Dead**	**Median**	**P-value**
Age	33.8	35.8	34.34 (17-77)	0.9
Factors	**Subtypes**	**Alive**	**Dead**	**P-value**
Sex	Male Female	141 (94%) 9 (6%)	52 (94.5%) 3 (5.4%)	0.883
Mechanism of injury	Blunt Penetrating	29 (19.3%) 121 (80.6%)	14 (25.4%) 41(74.54%)	0.221
Cause	GSW Stab MVC Other	97 (64.6%) 25 (16.6%) 15 (10%) 13 (8.6%)	33 (60%) 7 (12.73%) 9 (16.36%) 6 (10.91%)	0.515
Haemodynamics	Shock No shock	55 (36.67%) 95 (63.33%	33 (60%) 22 (40%)	0.003

Fluids	1L Crystalloids 2L Crystalloids Crystalloids/Colloids < 500 ml	78 (52%) 51 (34%) 5 (3.33%) 16 (10.67%)	23 (41.8%) 29 (52.7%) 0 (0%) 3 (5.45%)	0.074
Blood	1 PRBC 2 PRBC MTF Nil	15 (10%) 19 (12.67%) 26 (17.34%) 90 (60%)	11 (20%) 10 (18.18%) 9 (16.36%) 25 (45.45%)	0.13
Relooks	1 Relook More than 1	68 (45.33%) 82 (54.67%)	36 (65.45%) 19 (34.5%)	0.008
Metabolic acidosis	Present Not present	28 (18.67%) 122 (81.3%)	8 (14.5%) 47 (85.48%)	0.32
Contamination	Present Not present	100(66.6%) 50(33.3%)	36(65.4%) 19(34.5%)	0.83
Packs	Present Not present	63(42%) 87(58%)	30(54.4%) 25(45.4%)	0.075
Hypothermia	Present Not present	55(36.67%) 95(63.3%)	28(50.9%) 27(49.9%)	0.047
Haemodynamics	Present Not present	130(86.6%) 20(13.3%)	51(92.7%) 4(7.27%)	0.172
Coagulopathy	Present Not present	86(57.3%) 64(42.6%)	43(78.1%) 12(21.8%)	0.004
MTF	Present Not present	43(28.6%) 107(71.3%)	28(50.9%) 27(49.09%)	0.003
Complex repair	Present Not present	53(35.3%) 97(64.6%)	26(47.2%) 29(52.6%)	0.082
Vasopressors	Present Not present	95(63.3%) 55(36.6%)	45(81.8%) 10(18.18%)	0.008

Associated Injuries	Present Not present	10(6.67%) 140(93.3%)	11(20%) 44(80%)	0.008
Bowel Viable	Present Not present	2(1.3%) 148(72.9%)	0(0%) 55(100%)	0.53
Bowel oedema	Present Not present	9(6%) 141(94%)	3(5.4%) 52(94.5%)	0.59

For survival analysis, the following factors were found to have statistical significance in patients that demised post DCS, as listed in Table 3.4. The factors having a direct impact on length of survival was pH <7.2 (p-value 0.00), Lactate >2 (p-value 0.003), ISS (p-value 0.039), systolic blood pressure <90 mmHg (p-value 0.038) and coagulopathy (p-value 0.038).

Table 3.4: Factors associated with mortality

pH	0.00
BE	0.727
Lac	0.003
ISS	0.039
Systolic	0.038
Coagulopathy	0.038

Abbreviations: BE, Base excess; Lac, Lactate; ISS, Injury severity score

Kaplan Meier analysis was performed to assess how time of death varied among study participants according to different characteristics. The following were found to be significant, as shown in Figures 3.1, 3.2 and 3.3:

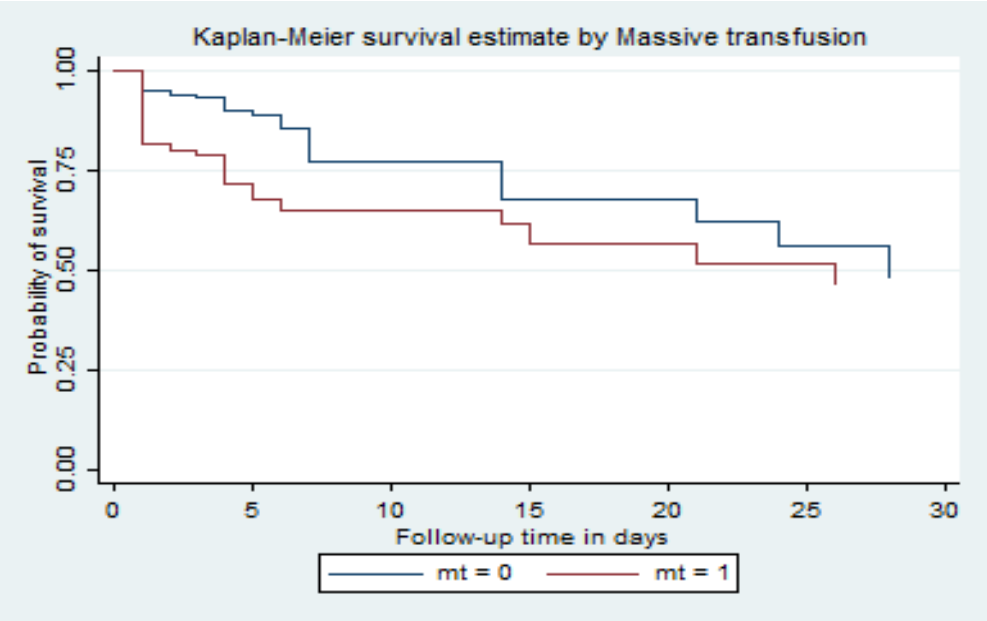

Figure 3.1: Kaplan- Meier survival estimate for massive transfusion

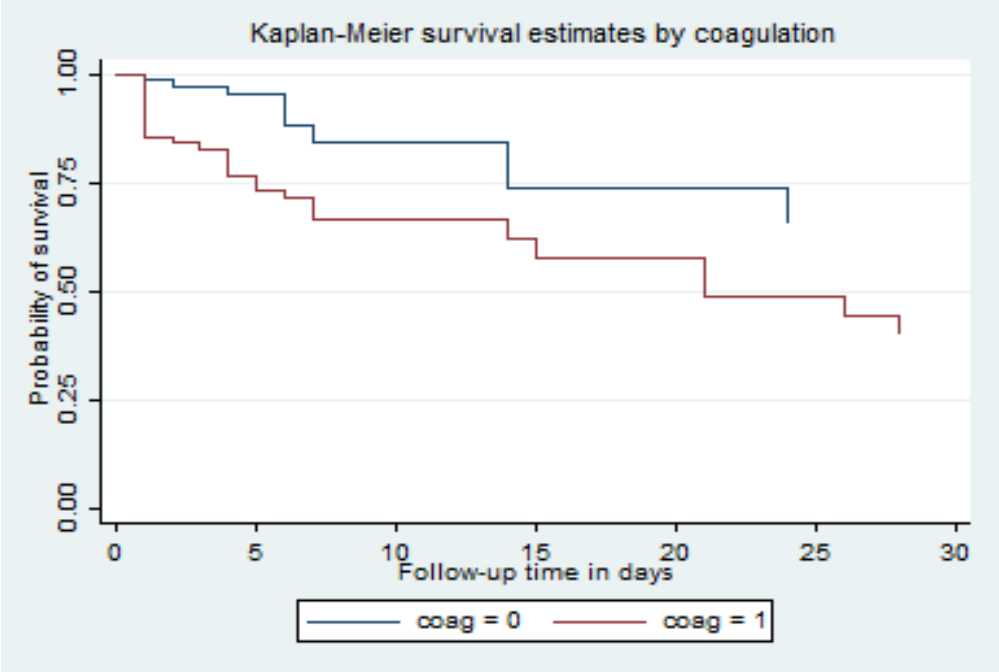

Figure 3.2: Kaplan- Meier survival estimates for coagulation

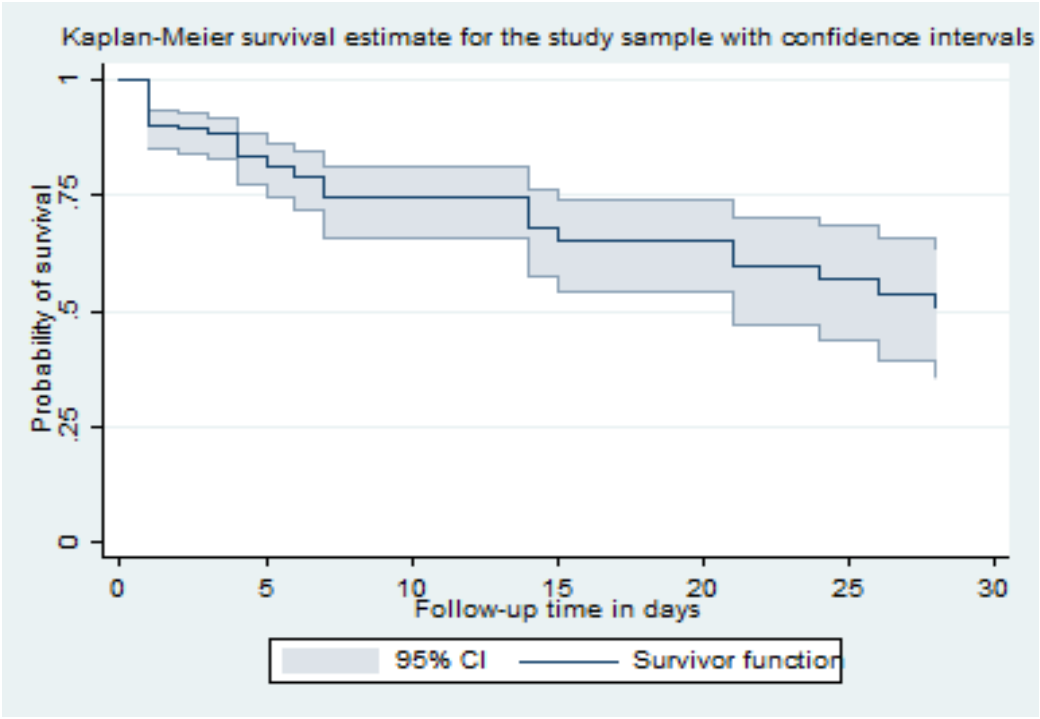

Figure 3.3: Kaplan-Meier survival estimates for the study example with confidence intervals

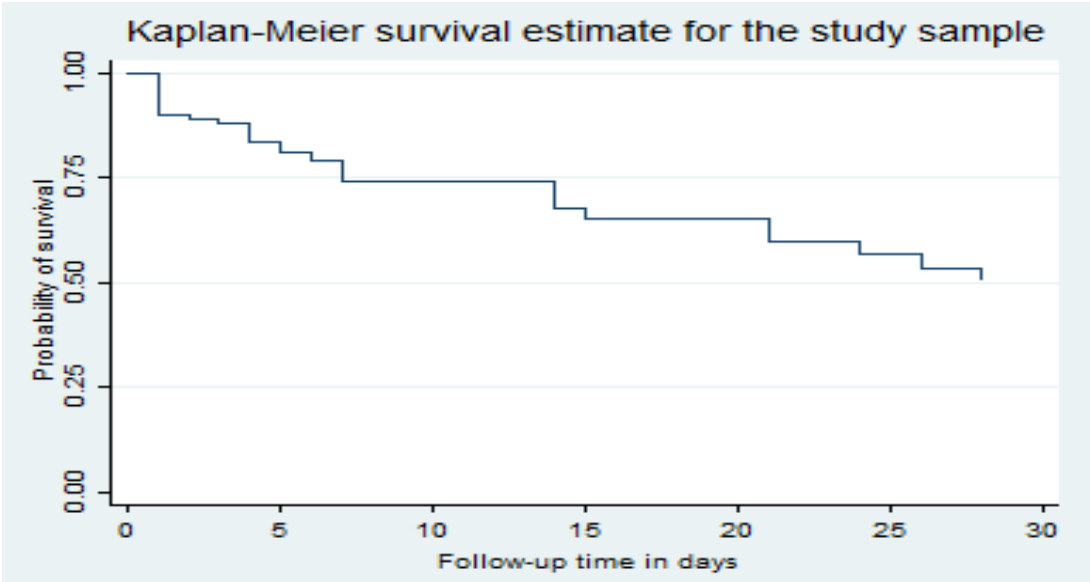

Figure 3.4: Kaplan- Meier survival estimate for the study sample

Table 3.5 lists the associated morbidity found in patients who underwent DCS. Fifteen patients (7.3%) developed entero-atmospheric fistula, 92 (45.36%) developed surgical site infection and 21 (10.24%) developed ventral hernias, diagnosed during hospital stay or on follow up at SOPD.

Table 3.5: Morbidities in open abdomen patients

EAF	15 (7.3%)
Surgical site infection	92 (45.36%)
Ventral hernia	21(10.24%)

The length of ICU stay was reviewed and found that 26 (12.68%) patients stayed <24 hours, 129 (62.93%) stayed 24-hours- 7-days, 36 (17.56%) stayed 8 - 28-days, and 14 (6.84%) more than one month.

Table 3.6: Length of ICU stay in damage control patients

<24 hours	26 (12.68%)
24 hours -7 days	129 (62.93%)
7 days – 28 days	36 (17.56%)
>28 days	14 (6.84%)

4. Discussion

This retrospective study investigated patients undergoing DCS with subsequent open abdomens in ICU. The study quantifies the mortality rate in these patients, associated morbidity and factors reported to be used in deciding to employ DCS. In previous literature, DCS was associated with shorter operating times, decreased post-operative complications, and early multi-organ failure prevention. (9)

Damage control surgery has become a cornerstone in the management of severe trauma patients. It is an integral part in the resuscitation and correction of physiology, and the steps toward the definitive repair. With the improved understanding of multi-organ failure in trauma and abdominal compartment syndrome, the open abdomen is an important strategy in the management of these patients. (9)

4.1 Mortality rate

Penetrating abdominal trauma is a major cause of hospitalisation in South Africa. (10) Some of these patients require DCS due to their physiology or contamination, leading to lengthy stays in ICU, potential morbidities, and mortality, in an already resource-limited setting. (10)

The timelines chosen in this study was to try determine at which period the patient is most vulnerable and at increased risk of mortality, also to assess the length of stay and impact on the health system.

Our findings show that the majority of mortalities (40%) happen within 24-hours – 7-days. Less than 24-hours was 34.54%, and after 8-days, the mortality rate dropped to 25.46%. The median mortality was found to be five days. Compared to timelines used in previous studies, 24% were reported to demise in <24 hours, and 27% demised >24 hours. These studies were done on a smaller group of patients with a broader timeline but do correlate to our findings. Local studies demonstrate a 27% mortality rate, not specifying certain time periods (17). We attribute the percentage of mortality within 24-hours - 7-days to the fact that these patients are critically ill and still requiring resuscitation and correction of physiology in this time period. (11)

In the literature, mortality rates of 64% were reported, with major causes relating to the primary injury, or complications developing from the open abdomen. In previous studies, age and injury severity scores (APACHE) were shown to directly impact the mortality rate. Other reported mortality rates were mentioned to be 46.7%, but the study populations were very small. (12)

In our study, we compared multiple variables, from the initial resuscitation to intra-operative findings. We found that the statistically significant contributions to mortality were haemodynamic instability (defined as a presenting systolic BP of <90), hypothermia (temperature <35), number of relooks, coagulopathy, massive transfusion, vasopressors, and associated injury. This correlates with the recent findings of Steven et al. that trauma patients in need of a damage control laparotomy due to acidosis, coagulopathy, and hypothermia are at risk of intra-abdominal hypertension, abdominal compartment syndrome and increased mortality. (13)

The ability to clear this acidosis, as analysed by lactate clearance, has been correlated to survival. In 1993, Abramson evaluated patients with trauma and found that if lactate was cleared within 24-hours, there was a 100% survival rate. If not, only 14% of patients would survive. (14). The finding of lactate being statistically significant, but Base excess not, cannot be explained, as both reflect tissue hypo perfusion and correlates to metabolic acidosis. The data was reviewed again, and these findings were confirmed.

The median age of those that died was 34, and of survivors was 39. In comparison to international studies, the median age of mortality varies between 39 and 55-years. Most of these studies do however have much less penetrating trauma (87% Blunt, 13% Penetrating), and the patients studied are older (Median age 47) and mostly blunt trauma. (14)

Factors assessed that were not found to contribute to mortality with no statistical significance were sex, mechanism of injury, cause of injury, fluids given, initial blood given in the Emergency Department (ED), contamination, packs placed, and bowel oedema.

The Kaplan Meyer graphs clearly demonstrate how patients receiving a massive transfusion had a higher chance of mortality at 15-days than the group without. Coagulopathy and the severity of injuries also decreased survival time significantly. Probability of survival decreased with length of stay, with a 64% chance of mortality at 15-days.

The most common factors associated with the decision to leave an abdomen open at DCS were found to be abnormal haemodynamics (88.29%), metabolic acidosis (82.43%), contamination (66.34%) as well as vasopressor usage (68.29%). The Eastern Association for the Surgery of Trauma (EAST) practice management committee performed a literature review of the management of the open abdomen in trauma and emergency general surgery in 2010. According to their published guidelines, level III evidence exists to support the use of the open abdomen technique in a trauma setting in the presence of acidosis (pH <7.2), hypothermia (temperature <35°C), and clinical coagulopathy with transfusion of > 10 units of red blood cells (RBCs). Our findings indicate that the use of DCS and open abdomen in this study was in accordance with the published guidelines. (15) A local study found that pH <7.2 is the best indicator of the need for DCS. Anatomic injuries in themselves are not predictive of the need for DCS. (18)

Our study showed that an increased number of relooks was associated with increased survival. We attribute this to the fact that these patients were still critically ill in the first 48 hours. Some relooks were on-demand before physiology had been corrected, while others, even once taken back for a planned relook, were still unstable and at high risk for decompensation and mortality, mostly with significant other injuries. Patients having survived longer have the opportunity of going for relook laparotomies, where those that demised do not, and thus this does not advocate that more relooks, decreases mortality.

The injury severity score was derived by Baker *et al.* (1974) as a standardised scoring system to assess the severity of injuries. It takes the three most severely injured compartments and add up the squares of these. This has been shown in the literature to have a direct correlation to increased mortality. In our retrospective review, the higher the ISS, the higher the chances of mortality. In earlier literature, ISS was found much more elevated in non-survivors, with p-values of 0.050. This is

in line with earlier studies where an ISS > 24 was associated with 25% mortality rate, > 45 had a 68% mortality rate, and > 70 had a 100% mortality rate. (15)

A trauma centre should have an agreement with the blood bank to have a protocol in place for massive transfusions. One study done on open abdomen patients found that an institutional protocol aimed at the early administration of blood products in a ratio of 3:2 RBC: FFP and 5:1 RBC: platelets for patients in haemorrhagic shock improved 30-day survival (56.8% vs 37.6%, p=0.001). The patients in the protocolised arm of the study also had a significantly lower incidence of ACS (0% vs 7%, p<0.001). These studies were, however, performed in general surgery patients with an open abdomen. (15)

4.2 Morbidity

Morbidity assessment found that surgical site infection was the most common complication (45.36%), followed by ventral hernias (10.24%), and then entero-atmospheric fistulas (7.3%). In literature reviews, fistula rates were documented at 1-15% and ventral hernia formation at 25%. (14) These percentages were documented after a 21 month follow up and might be why there is a discrepancy in comparison to our findings. Our patients were either identified during admission, or at any follow up visit, not within a specific time frame.

Further studies showed entero-atmospheric fistula (19.1%), ventral hernia (8.5%), and surgical site infections (19%). We had a large number of patients in comparison to these studies. (15). Local studies demonstrate 41% of patients had a ventral hernia, with 30% undergoing delayed fascial closure. (17).

4.3 ICU Stay

ICU stay was reviewed and found that 12% of patients stayed <24hours (this is mostly patients demising in this time as damage control patients' do not get discharged from ICU in this short time period), 62.93% stayed 24-hours to 7-days, and 17.56% were in ICU for 8-days to 28-days, and 6.84% were in ICU >28 days.

In the literature, 25 - 31-days of ICU stay was reported as an average stay for these patients, in our study we found the average to be 5 days. (14) In our setting, we are resource-limited, and we need to have a quick turnover of cases to open beds for new patients arriving in extremis. This is most likely why our patients are discharged sooner from ICU than in reported studies.

4.4 Study Limitations

Study limitations included incomplete records for some patients and having to rely on accurate record keeping. The study may also be biased with limited applicability outside of the setting in which the research is conducted. As this was a retrospective study, some aspects were difficult to interpret accurately as the sample size was small, e.g., bowel oedema, bowel viability, and associated injuries. The study was also performed in only one center, and this might attribute to certain findings. With regard to DCR, incomplete pre-hospital records is a weakness in this study, as we were unable to assess the use of permissive hypotension prior to arrival in the Emergency Department.

5. Conclusions

Our data demonstrated that patients undergoing damage control surgery are at risk of mortality due to multiple contributing factors. The majority of patients demised within 24-hours to 7-days (40%). The most common morbidity associated with an open abdomen was surgical site infection (45,46%). Open abdomen management remains an appropriate management in critically ill patients but does carry a high risk of mortality and morbidity.

6. References

1. Kritayakirana K, Maggio PM, Brundage S *et al*., Outcomes and complications of open abdomen technique for managing non trauma patients. *Journal of Emergencies, Trauma and Shock JETS* 2010; 3(2):118-122.
2. Frazee RC, Abenathy S, Jupiter D, *et al*., Long term consequences of open abdomen management. *Trauma* 2013; 16(1):37-40.
3. Falconi M, Pederzoli P, The relevance of gastrointestinal fistulae in clinical practice: a review, Gut 2002;49(Suppl IV):iv2–iv10
4. Waibel BH, Rotondo MF. Damage control surgery: it's evolution over the last 20 years. *Rev Col Bras Cir* 2012; 39(4):314-321.
5. Godat L, Kobayashi L, Constantini T, Coimbra R *et al*., Abdominal damage control surgery and reconstruction: world society of emergency surgery position paper. *WJES* 2013; 8:53.
6. Lamb CM, MacGoey P, Navarro AP, Brooks AJ. Damage control surgery in the era of damage control resuscitation. *Brit J Anaesth* 2014; 113(2):242-249.
7. Holcomb JB, Jenkins D, Rhee P *et al*. Damage control resuscitation: directly addressing the early coagulopathy of trauma. *J Trauma* 2007; 62:307-310.
8. Burch JM, Ortiz VB, Richardson RJ, *et al*. Abbreviated laparotomy and planned reoperation for critically injured patients. *Ann Surg* 1992; 215:476-483
9. Rotondo MF, Schwab CW, McGonigal MD, *et al*., "Damage control" and approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993; 35:373-382.
10. Asensio JA, McDuffie L, Petrone P, *et al*., Reliable variables in the exsanguinated patient which indicate damage control and predict outcome. *Am J Surg* 2001; 139:209-214.
11. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma* 2003; 54:1127-1130.
12. Cotton BA, Reddy N, Hatch QM, *et al*., Damage control resuscitation is associated with a reduction in resuscitation volumes and improved survival in 390 damage control laparotomy patients. *Ann Surg* 2011; 254:598-605.
13. Shamrock AE, Barker T, Yuen HM *et al.,* Management and closure of the open abdomen after damage control laparotomy for trauma. A systematic review and meta-analysis. *International Journal of the Care of the Injured Patient* 2016; 47(2):296-306.

14. Morais M, Goncalves D, Bessa-Melo R, *et al*., The open abdomen: analysis of risk factors for mortality and delayed fascial closure in 101 patients. *Porto Biomedical Journal*, 2018; 3(2)-14.
15. Oshita KO, Nakahara H, Oshita A, *et al*., Outcomes of Damage Control Surgery for Abdominal Trauma Evaluated Using the Trauma and Injury Severity Score and lethal triad in a single institution. *Hiroshima Journal of Medical Sciences* 2020; 69(1):9-14
16. Young UC, Seung HL, Jae GL *et al.,* Management of an Open Abdomen Considering Trauma and Abdominal Sepsis: A Single-Center Experience, *Journal of Acute Care Surgery,* 2019;9(2):39-44.
17. Open abdomen critical care management principles: resuscitation, fluid balance, nutrition, and ventilator management. AACN Journals.*Crit Care Nurse* (2017) 37 (5): 22–45.
18. Steenkamp CJ, Kong VJ, Clarke DL *et al.,* A selective vacuum assisted mesh mediated fascial traction approach following temporary abdominal containment for trauma laparotomy is effective in achieving closure, *S. Afr. j. surg.* vol.56 n.4 Cape Town Dec. 2018
19. Weale R, Long V, Buitendag J *et al.,* Damage control or definitive repair? A retrospective review of abdominal trauma at a major trauma center in South Africa, *Trauma Surg Acute Care Open* 2019;4:e000235.
20. KN Boolaky, Hassan A, Craig T. Open abdomen in the trauma ICU patient: who? when? why? and what are the outcome results? Eur J Trauma Emerg Surg, 2020 Nov; 10: 1543-6.

7. Appendices:

Appendix 1: Approved Protocol

The mortality rate of patient's with open abdomen and contributing factors: three-year audit in a major academic trauma unit.

Researcher: Estelle van der Merwe, MBChB(Pta)

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Protocol for MMed (Surg)

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Appendix A: Data extraction sheet

List of Abbreviations

DCS Damage Control Surgery

DCR Damage Control Resuscitation
PTT Partial thromboplastin time
BE Base excess
ICU Intensive Care Unit
WSACS World Society of Abdominal Compartment Syndrome

1. Introduction

South Africa is a country with a high level of trauma, both caused by blunt and penetrating mechanisms. In the context of abdominal trauma, a laparotomy remains the most effective way of assessing and treating an intra-abdominal injury.

Damage control surgery (DCS) is a well-known and widely used approach in trauma (1).Open abdomen has become one of the cornerstones in severe trauma compartment syndrome and in severe contamination (2).

The concept of DCS was introduced to civilian trauma care by Burch *et al.,* and Rotondo *et al.,* in the early 90's, aiming to reduce mortality in severe trauma by performing abbreviated surgery to control bleeding and contamination followed by active resuscitation in Intensive care and return to theatre for definitive repair once the physiological and metabolic insult have reversed .A key element of DCS is the need to leave the abdomen open with a temporary closure device in place (3).

The rationale behind the decision to perform an open abdomen during DCS is based on:(4).
-The need to prevent development of abdominal hypertension and abdominal compartment syndrome
-The need to re-examine the abdominal cavity when intestinal viability and potential residual contamination is present
-The need to shorten surgical time during DCS by using temporary closure techniques
-The need to return to the peritoneal cavity to perform complex gastro-intestinal anastomosis and to remove packs and vascular shunts (4).
Factors used to decide the need for open abdomen include:(3)
• Metabolic status: severe metabolic acidosis (pH < 7.2, Base Excess (BE) > -8)

- Haemodynamic status: sustained hypotension, inotropic support
- Multiple injuries: lengthy operations
- Volume of crystalloids infused during initial resuscitation
- Volume of blood infused during initial resuscitation: massive transfusion defined as use of 50% of blood volume in 6 hours, 100% of blood volume in 24 hours or ongoing transfusions needed.
- Intra-operative coagulopathy (increased partial thromboplastin time (PTT), prothrombin time, thrombocytopenia)
- Severe hypothermia < 35 degrees
- Bowel oedema at end of surgery (3)

An open abdomen, carries complications, of which the most common are secondary and tertiary infections and enteric fistula formation as well as problems such as failure to perform anatomical fascial closure with residual ventral hernia and the presence of stomas. These issues prolong ICU and hospital stay, delay recovery and return to normal quality of life, as well as impose the need for further surgeries which add an array of new complications (2).

A well-known complication as mentioned above is entero-cutaneous fistulae which develop due to the manipulation of viscera (3). Defined as an abnormal communication between the intestinal tract and the atmosphere, it is described in 2 - 43% of trauma patients. The number of laparotomies (re-looks) performed before definitive abdominal closure, and a delayed period, attributes to the risk of these patients developing fistulae. These patients experience an ongoing cycle of repeated surgeries, continuous losses of intestinal fluid with essential electrolytes, re-infection, septic wounds with malnutrition being the leading cause of mortality (5).

Recent developments leading to a deeper understanding of the patho-physiology of traumatic bleeding and acute coagulopathy associated with trauma have changed the approach to the resuscitation of severely injured patients. Damage control resuscitation (DCR) was first described in 2007 in a warzone, with the emphasis on using less volume of crystalloids, early use of blood and blood products, permissive hypotension leading to decreased clot disruption, and the use of point of care coagulation testing, allowing for a “better” resuscitated patient at the end of surgery (6).

Damage control resuscitation is aimed at allowing volume re-expansion along with increased oxygen carrying capacity. These new strategies may play a significant role in changing the need to perform an open abdomen during a trauma laparotomy (7).

There is currently no end point for the resuscitative period. It has been shown that lactate clearance to normal levels within 24 hours correlate with good survival rates (6). Mostly patients will be taken to theatre for definitive surgery once physiologically improved (24-48hours later), but a subgroup will require re-exploration before physiology has been corrected. This group will require ongoing transfusions and/or show no improvement in lactate or base excess, despite resuscitation. Commonly these patients will have a missed visceral or vascular injury (6).

A second group requiring re-look will be the patients developing intra-abdominal hypertension. Abdominal compartment syndrome is defined by the World Society of Abdominal Compartment Syndrome [WSACS] as pressures > 20 mmHg with new single or multi-organ dysfunction (Normal pressures 2 – 7 mmHg) (5). Abdominal compartment syndrome is subdivided into primary, with an abdomino-pelvic pathology, and secondary with pathology not involving the abdomino-pelvic regions. Clinically these patients can present with abdominal distention, impaired ventilation, hypoxia, hypercarbia and/or decreased urine output (8). Colloid rather than crystalloid resuscitation will decrease bowel oedema. Abdominal wall compliance can be improved by good sedation and neuromuscular blockades (3).

As for abdominal wall closures, current options include mesh, vacuum dressings, grafting and abdominal wall reconstruction (2). The ideal vacuum dressing or temporary abdominal wall closure should absorb fluid, prevent evisceration and allow expansion. If a mesh is used, there is a high risk of ventral hernia formation, but not all will require repair (3).

In our unit, laparotomy patients are frequently left with open abdomens post DCS. However, the factors influencing the surgeon's decision of an open abdomen and the role of open abdomen in the outcome of these patients has not been evaluated.

This study aims to understand the factors influencing the decision to create an open abdomen at the end of an index laparotomy within the context of a changing approach to trauma resuscitation. With advances in DCR, borderline patients who would normally receive DCS might now receive early definitive surgery due to correction of physiology.

Research question

What is the mortality rate in patients after DCS with an open abdomen, at 24 hours, 7 days and 28 days in the Charlotte Maxeke Johannesburg Academic Hospital ICU?

2. Study aim and objectives

2.1 Study Aim

Open abdomen is associated with high morbidity and mortality rates (5), and this study aims to assess these rates in a level I trauma centre.

2.2 Study Objectives

Primary objective

To quantify the mortality rate of patients with an open abdomen over a 24 hour, 7 day and 28 day period in the major trauma unit of the Charlotte Maxeke Johannesburg Academic Hospital.

Secondary objectives

- To determine factors influencing the decision to perform DCS
- To determine possible contributory factors to mortality
- To determine the number of laparotomies till definitive closure
- To assess morbidity in the open abdomen patient: wound sepis, hernia rate and entero-cutaneous fistula.

3. Methodology

Study design: A retrospective review of open abdomen patient records over a 24 hour, 7 day and 28 day period.

Study site: Charlotte Maxeke Johannesburg Academic Hospital ICU.

Study population: Open abdomen patients at 24 hours, 7 days and 28 days after a trauma laparotomy over a 3 year period from 01/01/2016 to 31/12/2018.

Sampling: Retrospective data to be collected from prospectively filled MediBank forms, RedCap trauma database and patient ICU files.

Sample size: All patients that underwent Damage control surgery with an open abdomen, over a time period of three years.

Inclusion criteria

- Information from patients 18 years or older admitted to CMJAH over the study period of 3 years from 01/01/2016 to 31/12/2018, who had a trauma laparotomy with an open abdomen will be collected for analysis.

Exclusion criteria

- Patients transferred to the unit with an open abdomen following a laparotomy performed at another institution

Data collection: A data collection sheet with all aspects of the patients assessed in this study will be completed for each open abdomen patient (Appendix A).

Study limitations:

There is a possibility of incomplete patient records.

: The study may be biased with limited applicability outside of the setting in which the research is conducted.

4. Data analysis

Retrospective data will be collected from prospectively filled MediBank forms, RedCap Trauma database and patient ICU files.

Variables included in the study

- Age and gender
- Mechanism of injury
- Haemodynamic status on arrival = blood pressure < 90/60

- Injury Severity Score (ISS)
- List of criteria used by the surgeon to decide on DCS and open abdomen
- 24h, 7 days and 28 day mortality
- Morbidity development: enterocutaneous fistulae, ventral hernia, wound sepsis
- Length of stay in ICU

Clinical outcome measures

Primary:

- Determine the overall mortality rate of patients with open abdomen

Secondary

- Understanding the factors associated with performing an open abdomen
- Determine number of laparotomies needed before definitive closure

5. Ethics

Data collection will only commence once ethics clearance is obtained from the Human Research Ethics Committee (HREC) (medical) of the University of the Witwatersrand with a written clearance certificate with a specific clearance number.

Permission to collect data will be obtained in writing from RedCap database gatekeeper.

Permission to collect data will be obtained in writing from the Head of The CMJAH Trauma Unit

Permission to access and collect patient data will be obtained from the hospital CEO by means of registering the research project online on the National Health Research Database (NHRD).

Patient confidentiality will be maintained as data will be collected anonymously since only a study number will be allocated to each data collection sheet without recording any patient names or hospital numbers.

No patient information sheet or patient informed consent forms are needed, since no direct contact with patients or any identifying data is required or will be collected for the study.

The patient information will be collected by the principal investigator 31on a prepared data collection sheet (Appendix A) and will be kept in a safe place only assessable to the principal investigator and assistants.

6. Study Time-Line 2019

Process	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb
Literature Review	x	x										
Preparing protocol	x	x										
Protocol Submission			x									
Protocol assessment				x								

Ethics application				x								
Data collection					x	x						
Data analysis							x	x				
Writing up report									x	x		
Writing up paper										x	x	x

7. Funding

This study is investigator-initiated research and will thus be funded by the principal investigator.

ITEM:	**COST:**
Stationary	R500
Photocopying	R2000
Congress registration	R3000

Transport	R1500
TOTAL	R7000

8. References

1. Kritayakirana K, Maggio PM, Brundage S *et al*., Outcomes and complications of open abdomen technique for managing non trauma patients. Journal of Emergencies, Trauma and Shock JETS. 2010 Apr-Jun; 3(2): 118-122.

2. Frazee RC, Abenathy S, Jupiter D, *et al*., Longterm consequences of open abdomen management. *Trauma* 2013;16(1):37-40.

3. Waibel BH, Rotondo MF. Damage control surgery: it's evolution over the last 20 years. *Rev Col Bras Cir* 2012;39(4):314-321.

4 Godat L, Kobayashi L, Constantini T, Coimbra R *et al*., Abdominal damage control surgery and reconstruction: world society of emergency surgery position paper. WJES 2013, 8:53.

5 Huang Y, Li Y. Open abdomen in trauma patients: a double edged sword. Military Medical Research 2016 3:10.

6**.** Lamb CM, MacGoey P, Navarro AP, Brooks AJ. Damage control surgery in the era of damage control resuscitation. *Brit J Anaesth* 2014;113(2):242-249.

7. Holcomb JB, Jenkins D, Rhee P, *et al*., Da,Damage control resuscitation: directly addressing the early coagulopathy of trauma. *J Trauma* 2007;62:307-310.

8. Burch JM, Ortiz VB, Richardson RJ, *et al*., Abbreviated laparotomy and planned reoperation for critically injured patients. *Ann Surg* 1992;215:476-483

9**.** Rotondo MF, Schwab CW, McGonigal MD, *et al*., "Damage control" and approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993:35:373-382.

10**.** Asensio JA, McDuffie L, Petrone P*, et al*., Reliable variables in the exsanguinate patient which indicate damage control and predict outcome. *Am J Surg* 2001;139:209-214.

11. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma* 2003;54:1127-1130.

12. Cotton BA, Reddy N, Hatch QM ,*et al*., Damage control resuscitation is assocd with a reduction in resuscitation volumes and improved survival in 390 damage control laparotomy patients. *Ann Surg* 2011;254:598-605.

13. Shamrock AE, Barker T, Yuen HM *et al.,* Management and closure of the open abdomen after damage control laparotomy for trauma. A systematic review and meta-analysis. International Journal of the care of the injured patient. 2016 Feb; 47(2):296-306.

Appendix: Data collection sheet

Tick appropriate box or enter numeric data

Consecutive Study No:

Age in years:

Gender:

Male
Female

Mechanism of injury:

Penetrating
Blunt

Cause of injury:

MVC	MBC	PVC
Stab wound	GSW	Impalement
Fall	Other(Specify)	

ISS:

Haemodynamic status on arrival: BP < 90/60

Shock	No shock

Total volume crystalloid during resuscitation

Type:

Milliliters:

Blood component during resuscitation

Units of blood:	Units FFP:

Platelets mega units:	Units Cryoprecipitate:
Other:	

Open abdomen

Yes/No

Factors used to decide open abdomen

Abnormal haemodynamics	High dose vasopressor	Complex bowel repair required
Hypothermia	Severity associated injuries	Packs in abdomen
Coagulopathy	Metabolic acidosis	Temporary vascular shunt
Gross contamination	Massive transfusion	Other
Bowel oedema	Doubtful bowel viability	

Number laparotomies before definitive care:

Length stay ICU:

Alive: Yes/No

Mortality: Day of hospital stay: 24 hours, 7 days, 28 days ?

Complications:

Fistulae	
Hernia	
Wound Sepsis	

Comments:

Appendix 2: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Estelle van der Merwe

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M190982

NAME: (Principal Investigator)	Dr Estelle van der Merwe
DEPARTMENT:	General Surgery Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The mortality rate and contributory factors of patients with an open abdomen: three year audit in a major academic trauma unit
DATE CONSIDERED:	27/09/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof MS Moeng, Dr M Joubert and Dr M Nel
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	30/09/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **September** and will therefore be due in the month of **September** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 3: Turnitin report

08901071:Estelle_MMED_FINAL_for_Turnitin!!!.docx

ORIGINALITY REPORT

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SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Elizabeth Chabot, Ram Nirula. "Open abdomen critical care management principles: resuscitation, fluid balance, nutrition, and ventilator management", Trauma Surgery & Acute Care Open, 2017 Publication	3%
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