Narrative review

Maternal body weight and estimated circulating blood volume: A non-linear approach

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Abstract

Postpartum haemorrhage continues to be a leading cause of morbidity and mortality in the obstetric population worldwide, especially in patients at extremes of body weight. Quantification of blood loss has been covered extensively in the literature. However, these volumes must be contextualised to appreciate the consequences of blood loss for individual parturients. Knowledge of a patient's peripartum circulating blood volume is essential to interpret the significance of haemorrhage and provide appropriate resuscitation. Greater body mass in obesity can lead to gross overestimation of blood volume, resulting in inappropriately high thresholds for blood product transfusion and delays in treatment. The most recent MBBRACE-UK surveillance report demonstrated the risk to this population; with over half of all maternal mortality recorded in parturients who were either overweight or obese. Current linear calculations used to estimate circulating blood volumes based on patients' weight may be contributing to this phenomenon, as blood volume increases at a disproportional rate to body composition. In this review, we summarise the relevant physiology and explore the existing literature on the estimation of circulating blood volume, both during pregnancy and in obesity. Building on key works and principal findings, we present a practical, non-linear approach to the adjustment of estimated blood volume with increasing body mass. This clinical tool aims to reduce the clinical bias influencing the management of obstetric haemorrhage in a population already at increased risk of morbidity and mortality. Discussion of the limitations of this approach and call for further research within this field completes this review.

Introduction

Postpartum haemorrhage is a substantial and ongoing issue, affecting 24% of pregnancies in England in 2020-2021.[1] As noted in the 2020 *Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries Across the UK* (MBRRACE-UK) report, there continue to be serious untoward outcomes relating to the underestimation of blood loss, especially in parturients of lower weights.[2] Guidance arising from this report includes the recommendation to "ensure that the response to obstetric haemorrhage is tailored to the proportionate blood loss as a percentage of circulating volume based on the woman's body weight".[2]

A key aspect in the management of obstetric haemorrhage is an accurate assessment of the volume of blood loss,[3] but this information is only half of the picture; knowledge of the patient's original circulating blood volume (CBV) is just as important. However, this value cannot be directly measured in clinical practice. Drawing upon values given in the Royal College of Obstetricians and Gynaecologists (RCOG) 'green-top' guideline on postpartum haemorrhage published in 2009,[4] the recent MBRRACE-UK report advocates using a weight-based calculation volume of 100 ml per kg of bodyweight to approximate maternal CBV.[2] Of note, these values were subsequently omitted in the 2016 update of the RCOG guideline, which instead recommends that the "clinical picture should be the main determinant of the need for blood transfusion".[5]

One of the difficulties that may arise from arbitrarily using 100 ml kg^{-1} as the basis for calculating CBV and guiding therapeutic measures, is the potential to create 'cut-off values' that may disproportionately influence patient management. For example, guidelines often use this approach to derive a value of 1.5 L blood loss (i.e., >20% of a 'typical' 70 kg patient's blood volume) to activate major haemorrhage pathways, as this will be sufficient for many patients. However, recent guidance acknowledges that arbitrary volumes for activation of protocols may be detrimental for women with a lower body mass.[2, 5]

Although the adoption of an individualised 'per kg' approach to blood volume estimation in parturients goes some way to addressing the risk of under-estimating the significance of haemorrhage in those with lower body weights,[2, 5] little attention is paid to how this method may affect those of a higher body mass, for whom predictions may yield unrealistic results (e.g., 12 L for a 120 kg patient). Overestimation of CBV leads to a risk of inadequate resuscitation and false reassurance. This discrepancy is likely to become more clinically significant in shorter patients with a high BMI, as blood volume does not increase proportionally to excess adipose tissue, resulting in potentially harmful underestimation of the significance of blood volume loss in obese patients.

Over a decade ago, approximately one per thousand parturients in the UK were classified as extremely obese,[6] a number that has increased in line with the prevalence of obesity in the general population; in 2018 over 60% of women in England were classed as overweight or obese,[7] alongside an annual rate of obesity in early pregnancy of 22.1%.[8] In the latest MBBRACE-UK report over half of maternal mortality was amongst women who were overweight or obese,[9] and raised body mass index (BMI) is independently associated with an increased risk of significant postpartum haemorrhage.[10] Therefore pregnant women with obesity are at least as likely as non-obese women to suffer adverse outcomes, further hindered by healthcare biases. This is likely to become yet more prevalent as obesity rates rise.

In this narrative review, we outline the physiological changes pertinent to blood volume in pregnancy, review the surrounding literature, and based on the available data, suggest a methodology for adapting the estimation of CBV with increasing body mass.

Physiological changes to blood volume in pregnancy in the context of obesity

The physiological changes associated with pregnancy are well documented. These include increased cardiac output secondary to increased CBV and baseline heart rate (HR). A concomitant decrease in systemic vascular resistance (SVR) mediated by a combination of factors, including the action of relaxin and progesterone, and the presence of the placental circulation means that mean arterial pressure (MAP) falls during the second trimester of pregnancy, returning to near baseline at term.[11, 12] Plasma volume and red cell mass increase during pregnancy, although the disproportionate increase in plasma volume results in a physiological anaemia due to haemodilution. CBV expansion, mediated by the renin-angiotensin and aldosterone system, begins at 6-8 weeks' gestation, and rises progressively to 28-30 weeks gestation before plateauing.[13, 14]

The effects of pregnancy on cardiovascular remodelling have been studied in the context of obesity, and multiple studies have analysed the impact of obesity on maternal haemodynamics.[15, 16] The majority of these studies focused on whether there is a correlation between obesity and the development of hypertensive diseases of pregnancy, such as preeclampsia.[17, 18] However, the few studies that have examined the cardiovascular response to pregnancy in the context of obesity demonstrate conflicting results, with some reporting no difference in the observed parameters between high BMI and control groups.[16]

Other studies suggest that obesity is associated with altered haemodynamics in pregnancy; including increased sympathetic activation, producing an increase in HR and myocardial contractility, and increased SVR and MAP due to vasoconstriction.[15] Obese parturients have an increased risk of

cardiovascular diseases such as ischaemic heart disease, increased left ventricular mass and peripartum cardiomyopathy, and therefore may poorly tolerate a reduction in oxygen-carrying capacity and volume depletion.[16, 19]

Estimation of blood loss

In many treatment protocols, blood product transfusion is triggered by specific quantities of blood loss, but the optimal methods to assess blood loss are yet to be determined. Visual estimations have recurrently been found to be inaccurate, especially as blood loss may be hidden; with accuracy degrading further with increasing volumes of haemorrhage.[20] Although quantification of blood loss lends itself to more suitable methodologies than historic studies of CBV, a recent Cochrane review identified only two trials suitable for comparison and was unable to advocate any one method of blood loss estimation.[21] Furthermore, there is little research to support the role of quantitative blood loss measurement in improving overall maternal morbidity or mortality.[22, 23] This is likely, at least in part, to be because of the ethical and practical problems of attempting to isolate the influence of blood loss measurement from other clinical interventions.

Studies examining blood loss often extrapolate from haemoglobin-based analysis to determine the accuracy of blood loss estimates.[24] However, it has been suggested that this technique may be inherently flawed due to the poor correlation between these estimates and postpartum maternal haemoglobin values.[23] Although this discrepancy has been previously explained by the influence of fluid shifts, starvation periods and crystalloid administration, it may reflect the variability of CBV at the population level. Gravimetry (weight-based evaluation, e.g., of swabs), volumetry (based on fluid volumes, e.g., of suction canisters), and colorimetry (based on colour density analysis) can all be used individually to help quantify blood loss.[25] However, it is likely that a multimodal approach, as recommended by the RCOG,[5] is superior. Contemporary methods for quantifying blood loss have been shown to be effective when integrated into care systems and used in conjunction with treatment bundles, as demonstrated by the quality improvement project 'The Obstetric Bleeding Strategy Wales' (OBS Cymru).[26]

To date, there are no studies specifically addressing the relationship between the numerator (estimated blood loss) and the denominator (estimated blood volume). This may be due to a lack of a 'gold standard' technique for quantification of blood loss, as existing research debates the superiority of any one method.[21, 22, 27] Whilst quantitative measurement techniques such as gravimetry are now recommended by multiple international bodies,[23, 28] it is not only knowledge of blood loss that is

important, but the significance of that volume for the individual parturient that is vital for clinicians to appreciate.

Estimations of maternal blood volume in the obese population

Haemodynamic Studies

In an extensive literature search, we identified a paucity of research addressing the estimation of maternal CBV in the obese population. As such, it is useful to analyse the methodologies used by studies exploring haemodynamic adaptation to pregnancy and review how estimates of CBV were derived.

A prospective, case-controlled study by Vinayagam and colleagues[15] compared morbidly obese pregnant women (BMI ≥ 40 kg m^{-2}) with a control population (BMI 20-29.9 kg m^{-2}), using a doppler ultrasound technique to measure HR, CO, SV and SVR, which they corrected for body surface area (BSA) to produce indexed variables. They found that the obese population had a lower cardiac index (CI) and higher systemic vascular resistance index (SVRI) when compared to the non-obese population.[15] They attributed this phenomenon to reduced cardiac function and an 'impaired cardiac adaptation' to pregnancy, although they were unable to elucidate any structural or functional anomalies during the study to explain this hypothesis.[15] These findings were later echoed by both Sarno and colleagues,[29] who also used continuous wave doppler ultrasound to measure cardiac output, and a haemodynamic study assessing a subset of the ASPRE trial that utilised a non-invasive bioreactance method to assess cardiac function.[30] Transthoracic echocardiography has been used to demonstrate left ventricular hypertrophy,[16, 31] and diastolic dysfunction,[31] in obese pregnant women, attributed to maladaptive response to volume overload. However, none of the studies above quantified maternal blood volume or specifically addressed its impact on maternal cardiac output.

Vonck and colleagues[32] used bioimpedance to compare body composition and total body water (TBW) of obese and non-obese parturients during each trimester of pregnancy. They found an increase in TBW in both populations throughout pregnancy, but non-obese controls demonstrated a more significant late gestational increase in TBW that was not observed in the obese population.[32] Their study also estimated volumes for extracellular water (ECW) and intracellular water (ICW), from analysis of different electrical frequencies,[32, 33] although their method was unable to provide estimates for individual ECW constituents such as plasma volume.

Whilst the methodologies employed above are validated, non-invasive techniques which may be translatable into clinical practice, they do not provide an accurate estimation of CBV. Assumptions can

be inferred from measuring stroke volume, which is directly affected by preload, but this does not take into consideration other compensatory mechanisms and cannot be presumed to truly reflect plasma volume.

Dilution-based studies

In their paper on postpartum blood loss, Hernandez and colleagues[3] developed a predictive formula to estimate CBV in relation to maternal height and weight at the time of delivery. This involves predicting the nonpregnant CBV, then adding an additional 50% to account for the average blood volume expansion in pregnancy:

$$\{\,[(maternal\ height\ in\ inches\ x\ 50)\ +\ (maternal\ weight\ in\ pounds\ x\ 25)\ \div\ 2]\ \times\ 1.5\,\}$$

This formula was derived from measurements of maternal blood volumes using chromium isotope (^{51}Cr) labelled red blood cells developed by Pritchard and colleagues at Parkland Memorial Hospital, Dallas, Texas in the 1960s.[34] This formula has been validated internationally,[31, 35] but can no longer be reproduced on ethical grounds. This equation was later used by Stafford and colleagues,[36] who multiplied this estimated CBV by the percentage drop in haematocrit to estimate total volumes of blood loss, which was then compared to visual estimations. However, neither Hernandez nor Stafford validated their estimated values for blood loss with volumetry, gravimetric measurement, or the 'gold standard' haemodilution technique that the original formula was based upon.

Various studies have used similar dilution-based methods for measuring blood volume, such as the Evans blue dye dilution[37] or the radiolabelled iodine-albumin (^{125}I-HSA) indicator dilution method, to produce a value for plasma volume per lean body mass (PV ml kg^{-1}).[38, 39] Radiolabelled iodine-albumin was used by Aardenburg and colleagues[40] to generate a standardised plasma volume, corrected for height and weight, by analysing the proportional contribution of each variable by multiple linear regression analysis of logarithmically transformed variables.

A systematic review and meta-analysis of studies evaluating plasma volume expansion in pregnancy by de Haas and colleagues[41] included thirty dilution-based studies in singleton pregnancies and found an average volume expansion at term (36 - 41 weeks gestation) of 1.13 litres (95% CI 1.07-1.19 L), a relative increase of 45.6% (95% CI 43.0-48.1%) from the reference values. The primary outcome of this analysis was plasma volume expansion, expressed in litres and percentage change, but this did not take account of any anthropometric measures. Interestingly, they found no statistical difference between the various dilution-based techniques for measuring plasma volume expansion, including Evan's blue dye, chromium isotopes, iodine-labelled albumin, and iron-dextran complex.

Haemoglobin concentration and haematocrit

Although knowledge of a patient's blood volume is important, targeting circulating plasma volumes without considering the oxygen-carrying capacity of blood may overlook the effect of anaemic hypoxia. The disproportionate increase in plasma volume relative to red cell count during gestation, often termed the physiological anaemia of pregnancy, is well documented.[42] However, there may be pathological causes of anaemia during pregnancy in patients who are euvolemic. Furthermore, antenatal anaemia itself has been found to be a risk factor for postpartum haemorrhage and increased blood loss.[43]

To address this issue, various guidelines advocate targeting haematological indices and haemoglobin concentration thresholds for transfusion.[44] Some recommend defining a significant postpartum haemorrhage as a 10% drop in haemoglobin or haematocrit levels from late pregnancy values.[45] However, recent blood results may be unavailable, making it difficult to distinguish whether post-delivery anaemia reflects blood loss or pre-delivery anaemia.[46] Furthermore, in acute blood loss the haematocrit often remains unchanged and may even be elevated.[47] Postpartum haemoglobin levels will also be significantly influenced by changes in intravascular volume due to factors such as crystalloid administration and dynamic fluid shifts.

Recent MBRRACE-UK reports and the European Society of Anaesthesiology advocate monitoring haematological and biochemical parameters including haemoglobin, haematocrit, base deficit, and serum lactate concentration using both point-of-care testing and laboratory analysis.[5, 48, 49] In view of reports of 'false reassurance' from near-patient testing, contributing to delays in transfusion and maternal deaths, these values should not be interpreted in isolation.[2] Serial measurements are recommended by the above guidelines, however, this approach has yet to be shown to improve major haemorrhage outcomes.[4]

Estimated blood loss (EBL) has been an outcome of many studies investigating postpartum haemorrhage; some of these studies have used haematocrit-based formulae as a surrogate measure for blood volume.[50-53] These studies assume a premorbid estimated blood volume (EBV), by multiplying the patient's weight in kilograms by 85 ml, which is then multiplied by changes in peripartum haematocrit.[50, 51]

$$EBL = EBV\ x\ \frac{(Preoperative\ haematocrit - Postoperative\ haematocrit)}{Preoperative\ haematocrit}$$

There is no clear explanation for the use of the 85 ml multiplication factor in any of the citing literature, and there are considerable discrepancies between which body weight is to be used for the calculation; some studies reference 'booking weight'[52], measured at the first antenatal appointment, whilst others use the patient's weight immediately prior to delivery.[3, 36, 53] Despite this, calculations using this equation have been shown to correlate well with gravimetric measurements of blood loss by Sentilhes and colleagues.[50] However, the comparative post-operative haematological tests were mainly conducted at 24-48 hours postpartum, so this estimation may not translate to the acute setting.

Vital signs

Assessment of a patient's volume status should include bedside assessment of haemodynamic stability, vasopressor requirements, and symptoms of shock such as light-headedness, nausea and vomiting, cortical blindness, or depressed conscious level. Astute judgement is vital, alongside situational awareness of both the rate and causes of blood loss, which is reliant on good communication with obstetric and midwifery colleagues. Losses may be hidden; therefore clinicians should retain a high index of suspicion. Although most international clinical guidelines refer to clinical assessment, there appears to be a reluctance to specify target parameters or give weight to their significance.[54]

Studies have shown poor correlation between individual parameters and quantification of postpartum bleeding; haemodynamic observations such as tachycardia or hypotension may yield a high sensitivity, but poor specificity due to multiple concurrent factors such as effects of anxiety, pain, and administered analgesia or anaesthesia. However, these are better at identifying hypovolaemia when used in combination, such as the obstetric 'shock index' (heart rate divided by systolic blood pressure).[55, 56]

Patients with signs and symptoms of hypovolaemia are likely to have lost a significant amount of their CBV and require blood product resuscitation.[3, 56] Definitions of postpartum haemorrhage based on a patient's developing symptoms have been criticised for having poor specificity, leading to delays in treatment.[57] Some national and international societies' guidelines recommend blood transfusion if blood loss is accompanied by unstable vital signs,[44] incorporating the 'classes of shock' taxonomy traditionally taught in advanced trauma life support (ATLS) which have been adapted into obstetric instruction such as the Managing Obstetric Emergencies Trauma (MOET) course.[58]

Though this classification of hypovolaemic shock provides a useful framework for understanding and grading severity, its clinical applicability and validity have been criticised for not reflecting clinical reality. This is particularly relevant in the obstetric setting due to altered physiology, including

autotransfusion post-delivery, and are a typically young and physically resilient population.[59, 60] Whilst comparisons are often drawn with major trauma cases, physiological adaptations to pregnancy mean that these patients often demonstrate sustained haemodynamic compensation despite significant blood loss.[61, 62]

The effect of obesity on blood volume

The influence of increasing body mass index on total blood volume is well documented. In 1977, Feldschuh and Enson administered radiolabelled albumin dilutions in healthy, non-pregnant volunteers to demonstrate that as BMI increases, blood volume per weight decreases non-linearly: from 100 ml kg^{-1} in individuals with body weight 40% lower than ideal body weight (IBW), to 43 ml kg^{-1} in individuals with body weight 200% greater than IBW.[63] Based on these findings, they proposed a method for predicting CBV based on a table of blood volume ratios derived from their data.

Lemmens and colleagues[64] further developed this work, and that of others,[65-68] and devised a formula to estimate CBV in obesity known as the Lemmens-Bernstein-Brodsky equation:

$$Circulating\ blood\ volume\ = \frac{70}{\left[\ \sqrt{(Body\ Mass\ Index\ \div 22)}\ \right]}$$

This formula relates the widely accepted 70 ml kg^{-1} estimate for CBV, which is the value taken from Nadler's original work,[68] indexed to the ratio of the patient's actual BMI to an 'ideal' BMI of 22 kg m^{-2}. Lemmens and colleagues validated their equation by comparing their predicted values against those already found in the literature, plotting their curvilinear decline in blood volume against BMI and %ΔBMI against other regression curves, demonstrating the same graphical relationship.

Their formula has been widely used in the literature to correlate total blood volume with BMI and has been used as the control reference in studies assessing biomarker concentrations.[14, 69] However, the obvious limitation is that it quantifies CBV for non-pregnant, surgical patients and has not been validated in the obstetric population. Nevertheless, these findings illustrate how the application of a linear formula can lead to gross overestimation of CBV in clinical practice.

The effect of obesity on blood volume in pregnancy

To our knowledge, only one study found quantifying the impact of obesity on maternal blood volume to date is by Vricella and colleagues,[70] who used a hydroxyethyl starch (HES) dilution technique to demonstrate the relationship between obesity and CBV in patients after 34 weeks gestation. Estimates

of CBV were calculated by comparing glucose concentrations of acid hydrolysed plasma samples taken immediately before and 10 minutes after injection of HES. These were then compared to patients' BMI and body composition values measured by air displacement plethysmography. Using simple linear regression, this study showed a decreasing relationship between CBV per kilogram and BMI: producing a line of best fit at: y = -1.372x + 130 [y = HES blood volume estimate (ml kg^{-1}), x = Body Mass Index (kg m^{-2})]. They produced estimated blood volumes in millilitres per kilogram for both the lean and obese populations (table 1), although only reported values for these two discrete categories.

Vricella and colleagues' findings are consistent with those of Lemmens[64] and their cited studies in the non-pregnant population.[65-68] Their estimated volumes were approximately 50% higher than non-pregnant reference values, echoing classical teaching regarding gestational volume expansion.[34, 57] However, as with many studies, their values were not compared to a 'gold standard' methodology, rather to the original formula derived by Feldschuh and Enson.[63]

Though it provides useful data in an under-researched setting, Vricella and colleagues' study is significantly hampered by the small sample size (30 patients per group). Hence their 95% confidence intervals are very wide: as low as 29 ml kg^{-1} and as high as 117 ml kg^{-1} in the obese group. The classification of participants into two dichotomous groups (obese or non-obese) also limits extrapolation when predicting CBV clinically. However, this study does suggest that trends in blood volumes with increasing BMI seen in studies on the non-pregnant population are replicated in pregnancy, indicating that linear weight-based estimations (e.g., 100 ml kg^{-1}) may cause significant inaccuracies.

The lack of research into how to best determine blood volume in pregnancy poses several questions when attempting to follow national guidance and take an individualised approach to major obstetric haemorrhage. Whilst patients' 'booking' height, weight, and BMI, measured at initial assessment, are most accessible in clinical practice in the UK,[71] this does not reflect international practice.[72] It is recognised that there is a wide spectrum of weight change during pregnancy, and current guidance on obesity in pregnancy from the RCOG advocates reweighing women during their 3rd trimester to allow for appropriate planning prior to delivery.[73]

The ability to estimate current circulating blood volume using available variables, such as height and weight at term, would offer practical benefits to the clinician. The authors acknowledge that this information may be less readily available in the UK due to differing antenatal documentation processes. However, obtaining an up-to-date patient weight is a simple intervention that may help quantify the significance of any postpartum blood loss.

A proposed approach to estimating circulating blood volume

Based on the literature reviewed above, we propose estimating CBV in late pregnancy by adapting the CBV curve developed by Lemmens and colleagues,[64] with 95 ml kg^{-1} as the reference volume at a BMI of 22 kg m^{-2}, accounting for the hypervolaemia of pregnancy as per Pritchard's original work.[3, 34] This is consistent with Vricella and colleagues' regression, which provides the mathematical foundation for our proposed model (CBV per kg = -1.372 BMI + 130), depicting the relationship between BMI and CBV after 34 weeks gestation.[70]

Figure 1 illustrates the application of this model for a woman of 160cm height. This produces a curvilinear decline in gradient illustratively similar to that of a natural logarithmic function. Further series illustrate significant percentages of blood loss: 15%, 30% and 40%. The line for CBV approaches an asymptotic value of approximately 70 ml kg^{-1} at a body weight of 100 kg which, interestingly, reflects the values found in the non-pregnant population by Feldschuh and Enson.[63]

Whilst the values in Figure 1 provided a useful and granular reference guide for an 'average' parturient at term (UK average female height is 161.7cm[74]), it cannot be used reliably for all patients, and a multitude of corresponding graphs for parturients of different heights would be unsuitable for clinical practice.

We therefore suggest that it is more practical to simplify the values obtained from the methodology described above and categorise these values according to the current NHS obesity classification[75] (Table 2), which is based upon anthropometric work published by the World Health Organisation (WHO).[76] This can then be used to derive the expected values with increasing patient weight. We chose the highest CBV value to be 95 ml kg^{-1} in line with Vricella's publication,[70] as all estimates of CBV in pregnancy from studies into maternal haemodynamics (referenced above) produced values below 100 ml kg^{-1}.

Table 3 shows the estimated total CBV for parturients of different BMI ranges according to the NHS obesity classification, at different weights. It includes sub-section values corresponding to 15%, 30% and 40% blood loss which have been rounded to the nearest ten to help facilitate instant reference. We acknowledge that producing a table with ranges of values for obesity classifications, and subsequent percentage blood loss values, would best reflect the wide confidence intervals from underpinning research.[64, 70] However, consideration of the practicality of these tables has led to this format after several iterations. To provide a useful reference tool for the majority of parturients, we have included potential values for females 145cm to 180cm tall to encompass the 0.4^{th} to 99.6^{th}

centiles of height as taken from cross-sectional surveys.[77, 78] Stature outside this range may reflect underlying pathology that could influence circulating blood volume.

Table 3 demonstrates the difference in estimated blood volumes for parturients of the same weight. For example, a tall 70 kg patient with a BMI of 20 kg m^{-2} has an estimated CBV of 6650 ml, whereas a shorter 70 kg patient with a BMI of 40 kg m^{-2} has an estimated CBV of 4900 ml, estimating a 26.3% lower CBV than their lean counterpart. This shows a significant difference of 1.75 L using our calculations, and over 2 L less than traditional linear estimations of 100 ml kg^{-1}. This means that an arbitrary threshold for blood product transfusion of 1500 ml blood loss represents 23% of CBV for the lean patient, but for the morbidly obese patient, it represents 31% of CBV.

This table was designed to be incorporated into our Trust's major obstetric haemorrhage protocol and is displayed alongside posters in theatres outlining stepwise management of postpartum haemorrhage intending to enhance patient care and facilitate communication.

Conclusion

Post-partum haemorrhage remains a significant cause of maternal morbidity and mortality. Since its inception, the triennial *Confidential Enquiry into Maternal Deaths* has consistently reported postpartum haemorrhage as both a direct and contributory cause of maternal death.[2, 4, 9, 48] Timely and effective treatment of postpartum haemorrhage is essential, while delays in definitive treatment and blood product transfusion have been shown to exacerbate both acute and chronic sequelae.[79]

To comply with national and international guidance, an individualised approach to risk management, assessment and intervention should be applied. One of the challenges faced by all clinicians is not only the accurate estimation of blood loss, but also the significance of that volume for each parturient. One way to address this is to 'correct' expected haemodynamic indices, resuscitation targets and estimated blood volumes for anthropometric characteristics.[80] This can help to limit underestimation of the significance of blood loss in patients with low body mass and may also help prevent erroneous overestimation of the circulatory capacity and physiological reserve in the obese population.

Unfortunately, the paucity of research on changes in circulating volumes with increasing body mass means that there is no definitive method for the estimation of CBV. However, we feel that the most pragmatic and reproducible model is based upon the work of both Lemmens and Vricella and their colleagues,[64, 70] both of which describe a non-linear relationship between CBV and obesity, with higher BMI associated with lower CBV per kg body weight. Drawing on these sources, we propose the use of

a table incorporating weight and BMI to more accurately predict CBV, and hence blood volume loss in the case of haemorrhage.

There are several potential limitations of our model: it is not as easy to remember or calculate as current 100 ml kg^{-1} guidance,[4] there are no adjustments for changes in CBV with increasing maternal age,[81] ethnicity,[82] multiple pregnancies,[83] pre-existing co-morbidities,[84] or foetal size.[37] As with all cited calculations, it also relies on the assumption that CBV equates to the capacity of the circulation to transport oxygen, which will be impaired with all forms of anaemia.[85]

The studies that this work is based upon are limited; often sampling small populations or producing high variability and interquartile ranges for published data. Values produced will also likely continue to overestimate CBV for patients with contracted circulations, such as those with hypertensive diseases of pregnancy, who are potentially more vulnerable to the consequences of blood loss.

Despite these critiques, we feel that this work helps to highlight an issue that is yet to be addressed substantially in the literature and provides a practical cognitive aid for clinical use in what is often a stressful situation. Nevertheless, further research into the topic is urgently required. With studies suggesting that approximately 90% of obstetric deaths due to haemorrhage are potentially preventable,[86] and an increasingly obese obstetric population,[87] it is especially important to take an individualised approach to estimating circulating blood volumes.

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Author Contributions

HK: Initial concept, design of proposed approach, writing up of the first draft of paper and subsequent revisions, final approval of the version submitted.

SLH: Article revision, intellectual input including accurate assessment of blood loss and haematological parameters, final approval of the version submitted.

CLS: Article revision, co-design of proposed approach and article tables, intellectual input including physiological adaptations and clinical assessment, final approval of the version submitted.

All authors are accountable for all aspects of the work and agree that all questions relating to the accuracy and integrity of this body of work have been investigated and resolved.

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Tables and figures

	BMI (kg m^{-2})	Estimated Blood Volume
Lean Pregnant	27 ± 2	95 ml kg^{-1} (95% CI 35-155)
Obese Pregnant	42 ± 4	73 ml kg^{-1} (95% CI 29-117)

Table 1: Blood Volume Estimates by HES dilution (adapted from Vricella et al[71])

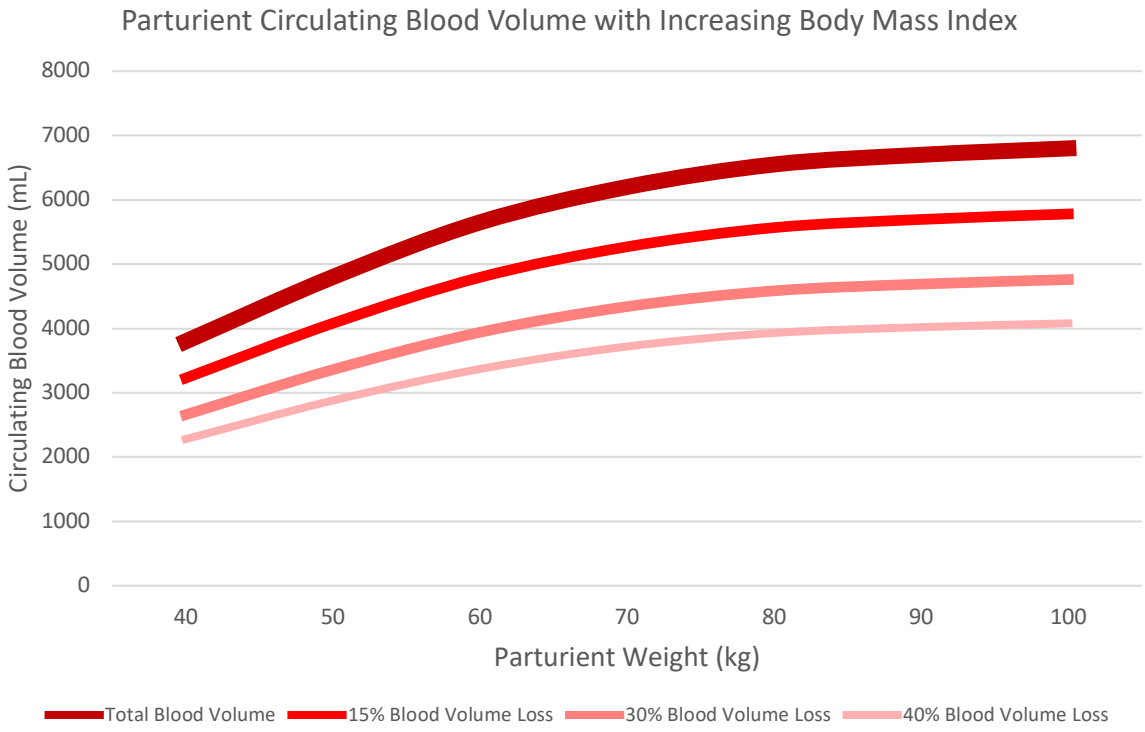

Figure 1: Circulating blood volume changes with increasing weight for 160cm parturient at term

NHS Obesity Classification	BMI Range	Blood volume
Healthy Weight	18.5 – 24.9 kg m^{-2}	95 ml kg^{-1}
Overweight	25 – 29.9 kg m^{-2}	85 ml kg^{-1}
Obese	30 – 39.9 kg m^{-2}	75 ml kg^{-1}
Severely Obese	> 40 kg m^{-2}	70 ml kg^{-1}

Table 2: Blood Volume Estimations by BMI Category

	'Healthy weight'[73]	'Overweight'[73]	'Obese'[73]	'Severely Obese'[73]
	18.5 – 24.9 kg m^{-2}	25 – 29.9 kg m^{-2}	30 – 39.9 kg m^{-2}	> 40 kg m^{-2}
	95 ml kg^{-1}	**85 ml kg^{-1}**	**75 ml kg^{-1}**	**70 ml kg^{-1}**
50 kg	**CBV = 4750 ml**	**CBV = 4250 ml**		
	15% = 710 ml	15% = 640 ml		
	30 % = 1430 ml	30 % = 1280 ml		
	40% = 1900 ml	40% = 1700 ml		
60 kg	**CBV = 5700 ml**	**CBV = 5100 ml**	**CBV = 4500 ml**	
	15% = 860 ml	15% = 770 ml	15% = 680 ml	
	30 % = 1710 ml	30 % = 1530 ml	30 % = 1350 ml	
	40% = 2280 ml	40% = 2040 ml	40% = 1800 ml	
70 kg	**CBV = 6650 ml**	**CBV = 5950 ml**	**CBV = 5250 ml**	**CBV = 4900 ml**
	15% = 1000 ml	15% = 890 ml	15% = 790 ml	15% = 740 ml
	30 % = 2000 ml	30 % = 1790 ml	30 % = 1580 ml	30 % = 1470 ml
	40% = 2660 ml	40% = 2380 ml	40% = 2100 ml	40% = 1960 ml
80 kg	**CBV = 7600 ml**	**CBV = 6800 ml**	**CBV = 6000 ml**	**CBV = 5600 ml**
	15% = 1140 ml	15% = 1020 ml	15% = 900 ml	15% = 840 ml
	30 % = 2280 ml	30 % = 2040 ml	30 % = 1800 ml	30 % = 1680 ml
	40% = 3040 ml	40% = 2720 ml	40% = 2400 ml	40% = 2240 ml
90 kg		**CBV = 7650 ml**	**CBV = 6750 ml**	**CBV = 6300 ml**
		15% = 1150 ml	15% = 1010 ml	15% = 950 ml
		30 % = 2300 ml	30 % = 2030 ml	30 % = 1890 ml
		40% = 3060 ml	40% = 2700 ml	40% = 2520 ml
100 kg			**CBV = 7500 ml**	**CBV = 7000 ml**
			15% = 1130 ml	15% = 1050 ml
			30 % = 2250 ml	30 % = 2100 ml
			40% = 3000 ml	40% = 2800 ml

Table 3: Estimated CBV by weight and BMI - with 15%, 30% and 40% blood loss volumes

Supplementary Material

To identify relevant studies, the titles and abstracts (limited to the English language) of papers in the MEDLINE, EMBASE and CINAAHL databases were searched according to the strategy detailed in Box 1, resulting in 89 potential articles. The titles and abstracts of the search results were reviewed for relevance to the topic of this review by one author (HK,) who obtained full text copies of relevant papers. Further papers were obtained by forward and backward citation searching, using the reference lists of relevant papers and Google Scholar. This process resulted in 26 papers which reported data relevant to this work.
"Maternal blood volume" OR "blood volume" OR "blood volume determination" OR "plasma volume" AND "Circulation" OR "circulating blood volume" OR "blood flow" AND "Gestation*" OR "pregnan*" OR "maternity" AND "Obese patient" OR "overweight" OR "maternal obesity" OR "body mass index" OR "BMI" OR "body mass"

Box 1. Search Strategy