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Low-titer group O whole blood transfusion in high-intensity war: an insight from Ukraine

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Dear Editors,

The renewed adoption of low-titer O whole blood (LTOWB) represents one of the most significant doctrinal shifts in Damage Control Resuscitation in both military medicine and civil critical care [1]. The war in Ukraine is high-intensity with the application of all kinds of weapons, resulting in acute trauma and frequent severe hemorrhage in combat patients [2]. Experience from recent U.S. combat operations and from Ukraine has demonstrated that forward deployment of whole blood is operationally feasible and clinically effective when supported by structured donor screening and standardized transfusion protocols. The ABO-type specific FWB should be transfused for patients with confirmed blood type. However, the translation of LTOWB doctrine from well-resourced NATO systems to a resource-limited, high-intensity warfare environment like Ukraine reveals a critical technological vulnerability: the absence of standardized, rapid isohemagglutinin screening.

The safety of LTOWB depends on verified low titers of anti-A and anti-B isohemagglutinins. Epidemiological data indicate that a substantial proportion of group O donors possess antibody titers exceeding commonly accepted low-titer thresholds, and donor demographic factors correlate with isohemagglutinin levels. Chatterjee et al. analyzed the prevalence of the IgM and IgG as well as reported the prevalence of group O donors up to 9% [3]. In contrast, Kryvda et al. showed 32.7% group O donors in civil population of Ukraine, which should also

reflect the similar proportion in military personnel [4]. Still, the exact data about the distinct proportion of the blood grouping in military personnel of Armed Forces of Ukraine is not available. Also, there are no studies addressing the analyses of the isohemagglutinin titers in Ukraine, which constitutes a scientific gap and justifies the need for further research in this area. Without systematic titration, a significant fraction of units labeled “universal” may carry hemolytic potential. Furthermore, titration methodology itself lacks standardization. It is worth mentioning, that the hemostatic potential of cold-stored whole blood is time-dependent, with critical parameters significantly diminishing beyond 14 days of storage at 4 °C (± 2 °C), which was also performed for our patients [5]. Comparative laboratory analyses demonstrate significant variability in measured ABO isoagglutinin titers across testing platforms, including tube hemagglutination, gel column agglutination, and automated erythrocyte-magnetized systems [6]. Automation and validation mitigate the abovementioned variability in well-resourced military medicine systems. In disrupted wartime environments such as in Ukraine, these safeguards are frequently absent.

The operational context of the Russia-Ukraine war illustrates the aforementioned gap in the military medical facilities in Ukraine. Role 2–3 medical facilities are frequently functioning under prolonged field care conditions, intermittent supply chains, and limited laboratory capacity. Confirmatory isohemagglutinin titration is not

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consistently available, particularly during mass casualty events. As suggested by clinical experience by Ukrainian critical care at Role 1 and 2 facilities in the battlefield area, blood type O WB may be administered without definitive verification of low titers. When multiple units are transfused to non-O recipients, cumulative exposure increases the probability of clinically significant hemolysis. Observations from wartime practice in Ukraine have included cases of mixed-field agglutination and transient dual red cell populations following massive transfusion of unverified O WB, complicating subsequent blood typing and associated with laboratory patterns consistent with hemolysis and secondary organ dysfunction. During the 2024–2026, we have identified approximately 30 patients with mixed-field agglutination specifically associated with the massive transfusion of untitrated “universal” group O whole blood (unpublished data). In these cases, the severity of hemolysis varied. However, it consistently complicated subsequent bedside blood typing, requiring the clinical team to maintain the patient on group O products for the remainder of the acute phase to prevent potential incompatible reactions with type-specific blood.

In our system, the prioritization of warm ABO-type specific FWB over cold-stored LTOWB represents a strategic adaptation to wartime constraints, which is in contrast to the Tactical Combat Casualty Care (TCCC) guidelines [7]. While TCCC prioritizes a pre-screened, ‘universal’ product (i.e. LTOWB) to minimize hemolytic risk, the Ukrainian experience highlights a shift toward warm FWB. This necessity arises from the logistical challenges of maintaining a cold chain and the lack of widespread titration facilities, prioritizing immediate hemostatic efficacy and availability over the standard LTOWB-first protocol used in other systems.

While retrospective observation cannot establish causality, the temporal association highlights an immunohematologic vulnerability inherent to unscreened universal transfusion.

An additional operational consideration is the biological degradation of stored LTOWB. Prolonged storage is associated with progressive structural and functional damage to erythrocytes, including membrane alterations and hemolysis-related changes that may affect oxygen delivery. Platelet function and coagulation factor activity also decline during storage, reducing the hemostatic potential of LTOWB over time. Experimental and field data suggest that the coagulation competence of stored LTOWB may be reliably preserved for approximately 14 days under austere conditions, after which functional deterioration becomes more pronounced. These findings indicate that shorter storage intervals (approximately 14–15 days) may represent a more biologically optimal

window for operational use of stored LTOWB in high-intensity conflict environments.

These concerns do not negate the life-saving value of an early LTOWB use. Systematic review data suggest early survival benefit compared with component therapy in acute hemorrhage, and forward military experience confirms its operational advantages in austere environments. However, in resource-limited high-intensity conflict in Ukraine, LTOWB is a very good option for prehospital transfusion (tactical bridge) rather than a definitive resuscitative solution.

In such environments, fresh warm ABO-type specific FWB collected from walking blood banks may represent an additional pragmatic solution. A LTOWB can provide optimal hemostatic function in austere settings, although the availability of suitable low-titer donors may be limited in operational donor pools. While LTOWB is the preference, the reality in Role 2 facilities often necessitates the use of ABO-type specific FWB as a pragmatic life-saving measure. It is a widespread necessity rather than a rare preference. When the cold chain is compromised or stored supplies are exhausted, warm ABO-type specific FWB becomes the primary transfusion resource. Only medical personnel are trained specifically in the collection process and the use of simplified, pre-assembled “walking blood bank” kits were crucial in reducing the time and personnel required for collection during mass casualty events. For patients with severe hemorrhagic shock, when rapid blood group determination is feasible, group-specific warm whole-blood transfusion may also be an effective alternative in resource-constrained environments. An EldonCard bedside kits are applied for rapid ABO and Rh(D) forward typing of both the donor and the recipient, but not the ID discs or documented records etc. to avoid mismatches. EldonCard bedside kits allow our teams to confirm blood group compatibility within minutes directly at the point of care. At Role 2 settings, when time and resources permit, this is supplemented by a simplified bedside cross-match to further ensure transfusion safety before administering group-specific warm FWB.

We therefore propose a two-level adaptation strategy:

1. Strategic level: implementation of standardized, high-throughput isohemagglutinin screening at regional donor centers (Role 3–4 hospitals) to pre-identify and label low-titer units before distribution.
2. Operational level (Role 1–2): deployment of reproducible, rapid titration methods to guide timely transition from universal O FWB to group-specific transfusion once stabilization is achieved.

An echelon-specific model for the organization of blood transfusion is considered optimal. The O FWB dominates

the tactical prehospital phase and is followed by a mandatory transition to group-specific products at the hospital level may represent a safer doctrinal adaptation in prolonged, resource-constrained warfare. The Ukrainian experience underscores a broader lesson for modern military medicine: the success of whole-blood doctrine depends not only on clinical efficacy but also on technological infrastructure. An immunological response after the transfusion of WB might happen at later stage of patients' management at Role 3 and higher, which is required additional investigation and appropriate reflection in treatment protocols [8]. While the implementation of "walking blood banks" (WBB) is a well-established practice in many military systems, it was not explicitly categorized as a separate pillar in Ukrainian two-level strategy for specific reasons. In the Ukrainian context, the immediate priority was the formalization of warm FWB transfusion within existing medical units under extreme logistical constraints. Furthermore, a truly "safe and effective" WBB requires pre-screening for high-titer antibodies to identify LTOWB donors - a capability that, as previously noted, remains limited in frontline conditions. Instead of a formal WBB system, our approach focused on point-of-care collection from available personnel, which we consider a pragmatic adaptation of the WBB concept necessitated by high-intensity conflict where pre-screened donor pools are difficult to maintain. In our clinical practice (unpublished data), we observed approximately 30 documented cases of hemolysis, several patients developed acute kidney failure requiring medical intervention. While it is often difficult to fully isolate the contribution of hemolysis from the multi-factorial impact of profound hemorrhagic shock and crush syndrome in combat trauma, the temporal association with un-titrated O whole blood transfusion was evident.

To better characterize these challenges, a prospective study is being planned to compare different transfusion strategies used in austere combat environments and to evaluate their clinical effectiveness. Particular attention will be given to the potential role of viscoelastic testing (VET) (e.g. rotational thromboelastometry) at Role 2 deployed field hospitals to support real-time assessment of coagulation status. It is worth mentioning that there are many Role 2 facilities are located in close proximity to small and large cities, which allows to maintain the provision of blood components alongside the whole blood. In these facilities, VET is not redundant, but essential. It allows clinical teams to perform goal-directed therapy, specifically identifying whether a patient requires further whole blood, or if targeted intervention with fresh frozen plasma, cryoprecipitate, or platelet concentrates is more appropriate. Such a hybrid approach of combining the immediate availability of whole blood with the precision of component therapy guided by VET is a key feature of

our current adoption strategy for Role 2 hospitals with established logistical links to regional blood centers.

Using available field resources, we aim to integrate clinical outcomes with physiological markers of shock and resuscitation adequacy, including lactate levels, base deficit, and other indicators of metabolic compensation.

Abbreviations

FWB	Fresh whole blood
LTOWB	Low-titer O FWB
VET	Viscoelastic testing
WBB	Walking blood banks

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Author contributions

I Mikheiev, R Kuziv and S Machuisky suggested the hypothesis, designed the study, performed literature search, I Mikheiev drafted a first version of the manuscript, I Lurin and A Dinets - critical revision and supervision, final approval, and submission of the manuscript.

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Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Committee at the Zaporizhzhia State Medical and Pharmaceutical University (Zaporizhzhia, Ukraine). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent for publication

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Competing interests

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