







A whole blood based resuscitation strategy in civilian medical services: Experience from a Norwegian hospital in the period 2017–2020

Kristin Gjerde Hagen¹  | Geir Strandenes^{1,2}  | Einar Klæboe Kristoffersen^{1,3} | Hanne Braathen^{1,4}  | Joar Sivertsen^{1,4}  | Christopher Kalhagen Bjerkvig^{3,5} | Nina Sommerfelt-Pettersen³ | Irmelin Beathe Aasheim¹ | Turid Helen Felli Lunde¹  | Tor Hervig^{1,3,6} | Torunn Oveland Apelseth^{1,2} 

¹Department of Immunology and Transfusion Medicine, Haukeland University Hospital, Bergen, Norway

²Department of War Surgery and Emergency Medicine, Norwegian Armed Forces Medical Services, Sessvollmoen, Norway

³Institute of Clinical Science, University of Bergen, Bergen, Norway

⁴Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

⁵Department of Anesthesia and Intensive Care, Haukeland University Hospital, Bergen, Norway

⁶Laboratory of Immunology and Transfusion Medicine, Haugesund Hospital, Haugesund, Norway

Correspondence

Kristin Gjerde Hagen, Helse Bergen HF, Department of Immunology and Transfusion Medicine, Haukeland University Hospital, P.O. Box 1400, N-5021 Bergen, Norway.
Email: kristin.gjerde.hagen@helsebergen.no

Funding information

Department of Immunology and Transfusion Medicine at Haukeland University Hospital, Bergen, Norway

Abstract

Background: Civilian and military guidelines recommend early balanced transfusion to patients with life-threatening bleeding. Low titer group O whole blood was introduced as the primary blood product for resuscitation of massive hemorrhage at Haukeland University Hospital, Bergen, Norway, in December 2017. In this report, we describe the whole blood program and present results from the first years of routine use.

Study design and methods: Patients who received whole blood from December 2017 to April 2020 were included in our quality registry for massive transfusions. Post-transfusion blood samples were collected to analyze isohemagglutinin (anti-A/-B) and hemolysis markers. Administration of other blood products, transfusion reactions, and patient survival (days 1 and 30) were recorded. User experiences were surveyed for both clinical and laboratory staff.

Results: Two hundred and five patients (64% male and 36% female) received 836 units in 226 transfusion episodes. Patients received a mean of 3.7 units (range 1–35) in each transfusion episode. The main indications for transfusion were trauma (26%), gastrointestinal (22%), cardiothoracic/vascular (18%), surgical (18%), obstetric (11%), and medical (5%) bleeding. There was no difference in survival between patients with blood type O when compared with non-group O. Haptoglobin level was lower in the transfusion episodes for non-O group patients, however no clinical hemolysis was reported. No patients had conclusive transfusion-associated adverse events. Both clinical and laboratory staff preferred whole blood to component therapy for massive transfusion.

Abbreviations: CPD, citrate-phosphate-dextrose; DAT, direct anti-globulin test; HEMS, helicopter emergency medical service; LTOWB, low titer group O whole blood; MTP, massive transfusion protocol; RBC, red blood cells; TA-GvHD, transfusion-associated graft-versus-host disease.

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Discussion: The experience from Haukeland University Hospital indicates that whole blood is feasible, safe, and effective for in-hospital treatment of bleeding.

KEYWORDS

Massive transfusion, massive transfusion protocol, low titer group O whole blood, whole blood, bleeding, hemorrhage, trauma

1 | INTRODUCTION

Life-threatening hemorrhage is a challenging medical emergency that requires immediate intervention to reduce the impact of hemorrhagic shock and subsequent coagulopathy to increase survival and reduce morbidity. Major hemorrhage is common in the trauma population, but major surgery, gastrointestinal disease, and obstetric complications frequently require activation of a massive transfusion protocol (MTP).¹ Over the past decades, significant changes in the resuscitation approach for uncontrolled bleeding and hemorrhagic shock have evolved.² National and international guidelines, both civilian and military, recommend early balanced transfusion in life-threatening bleeding to restore oxygen delivery, maintain blood volume, and support hemostasis.³⁻⁷ The ability to provide platelets, plasma, and RBCs early improves survival outcomes, but is logistically challenging in prehospital settings and for smaller hospitals with limited blood inventories.⁸⁻¹¹

The optimal choice of resuscitation fluid for this patient category is still under debate, with the controversy of whether a blood component-based strategy or a whole blood-based strategy should be preferred.¹² Whole blood affords plasma, RBCs, and platelets in a balanced ratio,^{6,7,12,13} and has been implemented in a significant number of trauma centers worldwide.¹⁴⁻¹⁶ Transfusion of whole blood has certain major advantages compared with blood components. Staff handles one bag instead of three in a time-critical situation. It solves the problem of managing the timing of the different blood components in a balanced transfusion. Reduced time to issue can further facilitate early balanced transfusion.

Restoring normal physiology from the shocked state requires rapid bleeding control and transfusion. The main goal is to avoid anaerobic metabolism due to insufficient oxygen delivery, which poses a great challenge in patients with life-threatening bleeding. Maintaining sufficient oxygen delivery in patients with severe hypovolemia requires optimal oxygen carrying capacity of transfused blood products.¹⁷⁻¹⁹ Providing sufficient hemoglobin concentration by reducing hemodilution is an argument for whole blood, as the volume of additive solutions is higher in a component-based strategy than in whole blood.²⁰⁻²²

In this publication, we describe our whole blood program and report our experience from the first years of routine use of whole blood as the primary blood product for resuscitation of massive hemorrhage, aiming to provide information relevant for other hospitals considering implementation of a whole blood program.

2 | MATERIALS AND METHODS

2.1 | Study design

This report is based on data from our local quality registry for the use of whole blood for massive transfusions at Haukeland University Hospital. The registry was approved by the local data protection officer (approval number 2016/07040). The registry includes patients who received whole blood, regardless of the number of units transfused, and blood components when transfused as part of an MTP. The Norwegian health authorities approved our use of low titer group O whole blood (LTOWB) prior to implementation.

2.2 | Implementation of a whole blood program at Haukeland University Hospital

Haukeland University Hospital is a level-one trauma center and a national burn center located in the western part of Norway. The hospital has 790 beds and supports the city of Bergen, with a population of 285,000. As a level-one trauma center, the hospital covers the Western part of Norway, with a population of 1.1 million and an area of 43,500 km². A landscape of fjords, mountains, and scattered settlements, sometimes facing harsh weather conditions, can make transport of patients from the site of injury or smaller local hospitals challenging. In 2015, we implemented procedures for donor selection and production of LTOWB for massively bleeding patients transported by our helicopter emergency medical service (HEMS). Bergen HEMS operates a three-crew staff (physician, rescue paramedic, and pilot) 24/7, responding with a helicopter or a rapid response vehicle. In December 2017, we implemented LTOWB for in-hospital patients, including children, as the preferred product for

massive transfusions and for contingency plan activation. Our hospital-based blood bank provides whole blood for Haukeland University Hospital, including HEMS and Voss hospital, a local satellite hospital 1.5 h from the main hospital. In addition, we collect whole blood for Norwegian military health services.

2.3 | Collection and preparation of whole blood units

Units of whole blood are collected from regular blood donors of both sex. RhD negative and RhD positive group O donors are included in the whole blood program. Donors are prescreened for isohemagglutinin titers (anti-A and anti-B) and only low titer donors are accepted. Donors are classified as low titer if the titers of anti-A and anti-B are less than 250 (IgM) and/or 500 (IgG). Titration is performed in gel cards (ID-Card 50540 Coombs Anti-IgG and 50520 NaCl, Enzyme Test and Cold Agglutinins, Bio-Rad Laboratories, Inc., Hercules, CA, US). Titer analyses are repeated after pregnancies and transfusions, and, for female donors below 50 years, if there has been more than 2 years since last donation. According to Norwegian guidelines, screening of female donors for HLA antibodies is currently not required.

Four hundred and fifty milliliter whole blood from group O donors is collected in citrate-phosphate-dextrose (CPD) using a whole blood collection set featuring a platelet-saving leukoreduction filter (Imuflex WB-SP, BB*LGQ456E6, Terumo BCT, Lakewood, CO, US) that preserves 80%–90% of platelets.²³ Normal production time of minimum 3 h, including cooling/resting, filtration, TTD screening, and control blood typing, gives a product ready for use the same day as collection. LTOWB is stored without agitation for up to 21 days at 2–6°C. Cold stored whole blood units are not irradiated before issue.

Fresh whole blood units collected for emergency use are filtrated immediately after collection and irradiated during production to prevent transfusion-associated graft-versus-host disease (TA-GvHD).^{24,25} Warm irradiated units, which are not issued immediately, can be stored cold for 14 days.

2.4 | Inventory and issue of whole blood for MTP

Our minimum in-hospital whole blood inventory consists of eight LTOWB units (four RhD positive and four RhD negative), all stored in the hospital blood bank. In addition, Bergen HEMS and Voss Hospital each have two units of RhD negative LTOWB in their inventory. If units from HEMS are not used within 1 week, they are returned to

inventory at the hospital blood bank, and are replaced by new units.²⁶ As a result, day-to-day inventory often exceeds 8 units. Before public holidays or large public events, the inventory is increased. LTOWB is the blood product of choice in our contingency plan for mass casualty events. In case of massively bleeding patients depleting both whole blood and platelet concentrate inventory, emergency collection by the walking blood bank principle can be initiated.¹⁵

MTP is activated for patients with a suspected or an identified larger bleeding. On initiation of the MTP, 4 units of LTOWB are issued. If LTOWB is not available in stock, a component-based MTP consisting of 6 units of red blood cells (RBCs), six thawed type A or AB plasma units (Octaplasma, Octapharma, Lachen, Switzerland), and two platelet concentrates with platelet additive solution (PAS-IIIM (T-PAS+, Terumo BCT)) are issued. If issuing of plasma is delayed due to thawing, locally stored units of single-donor lyophilized plasma (LyoPlas, German Red Cross, Berlin, Germany) can be used in designated departments (ER, surgical, intensive care, and obstetrical departments).

2.5 | Whole blood transfusion and follow-up procedures

Female patients under the age of 50 with unknown RhD blood type or known to be RhD negative receive RhD negative LTOWB. All other patients will receive RhD positive LTOWB. All LTOWB units available in inventory will be used before component-based MTP are issued, but female patients under the age of 50 with unknown or RhD negative blood type will receive RhD negative components if RhD negative whole blood units are not available. Patients receiving massive transfusion with LTOWB are, regardless of their blood type, followed with blood samples to evaluate the effect of transfusion. In addition, hemolysis markers are evaluated for patients receiving incompatible plasma from whole blood. Sample tubes and a prefilled requisition form are included in the issued cooler, and blood samples are collected after each transfusion episode. The samples are analyzed for hemoglobin, platelet count, haptoglobin, lactate dehydrogenase, total bilirubin, direct anti-globulin test (DAT), and analysis of passively transferred (unexpected) anti-A/-B according to patient ABO blood type. Thromboelastographic analysis of bleeding patients is available at the blood bank laboratory to guide transfusion therapy. If the patient needs subsequent transfusion of RBCs after receiving LTOWB, non-group O recipients are transfused with group O RBCs until unexpected anti-A/-B are no longer detected. If any level of anti-A/-B is detected, new samples are collected the following day. If DAT is positive, extended DAT testing is performed

(IgG/IgA/IgM, C3c/C3d). Eluate analyses are not routinely performed.

2.6 | User survey

Nurses and physicians working in surgical and anesthesiology departments and blood bank laboratory staff were surveyed to evaluate implementation and user experience. Survey questions are reported in Table S1.

2.7 | Data collection for the quality registry

Data entry for the local quality registry was performed manually at regular intervals during the study period. Clinical information was retrieved by manual review of hospital electronic medical records. We recorded indication for transfusion, information on survival, and results of biochemical hemolysis parameters (bilirubin and haptoglobin), hemoglobin levels, and platelet count. DAT, anti-A/-B, age, sex, ABO/RhD type of patient and blood units, time of first LTOWB issue, and blood component use in the 24-h period following the first whole blood issue (defined as a transfusion episode) were collected from the blood bank IT system. Additionally, we noted the age of each LTOWB unit at the time of transfusion.

2.8 | Statistical analyses

Statistical analyses were performed using R version 4.0.4 (The R Foundation for Statistical Computing). The results are presented as mean (95% confidence intervals, minimum–maximum), median (interquartile range, minimum–maximum), or count (percentage). The difference in number of products transfused and survival was compared using the Mann–Whitney U test or Fisher's exact test as appropriate. For calculations of plasma to RBCs ratio, the following volumes of plasma were used: LTOWB (270 ml), RBC unit (35 ml), platelet concentrates (100 ml), and frozen and lyophilized plasma (200 ml). When calculating the ratio of platelets to RBCs, the number of platelet concentrates was multiplied by five, as platelet concentrates are equivalent to five whole blood donations.

3 | RESULTS

A total of 205 patients received LTOWB in the period from December 11, 2017, to April 17, 2020 and were included in this report. These patients used 836 units of LTOWB in

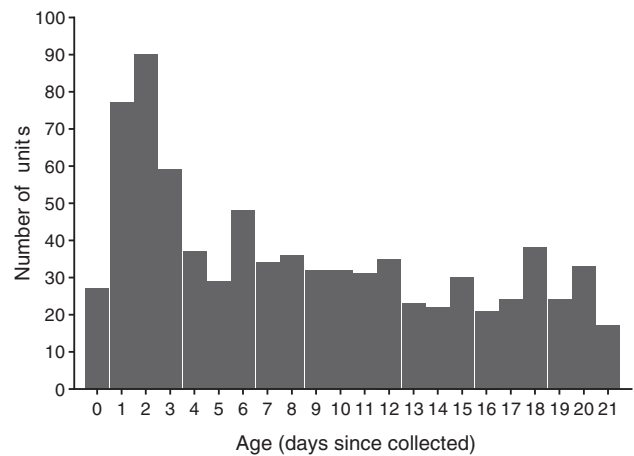


FIGURE 1 Age distribution of low titer group O whole blood units at the time of transfusion. Units with an age of 0 days were issued on the same days as collection. Some of these were issued as warm, fresh, and irradiated units, and some with ongoing (but not completed) TTD screening, due to emergency need for transfusion

226 transfusion episodes. The wastage rate of 30% included units outdated on shelf at day 21 of storage, units issued to clinical wards but not transfused, and units withdrawn due to production failure or donor-related causes. By April 17, 2020, 5077 group O donors have been titrated, of these 3979 (78%) are low titer donors.

The mean age of patients receiving LTOWB was 55 years (52–58, 1–92). Of the patients included, 131 (64%) were male and 74 (36%) were female. The age of the LTOWB units at the time of transfusion is presented in Figure 1.

The prescribing department for the first LTOWB unit was the emergency department for 87 (38%) of the transfusion episodes, and the obstetrical/gynecological, cardiothoracic/vascular, medical, and surgical departments were the first prescribing department for 27 (12%), 27 (12%), 31 (14%), and 25 (11%) of the episodes, respectively. The HEMS was the first prescribing department for 29 (13%) of the episodes, and nine (4% of total episodes) received only prehospital LTOWB.

An overview of blood product use, plasma-to-RBC ratio, platelet-to-RBC ratio, number of incompatible plasma products, and volume of incompatible plasma is presented in Table 1. The patients received a mean of 3.7 units of LTOWB (3.2–4.2, 1–35) per transfusion episode, and 77% of the transfusion episodes involved four or fewer units. The highest number of LTOWB given to one patient in a single episode was 35 as part of a contingency plan activation. The highest total number of LTOWB transfused to a single patient was 101 units, given throughout 17 transfusion episodes. Thirty-four percent of the patients received only LTOWB, while the

TABLE 1 Comparisons between non-group O and group O patients

	Non-group O (n = 123)	Group O (n = 103)	p
Blood products transfused per episode			
LTOWB	3 (1–4, 1–35)	3 (2–4, 1–16)	.277
Red blood cells	1 (0–3, 0–68)	0 (0–2, 0–42)	.015
Frozen plasma	0 (0–4, 0–71)	0 (0–3, 0–36)	.678
Platelet concentrates	0 (0–1, 0–18)	0 (0–1, 0–14)	.773
Lyophilized plasma	0 (0–0, 0–3)	0 (0–0, 0–3)	.621
Blood product ratios per episode			
Plasma:RBC ^a	1.35 (1.22–1.82, 0.41–4.35)	1.35 (1.35–1.78, 0.57–6.35)	.412
PLT:RBC ^b	1.00 (0.75–1.15, 0.20–6.00)	1.00 (1.00–1.25, 0.13–16.00)	.489
Incompatible plasma per episode			
Products	4 (3–10, 0–27)		
Volume	880 (340–1420, 0–3410)		
Markers of hemolysis per episode			
Haptoglobin ^c	0.6 (0.3–0.9, 0.1–2.4)	1.1 (0.6–1.4, 0.1–3.8)	<.001
Bilirubin ^d	18.0 (12.0–26.5, 3.0–102.0)	17.0 (10.0–26.5, 4.0–436.0)	.421
Positive DAT	29/77 (38%)	1/42 (2%)	<.001
Transfusion indication per patient ^e			
Trauma blunt	27 (23%)	15 (17%)	.386
Trauma penetrating	6 (5%)	4 (5%)	1.000
Cardiovascular surgery	24 (20%)	13 (15%)	.462
Surgery (other)	19 (16%)	18 (21%)	.365
Gastrointestinal bleeding	20 (17%)	24 (28%)	.060
Medical bleeding (other)	5 (4%)	5 (6%)	.745
Obstetric/gynecological bleeding	16 (13%)	6 (7%)	.173
Unknown	2 (2%)	1 (1%)	1.000
Age of whole blood units	9 (4–15, 0–21)	6 (2–12, 0–21)	<.001

Note: Results are shown as median (interquartile range, min–max) or counts (percentage) per transfusion episode. Indications for patients in counts (percentage). Groups were compared using the Mann–Whitney U test or Fisher's exact test, as appropriate (R version 4.0.4, The R Foundation for Statistical Computing).

^aIncludes the plasma contribution from frozen and lyophilized plasma (200 ml), whole blood (270 ml), platelet concentrates (100 ml), and red blood cell units (35 ml).

^bIncludes platelets in whole blood and platelet concentrates converted to whole blood-equivalent by multiplying by the number of donors pooled (5).

^c(Haptoglobin in g/L, normal reference level < 50 years 0.4–1.9 g/L, >50 years 0.5–2.1 g/L). n = 71 (Non-Group O), n = 51 (Group O) Haptoglobin <0.1 g/L are registered as 0.1, for 6 cases.

^d(Bilirubin, total in $\mu\text{mol/L}$, normal reference level < 20 $\mu\text{mol/L}$). n = 87 (Non-Group O), n = 74 (Group O).

^eIndication information reported per patient (not per transfusion episode); n = 119 (Non-Group O), n = 86 (Group O).

remaining 66% received additional blood component therapy (see Table S2).

Indications for whole blood transfusion are presented in Figure 2A. Of the 52 transfusions given to patients with trauma, 10 cases were due to penetrating trauma. All of these were in male patients. Five patients under the age of 18 received whole blood, all due to trauma. The relation between indication for transfusion and the number of LTOWB units given per transfusion episode is shown in Figure 2B. The

difference between indications for transfusion in female and male patients and the relation to the age of the patients are presented in Figure 2C,D. The distribution of the indications for transfusion for the patients with ABO type O and patients with ABO type A, B, or AB (non-group O) are shown in Table 1.

Passively transferred anti-A and/or anti-B were detected in 15 of 74 (20%) patients in the non-group O group, and a significantly higher proportion of these had been transfused with >4 units of whole blood (see Table S3). The results of

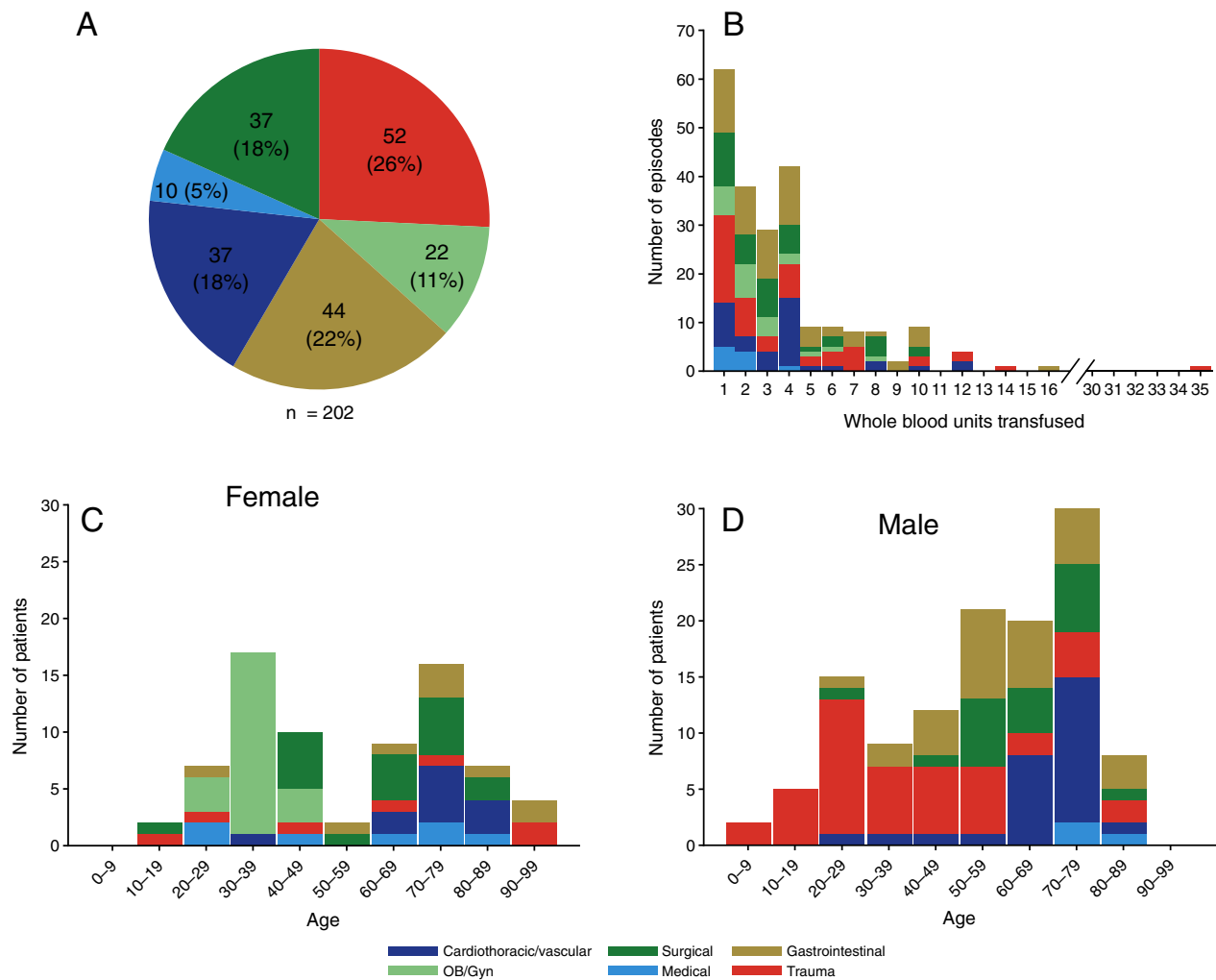


FIGURE 2 (A) Whole blood use by clinical indication, N = 202; N = 3 transfusion episodes with unknown indication (death before arrival at hospital) are not included in the pie chart. (B) the relation between indication for transfusion and the number of LTOWB units given. (C) Age distribution and number of whole blood units transfused for female, and (D) male patients. Colors indicate the transfusion indication

hemolysis markers are shown in Table 1. Positive DAT was observed in 29 of 77 (38%) transfusion episodes in the non-group O patients and in 1 of 42 (2%) group O patients. Eleven of 30 (37%) transfusion episodes with positive DAT had haptoglobin below normal levels. Significant lower haptoglobin values were observed in transfusion episodes for the non-O group patients when compared with the group O patients. Results above lower reference values for haptoglobin were observed in 40 of 71 (56%) non-group O and 40 of 51 (78%) group O transfusion episodes. No difference was observed in bilirubin levels between transfusion episodes in the two groups.

There were no reported cases of transfusion-associated clinical hemolysis. Among the patients receiving whole blood, one patient had a report of an acute transfusion-related adverse event, with symptoms of

chills and body temperature of 38.5°C during the transfusion of LTOWB. The laboratory and clinical evaluation concluded that concurrent infection could explain the symptoms. Three patients (1.4%) developed an alloantibody (one patient with anti-D and two patients with unidentified antibodies) following the transfusion episodes. These patients also received RBC concentrates and/or platelet concentrates.

Survival rates are presented in Table 2. No significant differences in survival rates were observed between non-group O patients receiving incompatible plasma and group O patients receiving compatible plasma. A significant difference was seen in the group with <24 h survival for patients who received 1–4 compared with >4 units of whole blood (see Table S4). Table S5 describes indications and blood groups for the patients with <24 survival.

TABLE 2 Survival rates

Survival status	All patients (n = 199) ^a	Group O (n = 82)	Non-group O (n = 117)	p
>30 days	147 (74%)	64 (78%)	83 (71%)	.531
1–30 days	21 (11%)	8 (10%)	13 (11%)	.817
≤24 h	31 (16%)	10 (12%)	21 (18%)	.323

Note: There were no significant differences in survival based on blood group or transfusion of other blood products. (Fisher's exact test, R version 4.0.4, The R Foundation for Statistical Computing).

^aAn additional six patients were transferred to hospitals outside of Norway in stable conditions. Survival status for these patients is unknown.

The survey of end-user experience was performed in June 2020. Twenty-one of 24 (88%) blood bank laboratory staff and 65 of 206 (32%) clinical staff (nurses and physicians) replied to the survey. Both clinical and laboratory staff preferred whole blood to component therapy for massive transfusion. See Table S1 for complete survey questions and results.

4 | DISCUSSION

Whole blood is an easily accessible contingency blood product, and production is possible within a short timeframe compared with more time-consuming production of blood components, especially production of platelet concentrates.^{15,27,28} As shown in our end-user survey, whole blood has logistical and practical advantages for the blood bank and clinical staff. In the prehospital setting, whole blood is the easiest way to ensure balanced transfusion therapy.²⁶ Similarly, LTOWB can serve as the only platelet-containing product in smaller hospitals where platelets are not readily available.²⁷ In the larger hospitals, where all blood components are available, the role for whole blood might be less obvious. However, a significant number of trauma centers worldwide have implemented LTOWB for massive transfusion.²⁹

The planning of a whole blood inventory may be challenging as the demand for LTOWB varies. We experienced some weeks with high demand and need for daily restock, including emergency collections of up to 30 units of whole blood for patients with acute bleeding. Other weeks' demand was low, and LTOWB became outdated. As seen in Figure 1, whole blood units were used throughout the storage timeframe of 21 days. Our minimum inventory of eight units of LTOWB was based on previous use of component-based MTP activations. The principle of rotating units back to the hospital from HEMS reduces the risk of outdates. In other institutions, RBCs are produced from outdated whole blood units to reduce wastage. Experiments on production of RBC from whole blood stored for 7 days have been performed with success in our Department.³⁰ However, production of RBC from stored whole blood is a manual procedure and as we have automated

the production of RBC, this has not been implemented in our institution on a routine basis.

Routines for emergency collection and massive transfusion should be trained and audited regularly. For both clinical and blood bank laboratory staff, training and education sessions were given before and during implementation of LTOWB, in addition to later education sessions to maintain knowledge, to train new personnel, and to audit the operating procedures for emergency collections. We have activated our system for emergency collection of LTOWB on a few occasions during this period, for patients with acute and massive bleeding, including a previously reported trauma patient.¹⁵ The use of LTOWB in these situations was of great benefit to ensure a balanced transfusion. We find that LTOWB is an ideal contingency product, as it can be available in a short timeframe in case of a depleted inventory of platelet concentrates.

Male patients dominate the population of patients receiving whole blood. This is seen particularly for trauma, gastrointestinal bleeding, and cardiovascular surgery. In a previous retrospective review of all massive transfusion episodes given in Haukeland University Hospital in the period 2002–2015, the same male predominance was observed.¹ For this period, 87.1% of all massive transfusion episodes were in support of surgery, with 42.7% for cardiac services. Whereas the retrospective review defined a massive transfusion episode as transfusion of 10 RBCs per 24 h, our present report includes all patients issued whole blood regardless of number of units given. The difference between these two studies can be explained by different inclusion criteria, but also by a change in the transfusion strategy for bleeding patients in our hospital over time.

Four transfusion-associated adverse events were recorded throughout the period. This included three cases of alloimmunization detected in blood samples taken 1–2 weeks after transfusion, and one event with increased body temperature and chills, which was not considered transfusion-related. In patients with massive hemorrhage, symptoms of the condition and underlying disease may be similar to symptoms of a transfusion

reaction and therefore make it difficult to recognize a transfusion reaction. This may result in underreporting of transfusion-related adverse events in this patient population. The rate of anti-D alloimmunization varies between different patient populations, with higher rates in the trauma patient population.³¹ However, several institutions provide only RhD positive LTOWB also for female patients,²⁹ and the question has been raised whether it is time to consider using RhD positive RBCs to all patients in bleeding emergencies, including women of childbearing age.³²

Survival in patients who received 1–4 and >4 units of whole blood can be related to severity of the condition of a patient who receives a larger massive transfusion during a shorter timeframe. No difference in survival was seen in the patients who survived >24 h related to the number of whole blood units received.

As our results show, both group O and non-group O patients had evidence of changes in the biological markers of hemolysis. Haptoglobin is a highly sensitive marker due to rapid consumption in the case of minor hemolysis, in addition to the influence of other factors like the use of cardiopulmonary bypass device and transfusion of older blood.^{33–35} Our results may indicate that some hemolysis takes place due to the transfusion of incompatible plasma, but median values for both groups were within normal reference level and patients from both groups had low haptoglobin levels. Detection of anti-A/anti-B in 20% of patients relates to passively transferred anti-A and anti-B in the total volume of incompatible plasma given, including plasma from platelet concentrates of blood type O, where one-third of the volume is plasma. We received no reports on clinical symptoms of hemolytic transfusion adverse events, and no difference was seen in survival between group O and non-group O patients or in bilirubin levels. The differences between the groups are therefore not considered to be of clinical significance. However, further studies should be performed to explore these findings.

Our data are limited by the fact that we received follow-up samples from only 60% of the non-group O transfusion episodes, in addition to variation in the timing of the samples in relation to the transfusion of whole blood. Early in the study period, the percentage of completed follow-up tests was low. Tests had to be ordered manually by the clinical staff and were often postponed or forgotten because of the acute tasks at hand. The blood bank would not be able to identify missing samples before a new order of blood products were received. Hence, on some occasions, follow-up samples were taken several days after whole blood transfusion. During the study period, routines were adjusted and the blood bank took responsibility to obtain samples. This

increased the number of patients with follow-up samples after LTOWB use.

In this quality assurance study, we have reported our experience based on our quality registry for massive transfusion. We conclude that whole blood is an easy-access, safe, and balanced resuscitation blood product for patients with massive hemorrhage of different etiologies. We encourage further clinical studies evaluating the effects and safety of whole blood transfusion.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest. The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Norwegian Armed Forces Medical Services.

ORCID

Kristin Gjerde Hagen  <https://orcid.org/0000-0003-1679-6413>

Geir Strandenes  <https://orcid.org/0000-0002-3168-3786>

Hanne Braathen  <https://orcid.org/0000-0002-4750-0681>

Joar Sivertsen  <https://orcid.org/0000-0001-5501-5486>

Turid Helen Felli Lunde  <https://orcid.org/0000-0001-6798-1630>

Torunn Oveland Apelseth  <https://orcid.org/0000-0001-8823-2719>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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