Is Obesity a risk factor for increased Perioperative Blood loss following Laparotomy? A Matched Cohort Study from South Africa.

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Abstract

Background:
The prevalence of obesity is growing in the South African (SA) population. Some of these obese individuals might require surgery during their lives. However, there are no specific studies from this setting which have investigated the impact of obesity on perioperative complications, such as blood loss, following high-risk abdominal surgery. This knowledge has potentially important implications for the perioperative management of obese SA abdominal surgery patients. Our objective was to address the identified gap in the published literature.

Methods:
We conducted a matched cohort study involving data from an existing laparotomy database at a SA tertiary hospital. Non-obese and obese patients were matched on established factors associated with perioperative blood loss. The Gross Equation was used to calculate the estimated perioperative blood loss. Mean estimated perioperative blood loss (with standard deviation - SD) was then statistically compared between obese and non-obese patient groups.

Results:
There were 58 patients who were matched (29 non-obese and 29 obese). The estimated mean (SD) perioperative blood loss in non-obese patients was 806.96 (536.9) mL. The estimated mean (SD) perioperative blood loss in obese patients was 725.06 (513.9) mL. Overall, there was similar perioperative blood loss between non-obese and obese patients (p=0.438).

Conclusion:
Obese and non-obese patients undergoing laparotomy experienced similar blood loss.

Recommendations:
Obese patients in our setting should be managed for perioperative bleeding in the same way as non-obese patients.

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1 Introduction:

The World Health Organisation reports that there are 650 million adults worldwide who are obese, defined as a body mass index (BMI) greater than 30kg/m^2 [1]. The prevalence of obesity in the general South African (SA) population ranges between 31% and 70% [2]. Obesity is more common in surgical patients when compared with the general population, ranging from 17.3% to 31.7% [3, 4]. Given the additional disease challenges facing the SA population, a proportion of these obese individuals are likely to require surgical intervention for these pathologies at some point in their lives.

Irrespective of BMI, all patients who undergo open intra-abdominal surgery are likely to experience at least some perioperative blood loss. Excessive blood loss might result in anaemia, which has serious consequences in surgical patients [5, 6, 7]. Perioperative anaemia is associated with mortality, renal impairment, and infectious complications. Excessive blood loss also has implications for the utilisation of blood products, which are a scarce commodity in SA. Overall, the published literature from outside SA is unclear around the relationship between obesity and perioperative blood loss. There is evidence which suggests that obese patients undergoing intra-abdominal or general surgery bleed more than non-obese patients [8]. Paradoxically, there is also evidence suggesting that obesity has a "protective" effect against perioperative bleeding [8]. Furthermore, there is also evidence of similar levels of bleeding in obese and non-obese surgical patients [9].

There are no studies which have sought to investigate the potential impact of obesity on perioperative blood loss in SA patients undergoing open intra-abdominal surgery. Given the mixed findings in the international published literature, a SA study on this topic would be useful for several reasons. Firstly, the findings could be used by anaesthetists and surgeons to improve patient blood management. More specifically, the findings could guide clinical decision-making around which patients are likely to suffer significant blood loss and require transfusions in a setting where the supply of blood products is often limited. Secondly, if obese patients are shown to have higher levels of perioperative blood loss, it can be used as an additional incentive to reduce BMI well in advance of elective surgery. Lastly, it could be used during the informed consent process to communicate risk of bleeding to patients undergoing major surgery. Our objective was to determine the relationship between obesity and perioperative bleeding in a cohort of SA intra-abdominal surgery patients.

2 Methods:

This was a matched cohort study involving data from an existing database of patients who had undergone laparotomy at the tertiary-level Inkosi Albert Luthuli Central Hospital in SA during 1 January 2006-31 December 2010. IALCH is a central and a tertiary-level hospital located in Durban, SA. This 846-bed public facility is amongst the first large, government-funded hospitals to be built in SA since the fall of Apartheid in 1994. The hospital offers specialist services across most medical and surgical disciplines to the population of the eastern seaboard of SA, particularly those living in the provinces of KwaZulu-Natal and the Eastern Cape. The demographics of the hospital's admissions reflect the diverse, multiracial population of the KwaZulu-Natal and Eastern Cape Provinces. IALCH is also one of the designated teaching hospitals affiliated to the Nelson R. Mandela School of Medicine at the University of KwaZulu-Natal. Given the specialist nature of the medical and surgical services offered at IALCH, admission to the hospital is based on a strict referral pathway with most patients being referred from regional hospitals that form the second tier of the public healthcare system in SA.

A set of eligibility criteria (Table 1) was used to create a pool of patients for the matching process.

Patients had data collected for various characteristics during a review of their medical charts. Characteristics collected for each patient included: Demographic criteria such as age and sex; clinical characteristics such as comorbidities, American Society of Anaesthesiologists (ASA) Score and BMI; preoperative anaemia, thrombocytopenia, hypoalbuminemia pre- and postoperative haematocrit; and surgery-related variables (type of anaesthesia used, tranexamic acid use, total surgery time, nonsteroidal anti-inflammatory use, thromboprophylaxis, and transfusion). A BMI threshold of > 30 $kg/m^2$was used to define obesity. Patients were matched on all characteristics, with the exception of obesity, using a 1:1 matching ratio. This was done to eliminate the potentially confounding effects of other characteristics which might impact blood loss. We used the Gross Equation to calculate blood loss in mL [10]. This method of estimating perioperative blood loss was preferred as clinical methods of counting blood-soaked swabs and measuring blood collected in drains often underestimate perioperative blood loss. Furthermore, clinical methods of estimating blood loss do not account for hidden blood loss, while the Gross equation accounts for this [11, 12].

We used the McNemar test to analyse categorical data. This was primarily done to evaluate the efficiency of the matching process. In order for optimal matching to have been achieved, the Mc-

Table 1. Patient eligibility criteria to be included in this matched cohort study

Inclusion Criteria	Exclusion Criteria
Patients already included in the pre-existing laparotomy registry	Missing height and or weight data
Age >18 years old (adults)	Patients with missing pre- or post-operative haematocrit tests
	Patients with other missing data which was required for the matching process
	Patient could not be paired/matched

Nemar test for all matched variables would need to have returned a p-value of >0.050. A paired t-test was used to evaluate a potential difference in mean perioperative blood loss between the two patient groups (non-obese and obese patients). Any results with $p<0.05$ were considered statistically significant. We used R version 4.1.1 (R Foundation, Vienna, Austria) to analyse our data.

We received ethical approval for this research from the University of KwaZulu-Natal's institutional review board (Study number BCA208/18).

3 Results:

A flow diagram showing the process through which the matched cohort was derived is outlined in Figure 1. The final study sample was comprised of 58 patients (29 obese and 29 non-obese patients).

A description of the study sample is presented in Table 2. Very few patients in the matched cohort were >65 years old (4 patients, 6.9%). Most patients were female (52 patients, 89.7%). Just under half of all patients comprising the matched cohort had an ASA score >2 (27 patients, 46.6%).

The most common comorbidity was preoperative anaemia (43 patients, 74.1%). Nine patients received a perioperative transfusion of >2 red cell units (15.5%). Surgery lasted >2 hours in 18 patients (31.0%). The most common indication for surgery was non-communicable disease (55 patients, 94.8%). With regard to medication use, preoperative NSAIDs were used in 11 patients (19%), tranexamic acid was used in 2 patients (3.4%), aspirin was used in 2 patients (3.4%) and thromboprophylaxis was used in 35 patients (60.3%). The results from the McNemar tests confirmed that our cohort was effectively matched (Table 3).

The findings from the analysis comparing perioperative blood loss between the two groups of patients (obese and non-obese) are shown in Figure 2. The mean (standard deviation - SD) perioperative blood loss for the non-obese and obese patients was 807.0 (536.9) and 725.1 (513.9) mL, respectively. Mean perioperative blood loss was not statistically different between non-obese and obese patients ($p=0.438$).

4 Discussion:

Our study did not find any clear relationship between obesity and perioperative blood loss in SA patients undergoing laparotomy. As previously alluded to, the international published literature reports mixed results regarding the relationship between obesity and perioperative blood loss. There are some studies that have found increased blood loss in obese patients compared with their non-obese counterparts [3, 13, 14, 15], while some studies have found obesity to have a protective effect against blood loss [8, 16]. Lastly, there are studies which in a manner similar to ours show similar perioperative blood loss between obese and non-obese patients [9].

There are a number of reasons why obese surgical patients might bleed more than non-obese surgical patients. Many studies have shown longer operating times in obese patients versus non-obese controls [3, 9, 14]. The longer period during which the surgical incision remains open in obese patients might result in higher levels of blood loss when compared with non-obese patients. Obtaining surgical access may be more difficult in obese patients, requiring larger surgical incisions through which more blood is lost. The thick layer of adipose tissue is highly vascular and surgical incisions in this tissue can contribute toward additional blood loss. Anticoagulants reduce the risk of perioperative embolism, for which obese patients are at high-risk [17]. However, anticoagulants might ex-

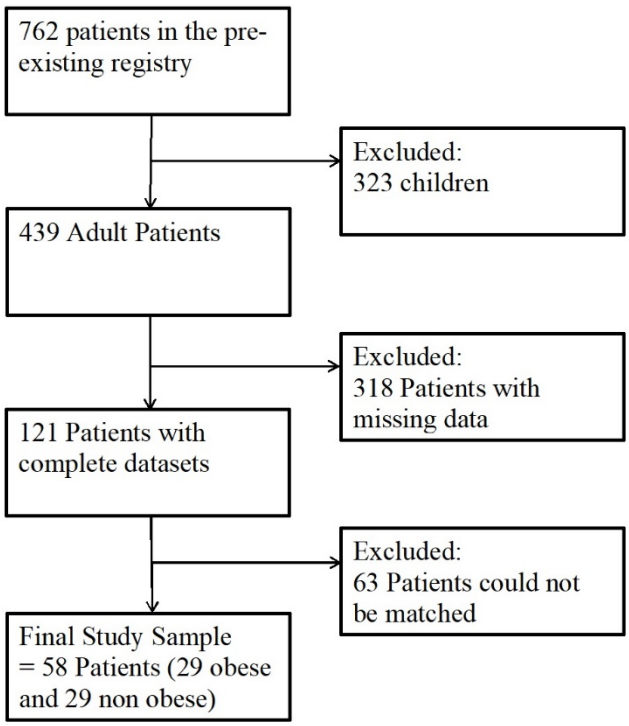

Figure 1. Flow diagram showing how the final matched cohort was derived

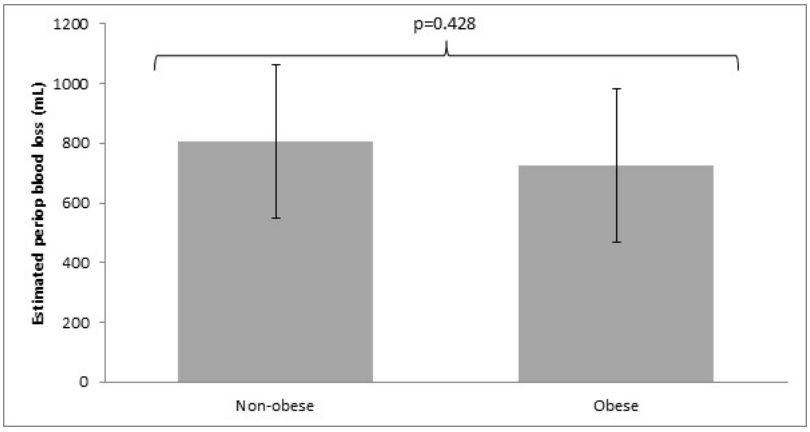

Figure 2. Blood loss in non-obese versus obese patients

acerbate bleeding in the obese surgical patient if these are not carefully administered.

There are three possible reasons why some studies have shown obesity to impart a protective effect on perioperative blood loss. Firstly, adipocytes produce plasminogen activator inhibitor and obese patients exhibit increased levels of factor VIII, fibrinogen, and von Willebrand factor. This results in a pro-thrombotic state [18], which would then reduce blood loss. Secondly, it is also possible that bleeding risk factors are more readily identified by physicians in obese patients than in non-obese patients. This might be attributed to more aggressive screening for these risk factors in patients who present with obesity. Therefore, some bleeding risk factors might be underdiagnosed and not treated in some non-obese patients. Thirdly, this protective effect of obesity might not actually exist, and the reported effect may be due to selection bias which is common in many epidemiological studies.

The findings of our research are not unique. In a published retrospective analysis of 151 patients undergoing elective colorectal resection for carcinoma in a tertiary hospital in the United States,

Table 2. Distribution of patient, clinical, and surgical characteristics in the study sample

Characteristics or Variables	n (% of N=58)
Patient demographics	
Age > 65 years old	4 (6.9)
Female gender	52 (89.7)
Comorbidities	
Hypertension	24 (41.4)
Diabetes	9 (15.5)
Cardiovascular disease	11 (19)
HIV	4 (6.9)
ASA > 2	27 (46.6)
Metastatic cancer	12 (20.7)
Asthma COPD	1 (1.7)
Gastric ulcer	1 (1.7)
Renal failure	6 (10.3)
Current smoker	9 (15.5)
Preoperative anaemia	43 (74.1)
Preoperative thrombocytopaenia	2 (3.4)
Preoperative hypoalbuminaemia	9 (15.5)
Surgery-related variables	
Transfusion > 2 units	9 (15.5)
Relaparotomy following index surgery	7 (12.1)
Duration of Surgery > 2hours	18 (31.0)
Emergency Surgery	4 (6.9)
Non-communicable disease indication	55 (94.8)
Medication	
Preoperative NSAID	11 (19)
Tranexamic acid	2 (3.4)
Preoperative aspirin	2 (3.4)
Perioperative thromboprophylaxis	35 (60.3)

ASA: American Society of Anaesthesiologists, COPD: Chronic obstructive pulmonary disease, NSAID: Nonsteroidal anti-inflammatory drugs, HIV: Human Immunodeficiency virus.

Blee and colleagues reported that obese and overweight patients had similar intraoperative blood loss when compared with patients who had normal BMIs [9]. Blood loss for normal BMI, overweight and obese groups were 212.6 mL, 295.9 mL and 312.3 mL (overall comparison between groups was not deemed to be statistically significant). Haemostasis involves an intricate balance between a pro- and antithrombotic state. This process is mediated by physiological processes such as vasospasm, platelet activation, and activation of the clotting cascade. In surgical patients there are additional factors to consider, such as preoperative aspirin/anticoagulants use, tranexamic acid administration, and preoperative optimization of comorbid diseases associated with perioperative bleeding. This points toward a multifactorial basis for perioperative blood loss. When this is taken into consideration along with our findings for obesity, it is likely that obesity acts as a moderating variable (i.e. a variable which moderates the way in which an exposure/determinant and outcome are related, but is itself not associated with the exposure/determinant or outcome) for perioperative blood loss in our setting.

Our findings have several potentially important implications related to patient blood management. Blood is a finite resource with considerable processing costs. Our findings suggest that within our SA tertiary hospital setting, obesity alone should not be used to stratify for bleeding risk for laparotomy. Furthermore, perioperative blood product management decisions should not be based solely on whether the patient is obese or not. No additional

Table 3. Evaluation of the matching process

Characteristics or Variables	Non-obese n (% of N=29)	Obese n (% of N=29)	p-value
patient demographics			
Age > 65 years old	2 (3.4)	2 (3.4)	0.999
Female gender	26 (44.8)	26(44.8)	0.999
Comorbidities			
Hypertension	9 (15.5)	15 (25.9)	0.238
Diabetes	3 (5.2)	6 (10.3)	0.508
Cardiovascular disease	3 (5.2)	8 (13.8)	0.227
HIV	1 (1.7)	3 (5.2)	0.625
ASA > 2	14 (24.1)	13 (22.4)	0.999
Metastatic cancer	8 (13.8)	4 (6.9)	0.388
Asthma/COPD	0 (0.0)	1 (1.7)	0.999
Gastric ulcer	1 (1.7)	0 (0.0)	0.999
Renal failure	3 (5.2)	3 (5.2)	0.999
Current smoker	5 (8.6)	4 (6.9)	0.999
Preoperative anaemia	25 (43.1)	18 (31)	0.065
Preoperative thrombocytopaenia	2 (3.4)	0 (0.0)	0.500
Preoperative hypoalbuminaemia	6 (10.3)	3 (5.2)	0.453
Surgery-related variables			
Transfusion > 2 units	5 (8.6)	4 (6.9)	0.999
Relaparotomy following index surgery	3 (5.2)	4 (6.9)	0.999
Duration of surgery > 2 hours	11 (19.0)	7 (12.1)	0.289
Emergency surgery	3 (5.2)	1 (1.7)	0.625
Non-communicable disease indication	26 (44.8)	29 (50.0)	0.250
Medication			
Preoperative NSAID	4 (6.9)	7 (12.1)	0.549
Tranexamic acid	1 (1.7)	1 (1.7)	0.999
Preoperative aspirin	1 (1.7)	1 (1.7)	0.999
Perioperative thromboprophylaxis	15 (25.9)	20 (34.5)	0.289

ASA: American Society of Anaesthesiologists, COPD: Chronic obstructive pulmonary disease, NSAID: Nonsteroidal anti-inflammatory drugs, HIV: Human Immunodeficiency virus

risk reduction interventions for perioperative bleeding are required for obese patients undergoing laparotomy. Our findings could limit the amount of unnecessary blood being ordered for a group of patients who have traditionally been considered high risk for perioperative blood loss. It should also be noted that blood transfusion itself carries a risk of postoperative complications [19]. Decreasing blood transfusions would therefore also decrease the risk to the patient. In addition to this, our findings are also relevant to communication of risk during the perioperative patient informed consent process and communication of possible risk of surgery. Obese patients should be counselled and informed prior to surgery that they will suffer some blood loss during the procedure, but this expected blood loss would not be any different to that in non-obese patients.

A limitation in our study is that it only involves data from a single institution. This might limit the generalizability of our findings to obese/non-obese intra-abdominal surgery populations elsewhere. Our findings are also limited to laparotomy patients and might not be generalizable to other types of surgeries. This was a retrospective study and was subject to all the challenges innate to retrospective studies, including a reliance on adequate record keeping, and missing data. Lastly, patients with missing data which was necessary to calculate estimated blood loss were excluded from our analysis. This reduced our overall pool of patients which we used to derive our final study sample.

5 Conclusions:

We found that obese and non-obese patients undergoing laparotomy experienced similar levels of

blood loss. Obese patients in our setting should be managed for perioperative bleeding in the same way as non-obese patients. However, given that our research does have some limitations, we recommend that more studies on this topic be conducted to confirm the lack of association between obesity and perioperative bleeding.

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