



## Characteristics of Nontrauma Patients Receiving Prehospital Blood Transfusion with the Same Triggers as Trauma Patients: A Retrospective Observational Cohort Study

Susanne Ångerman, Hetti Kirves & Jouni Nurmi

To cite this article: Susanne Ångerman, Hetti Kirves & Jouni Nurmi (2021): Characteristics of Nontrauma Patients Receiving Prehospital Blood Transfusion with the Same Triggers as Trauma Patients: A Retrospective Observational Cohort Study, Prehospital Emergency Care, DOI: [10.1080/10903127.2021.1873472](https://doi.org/10.1080/10903127.2021.1873472)

To link to this article: <https://doi.org/10.1080/10903127.2021.1873472>



© 2021 The Author(s). Published with license by Taylor & Francis Group, LLC



Published online: 24 Feb 2021.



Submit your article to this journal [↗](#)



Article views: 601



View related articles [↗](#)



View Crossmark data [↗](#)

# CHARACTERISTICS OF NONTRAUMA PATIENTS RECEIVING PREHOSPITAL BLOOD TRANSFUSION WITH THE SAME TRIGGERS AS TRAUMA PATIENTS: A RETROSPECTIVE OBSERVATIONAL COHORT STUDY

Susanne Ångerman, MD, Hetti Kirves, MD, PhD, Jouni Nurmi, MD, PhD

## ABSTRACT

**Objective:** While prehospital blood transfusion (PHBT) for trauma patients has been established in many services, the literature on PHBT use for nontrauma patients is limited. We aimed to describe and compare nontrauma and trauma patients receiving PHBT who had similar hemodynamic triggers. **Methods:** We analyzed 3.5 years of registry data from a single prehospital critical care unit. The PHBT protocol included two packed red blood cell units and was later completed with two freeze-dried plasma units. The transfusion triggers were a strong clinical suspicion of massive hemorrhage and systolic blood pressure below 90 mmHg or absent radial pulse. **Results:** Thirty-six nontrauma patients and 96 trauma patients received PHBT. The nontrauma group had elderly patients (median 65 [interquartile range, IQR, 56–73] vs 37 [IQR 25–57] years,  $p < 0.0001$ ) and included patients with gastrointestinal bleeding ( $n = 15$ ; 42%), vascular

catastrophes ( $n = 9$ ; 25%), postoperative bleeding ( $n = 6$ ; 17%), obstetrical bleeding ( $n = 4$ ; 11%) and other ( $n = 2$ ; 6%). Cardiac arrest occurred in nine (25%) nontrauma and in 15 (16%) trauma patients. Of these, 5 (56%) and 10 (67%) survived to hospital admission and 3 (33%) and 2 (13%) to hospital discharge. On admission, the nontrauma patients had lower hemoglobin (median 95 [84–119] vs 124 [108–133],  $p < 0.0001$ ), higher pH (median 7.40 [7.27–7.44] vs 7.30 [7.19–7.36],  $p = 0.0015$ ) and lower plasma thromboplastin time (median 55 [45–81] vs 72 [58–86],  $p = 0.0261$ ) than the trauma patients. **Conclusions:** We identified four nontrauma patient groups in need of PHBT, and the patients appeared to be seriously ill. Efficacy of prehospital transfusion in nontrauma patients should be evaluated further in becoming studies. **Key words:** blood transfusion; helicopter emergency medical services; nontrauma; prehospital; freeze-dried plasma; packed red blood cells

PREHOSPITAL EMERGENCY CARE 2021;00:000–000

Received September 21, 2020 from Emergency Medicine and Services, Helsinki University Hospital, Vantaa, Finland (SÅ, HK, JN); Department of Emergency Medicine, University of Helsinki, Helsinki, Finland (SÅ, JN); Hyvinkää Hospital Area, Hospital District of Helsinki and Uusimaa, Prehospital Emergency Care, Finland (HK); FinnHEMS Research and Development Unit, Vantaa, Finland (JN). Revision received November 12, 2020; accepted for publication December 30, 2020.

The authors declare that they have no conflict of interest and that there is no relationship between any of the authors and any commercial entity or product mentioned in this manuscript. No inducements have been made by any commercial entity to submit the manuscript for publication.

No competing interests declared. This work was funded by Helsinki University Hospital (state funding, VTR TYH2017220) and by FinnHEMS Research and Development Unit.

Address correspondence to Susanne Ångerman, MD FinnHEMS 10 Vesikuja 9, FI-01530 Vantaa, Finland. E-mail: [susanne.angerman-haasmaa@hus.fi](mailto:susanne.angerman-haasmaa@hus.fi)

© 2021 The Author(s). Published with license by Taylor & Francis Group, LLC

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

doi:10.1080/10903127.2021.1873472

## INTRODUCTION

The current literature about treatment strategies for massive hemorrhage focuses mostly on trauma (1). Improved survival, decreased need for blood products and fewer inflammatory reactions are achievements related to balanced massive transfusion protocols (2). Acute traumatic coagulopathy is an acknowledged threat to trauma patients, emphasizing early transfusion therapy as part of hemostatic resuscitation (3).

Balanced prehospital blood transfusion (PHBT) including both red blood cells and plasma possibly improves outcomes for trauma patients suffering from severe hemorrhage (4, 5). Thus, it is established practice in treating trauma patients, even though the quality of evidence is not strong (4). The therapy aims to bridge the gap between the accident scene and the hospitals providing surgical interventions. Adverse events have been reported in only 1% of prehospital transfusion cases (4). At present, prehospital transfusion therapy is a complex entity of different blood products and their combinations – including packed red blood cells (pRBCs), plasma (fresh-frozen or freeze-dried) and whole blood used in a variety of prehospital systems (5, 6).

Current PHBT protocols are adopted from in-hospital trauma resuscitation procedures and designed

for treating trauma patients with major hemorrhage. However, prehospital transfusion is also used to treat nontrauma patients (7, 8). The heterogeneous nontrauma population depends on the case-mix of the prehospital units providing PHBT (9). For example, patients suffering from gastrointestinal or obstetric hemorrhage may benefit from early transfusion (10, 11). The literature on the use of blood products for nontraumatic patients in the prehospital setting is limited (12, 13).

The efficacy of using prehospital trauma transfusion protocols to treat nontrauma patients is not well-established. Thus, we aimed to describe and compare the characteristics of nontrauma and trauma patients and their response to PHBT triggered by the same physiological measurements originally intended for predicting the need for a massive transfusion in trauma patients.

## METHODS

The study protocol was approved by the management of Helsinki University Hospital (HUS/278/2018). According to Finnish legislation, additional approval by an ethical committee was not needed, as only registry data were used and the study had no effect on patient's treatment. The change in clinical practice was based on the implementation of the prehospital transfusion protocol regardless of the data collection process. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were followed in the reporting of this study (14).

We performed a retrospective cohort study based on the quality registry of patients who received prehospital transfusion in one HEMS unit. We analyzed the data descriptively and compared the characteristics, prehospital treatment and the early emergency department data of nontrauma patients with those of trauma patients.

The HEMS unit used in this study serves a population of 1.3 million in Southern Finland, covering an area of 10,000 square km. The intensive care of the most critical patients is centralized and provided at the university hospital clinics in the capital area, where a HEMS unit transports and escorts patients. The unit is staffed by a crew of three members: a physician, a HEMS crew member and a pilot. The physicians are mainly consultant anesthesiologists working full time in the prehospital system. During the study period, 16 different physicians were employed in the service, including four fellows in anesthesia and intensive care medicine. The HEMS crew members are firefighters and prehospital nurses trained in aviation and prehospital critical care. Their

medical licensure varies and corresponds the EMT or paramedic level. The unit utilizes special equipment for point-of-care laboratory tests, continuous invasive blood pressure measurement and portable ultrasound scans. A HEMS unit is dispatched based on predefined criteria by emergency dispatchers. The most common dispatching categories are major trauma, cardiac arrest and unconsciousness. The unit does not have a role in interfacility transfers. Ambulance crews can also request the HEMS unit to join their mission – for instance, when they recognize a possible need for PHBT based on their clinical judgment. The EMS personnel has been informed about the PHBT criteria of the HEMS unit but no mandatory protocol for activation exists. The HEMS unit meets approximately 1,100 patients and provides PHBT in 35 cases annually.

Triggers for PHBT in the unit were designed to meet the massive transfusion protocol criteria of a level I trauma center. The main triggers and the supporting factors for PHBT are (a) a strong suspicion of major bleeding according to the mechanisms of injury and the clinical status and (b) systolic blood pressure under 90 mmHg or absent radial pulse. Supporting factors include a heart rate over 120 beats per minute, peritoneal or pleural fluid in ultrasonography examination, high-energy pelvic injury and penetrating injury. According to the protocol in the unit, PHBT can also be given to nontrauma patients – for example, patients suffering from a ruptured aortic aneurysm, major bleeding of obstetric reasons or bleeding from the gastrointestinal tract with same triggers.

The prehospital transfusion process was planned and executed together with Helsinki University Laboratory Blood Bank. The HEMS unit started to carry aboard two O RhD negative units of red blood cells in March 2016. In January 2017, the PHBT protocol was complemented with two units of freeze-dried plasma (Lyoplas<sup>®</sup> N/P-w AB, Deutsches Rotes Kreuz, Germany). The product was planned to be part of the protocol already in the planning phase. Consequently, it was implemented immediately after it became commercially available in Finland. Tranexamic acid (1 g intravenously) was already used for bleeding patients before the implementation of prehospital transfusion therapy, and it was included in the PHBT protocol. Calcium gluconate corresponding to Ca<sup>2+</sup> 90 mg was added to the protocol together with the implementation of freeze-dried plasma to reduce possible hypocalcemia caused by the citrate load after rapid blood product transfusion.

The pRBCs are stored in temperature-controlled portable medical transport bags (Credo S4 2 48

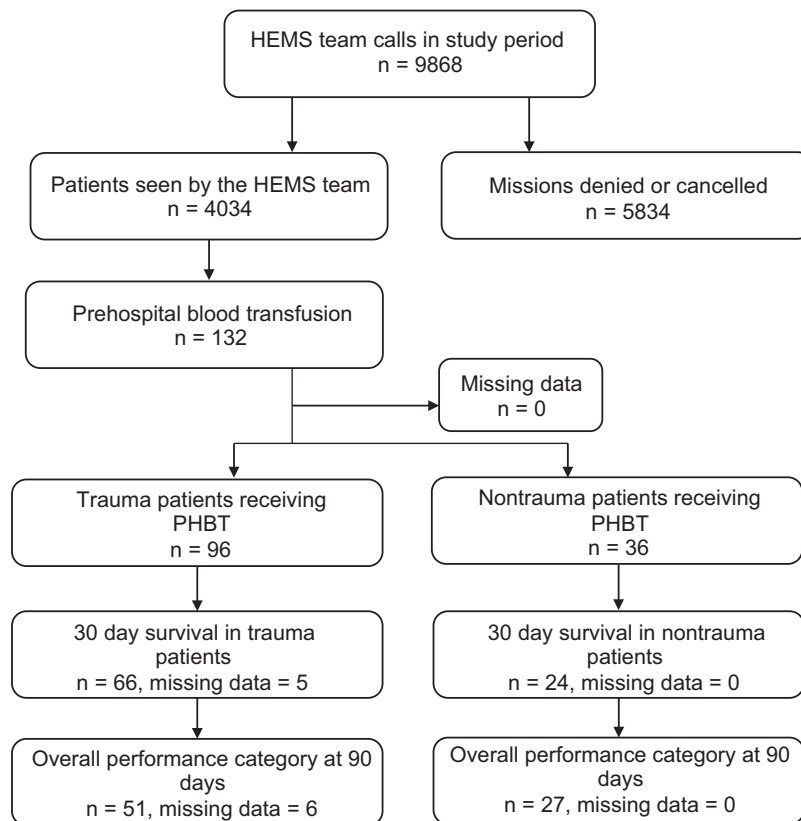


FIGURE 1. Flow chart of the study population (study period 22.3.2016–21.10.2019). HEMS, helicopter emergency medical services; PHBT, prehospital blood transfusion.

PROMED®, Pelican BioThermal, USA). Every pRBC unit has its temperature logger (Libero Ti1®, Elpro, Switzerland) with programmed alarm limits (+2°C–+6°C). The local hospital blood bank near the HEMS base provides new pRBCs 24-hours per day after usage and recycles the units for hospital utilization after three weeks if not used in prehospital setting. pRBCs (and all other resuscitation fluids, if possible) are always infused through a fluid warmer (Belmont Buddy Lite®, Belmont Instrument Corporation, MA, USA).

PHBT is prepared and delivered by the HEMS crew using a checklist. Blood components, crystalloids and medications are administered through standard intravenous or intraosseal accesses. Blood samples for blood group and compatibility testing are taken before initiating pRBC transfusion, but samples are not analyzed until hospital arrival. The patients are closely monitored to note the response to the hemostatic resuscitation and detect possible adverse reactions. All given treatments and their timestamps are documented in the prehospital patient report.

All PHBT cases were prospectively collected from a quality registry. Operational data was collected from the national HEMS mission database and the data concerning prehospital treatments and vital parameters were gathered from electronic

prehospital patient records. HEMS-physician on call is responsible for entering the data to the HEMS-mission database and prehospital patients' records. The PHBT registry data are completed from the hospital patient record system. The PHBT registry is maintained and validated by a single physician (SÅ) responsible for the PHBT process. The data is regularly compared to blood bank records to ensure its completeness. The registry is used in quality control, development of PHBT protocol and research.

The physician responsible for the PHBT process followed the patients using the electronic patient record system to determine the survival status at 30 days and the overall performance category (OPC) at 90 days based on the patient charts. The OPC scale extends from one (normal) to five (death), and values less than three are considered as favorable outcome (15). These served as the outcome measurements in the current study.

We included all PHBT patients, to whom the HEMS team administered either red blood cells, plasma or both, in this study. The data were collected over 42 months, from March 2016 to October 2019.

The normal distribution of the continuous variables was tested using the D'Agostino and Pearson

TABLE 1. Patient characteristics. Data are presented as value (%) or as median (interquartile range, [range]). Vital signs and laboratory results on hospital arrival are presented only for patients that survive to emergency department admission (nontrauma, n = 32; trauma, n = 91)

	Nontrauma patients (N = 36)		Trauma patients (N = 96)		p-value
	Data missing, n		Data missing, n		
Sex, male	0	24 (68)	0	79 (82)	0.0622
Age, years	0	65 (56-73 [19-71])	0	37 (25-57 [8-87])	<0.0001
HEMS unit reaching the patient, minutes from emergency call	0	52 (33-68 [19-122])	0	30 (22-42 [10-113])	<0.0001
Cardiac arrest before hospital admission	0	9 (25)	0	15 (16)	0.2165
Deceased before hospital admission	0	4 (11)	0	5 (5)	
Haemodynamic parameters					
Lowest systolic blood pressure before transfusion, mmHg	0	73 (67-84 [41-129])*	0	75 (65-85 [46-154])#	0.9544
Heart rate at lowest blood pressure, bpm	0	94 (80-112 [52-163])	0	108 (84-130 [45-160])	0.0758
Systolic blood pressure on hospital arrival, mmHg	3	113 (101-123 [74-155])**	3	109 (96-121 [49-170])##	0.3625
Heart rate on hospital arrival, bpm	2	91 (75-113 [53-153])	2	94 (81-115 [25-169])	0.6086
Prehospital point-of-care tests					
Hemoglobin, g/l	16	101 (75-114 [25-133])	16	119 (102-139 [65-170])	0.0009
pH	16	7.34 (7.20-7.45 [6.73-7.50])	16	7.33 (7.25-7.38 [6.58-7.50])	0.4040
Base excess, mEq/l	16	-6 (-11 - -3 [-29-0])	16	-5.0 (-6.0 - -2.0 [-30-3])	0.2953
Laboratory results on hospital arrival					
Haemoglobin, g/l	5	95 (84-119 [55-166])	5	124 (108-133 [72-156])	<0.0001
pH	6	7.40 (7.27-7.44 [6.83-7.55])	6	7.30 (7.19-7.36 [6.62-7.49])	0.0015
Base excess, mEq/l	7	-5.4 (-11.4 - -2.8 [-25.0-1.6])	7	-5.4 (-9.6 - -2.9 [-30.9-3.3])	0.8878
Thromboplastin time, %	9	55 (45-81 [22-113])	9	72 (58-86 [28-136])	0.0261
Lactate, mmol/l	6	3.9 (1.8-8.87 [0.6-18.8])	6	3.9 (2.4-7.0 [0.7-34])	0.7155

HEMS – helicopter emergency medical services.

For the patients with unmeasurable blood pressure.

\* Two without a palpable radial pulse, and one with palpable radial pulse.

\*\* One patient without and one with palpable radial pulse.

# Six patients in cardiac arrest, 16 without a palpable radial pulse, 1 with palpable radial pulse.

## Six with palpable pulses.

One pH measurement in trauma group under measurement level.

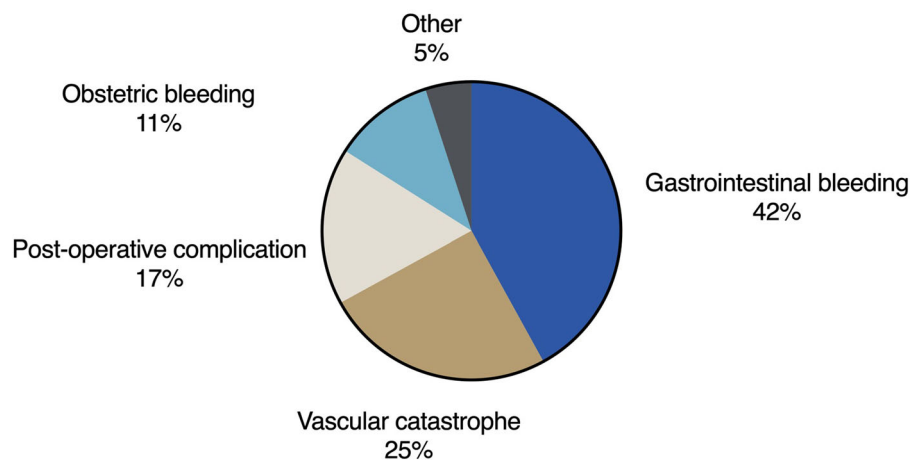


FIGURE 2. Etiology of hemorrhage on nontrauma patients receiving prehospital transfusion (n = 36).

omnibus normality test. As virtually all the parameters had skewed distribution, we reported continuous variables as the median and interquartile range (IQR). For proportions, 95% confidence intervals were calculated using the modified Wald method. Categorical parameters were compared between groups with Fisher's exact test in case of two categories and the Chi-square test in cases of three or more categories. Continuous variables were compared with the Mann-Whitney U test. Analyses were performed using GraphPad Prism version 9.0.0 for Mac OS X (GraphPad Software, USA). A p-value of less than 0.05 was considered significant.

## RESULTS

A total of 132 patients received PHBT during the study period, 36 (27%) of them were nontrauma and 96 (73%) were trauma patients (Figure 1). There were six patients aged < 18 years, and they were all transfused after major trauma. All the cases were included in the analysis. The characteristics of the patients are presented in Table 1. The number of males were 24 (68%) and 79 (82%) in nontrauma and trauma groups, respectively ( $p = 0.622$ ). The nontrauma group was significantly older (median age 65 vs. 37,  $p < 0.0001$ ). The proportion of nontrauma patients was 10/29 (35%) before and 26/103 (25%) after implementation of freeze-dried plasma.

The nontrauma group consisted of patients with various etiologies of hemorrhage (Figure 2). The most common reason for massive hemorrhage was gastrointestinal bleeding (n = 15, 42%). Patients with vascular catastrophes (n = 9, 25%) were suspected to suffer from a ruptured abdominal aortic aneurysm except for one case of suspected aortic dissection. Postoperative complications (n = 6, 17%) involved three patients suffering from late postoperative

bleeding after major vascular surgery, two post-tonsillectomy bleedings and one patient with bleeding from the microvascular free flap in the lower limb. Gynecologic/obstetric hemorrhage (n = 4, 11%) was caused only by pregnancy-related reasons – for example, uterine rupture and extrauterine pregnancy. Other indications for PHBT were one case of severe epistaxis and one case of anemic point-of-care test finding in a patient resuscitated from pulseless electrical activity.

The trauma group consisted of 70% (n = 67) blunt injuries and 30% (n = 29) penetrating injuries. The penetrating injuries included 23 stabbings, 3 shootings and 3 other mechanisms. The blunt injuries included 35 traffic accidents, 18 falls from height (over 4 meters), 10 falls from under 4 meters and other impacts and 4 patients with other mechanisms (e.g., railway accidents, watercraft accident and compression injury).

The HEMS unit was dispatched by the emergency response center in two (6%) of nontrauma and 66 (69%) of the trauma cases. In the rest of the cases, the HEMS dispatch was requested later by the paramedics on the scene. Consequently, nontrauma patients were reached significantly later by the HEMS unit (Table 1) and the delay from emergency call to PHBT initiation was longer (Table 2).

No significant differences were observed in accomplishing PHBT for nontrauma and trauma patients except for a longer delay in the nontraumatic group (Table 2). During the first 12 hours in the hospital, blood products were needed more frequently in nontrauma patients (84.4% vs. 60.4%,  $p = 0.0161$ ). The rate of massive transfusion, defined as more than 9 pRBC units transfused, was similar (15.6% vs. 15.4% in nontrauma and trauma patients, respectively).

Cardiac arrest occurred in 9 (25.0%) nontrauma and 15 (15.6%) trauma patients during prehospital

TABLE 2. Timelines and treatment before and within 12 hours after hospital arrival. Hospital data are presented only for patients that survived to emergency department admission (nontrauma, n = 32; trauma, n = 91). Data are presented as n (%) or median (interquartile range [range])

	Nontrauma (N = 36)		Trauma (N = 96)		p-value
		Data missing, n		Data missing, n	
Delay from emergency call to hospital admission, min	97 (71–114 [58–182])	0	83 (61–107 [31–202])	0	0.0634
to the start of PHBT, min	64 (48–78 [32–130])	6	49 (37–65 [14–140])	11	0.0170
Prehospital treatment					
Patients receiving pRBCs	34 (94%)	0	73 (76%)	0	
pRBC units per patient	2 (1–2 [0–2])	0	2 (1–2 [0–4])	0	
Patients receiving FDP	25 (69%)	0	74 (77%)	0	
FDP units per patient	2 (0–2 [0–2])	0	2 (0–2 [0–2])	0	
Crystalloids, ml	1000 (500–1500 [500–2500])	5	1000 (500–1500 [500–2500])	13	
Tranexamic acid	33 (92%)	0	87 (91%)	0	
Blood products after hospital admission					
No blood products	5 (15.6%)	0	36 (39.6%)	0	0.0027
1–4 pRBC/plasma	13 (40.6%)	0	11 (12.1%)	0	
5–9 pRBC and other blood products	9 (28.1%)	0	30 (33.0%)	0	
>9 pRBC	5 (15.6%)	0	14 (15.4%)	0	

PHBT – prehospital blood transfusion.

pRBC – packed red blood cells.

FDP – fibrin degradation products.

TABLE 3. Outcome of nontrauma and trauma patients receiving prehospital blood transfusions

	Nontrauma (n = 36)	Trauma (n = 96)	p-value
Prehospital mortality	4 (11.1%)	5 (5.2%)	0.2550
30-day mortality	12 (33.3%)	30 (33.0%)*	1.0000
OPC 1–2 at 90 days	27 (75.0%)	51 (56.7%)**	0.0685

OPC – Overall performance category (1–2 corresponds normal functionality or moderate disability).

\*Five missing data.

\*\*Six missing data.

care,  $p = 0.2165$ . After resuscitation from cardiac arrest five (55.6%) nontrauma and ten (66.7%) trauma patients survived to the hospital with spontaneous circulation ( $p = 0.6785$ ). Further, three (33%) nontrauma and two (13%) trauma patients survived to hospital discharge after resuscitation ( $p = 0.3256$ ). All cardiac arrest patients had PEA as their primary rhythm. The three nontraumatic cardiac arrest survivors suffered from bleeding from ruptured uterus, GI bleeding detected after a successful cardiopulmonary resuscitation and post-operative bleeding from femoral artery.

There was no significant difference in the 30-day mortality (33.3% vs. 33.0% in nontrauma and trauma patients, respectively,  $p = 1.000$ ) or in the rate of favorable functional outcome at 90 days (75% vs. 56.7% in nontrauma and trauma patients, respectively,  $p = 0.0685$ ). The outcome data is presented in Table 3. We performed a sensitivity

analysis to address the missing data. We tested scenarios with patients missing OPC data with favorable or unfavorable outcome. The estimate of OPC 1–2 rate in trauma patients would vary between 53.1% ( $p = 0.0287$ ) and 59.4% ( $p = 0.1081$ ) in comparison to nontrauma patients. Accordingly, the limits of 30-days survival rate in trauma patients would be 31.3% to 36.5% (both non-significant).

No transfusion-related adverse events were observed during prehospital phase or reported in the hospital records (incidence 0%, 95% confidence interval 0.0% to 2.8%).

## DISCUSSION

The main findings of the current study include the following. First, nontrauma patients treated with PHBT include patients with gastrointestinal bleeding, vascular catastrophes, obstetric emergencies and, little surprisingly, postoperative complications. Second, based on the laboratory findings and vital signs, these patients were seriously ill and presented for example with lower hemoglobin level than trauma patients transfused with similar triggers. Third, a majority of both nontrauma and trauma patients did receive transfusions at the hospital.

PHBT is a potentially life-saving treatment for trauma patients (16). Even though the PHBT protocols were primarily designed for trauma patients,

they are successfully applied in nontrauma patients by increasing number of prehospital systems (7, 8, 13). The need for PHBT by nontrauma patients is notable. In our study, almost one-third of the patients receiving PHBT therapy were bleeding due to heterogeneous nontraumatic reasons. Even higher rates from 46.5% to 64% have been reported (7, 9, 13). The main etiologies for nontraumatic bleeding in our study were gastrointestinal, vascular catastrophes, postoperative and obstetrical bleeding. Their proportions are mostly similar as previously reported. For instance, the proportion reported for gastrointestinal hemorrhage has been 35%–66.7%, for postoperative complications 11%–15% and for gynecological/obstetrical bleeding 5%–7% (7, 13). The proportion of vascular catastrophes (patients in possible need of cardiothoracic or vascular surgery) varied from 15% to 30%, which was probably due to divergence in categorization and hospital centralization of patients.

Gastrointestinal hemorrhage is a common emergency and usually presents as hematemesis in the prehospital setting (17). The mortality rate of the patients presenting with signs of shock and exteriorized bleeding is high – 5%–40% depending on the cause of bleeding (17, 18). According to international guidelines, hemodynamically unstable patient with upper gastrointestinal bleeding should be resuscitated with blood components using a major hemorrhage protocol (fixed-ratio) to avoid overtransfusion (19).

Identification of a ruptured abdominal aortic aneurysm in the prehospital setting is conventionally based on the triad of hypotension, abdominal and/or back pain and pulsatile abdominal mass. However, the triad presents only in about 50% of the patients (20). Prehospital ultrasound may be useful in identifying the presence of an abdominal aortic aneurysm, but the detection of retroperitoneal hemorrhage is difficult (21). To secure the perfusion of vital organs, the current European guidelines recommend restricted transfusion strategy using blood products but not necessary targeting to normotension (20). The prehospital service should transport these patients directly to a specialized center as centralization may lower mortality even by 20% (22).

The proportion of major obstetric hemorrhage in nontrauma patients in this study was 11%. The incidence of out-of-hospital deliveries appears to be increasing, as well as the incidence of major obstetrical hemorrhage (23, 24). The most common cause of primary postpartum hemorrhage is atony of the uterus, treated initially with manual uterine massage, uterotonic agents and prompt resuscitation with blood products and tranexamic acid. The

current evidence favors application of massive transfusion protocol and early use of fibrinogen concentrate (11).

On hospital admission, nontrauma patients were characterized by lower hemoglobin, higher pH and lower plasma thromboplastin time. These are convergent findings with previous literature (7). Other comorbidities (e.g., baseline anemia) are more likely to affect the manifestation of shock with elder patients. Polypharmacy, especially anticoagulants, complicate the situation (25). Various etiologies for nontraumatic bleeding entails several mechanisms of hemorrhage and coagulopathy, which may differ from the nature of traumatic bleeding (26).

Majority of the patients in both groups received blood transfusions in the hospital within 12 hours. However, it is possible that some patients were overtransfused due to the challenging diagnostics and decision-making in the prehospital setting. The shock index, acquired by dividing the heart rate by the systolic blood pressure, is an established and validated tool for identifying hemodynamically instable trauma patients (27, 28). It has recently been developed further to achieve more precise tools, such as modified shock index and age shock index (29). Furthermore, PHBT therapy could probably be targeted more precisely by analyzing point-of-care markers, such as lactate. In a study by Guyette et al., prehospital lactate outperformed shock index and systolic blood pressure in detection of resuscitative interventions in 387 trauma patients (30). The same physiological triggers may not be optimal in all age groups. In the current study, nontrauma patients were significantly older than trauma patients. This finding needs to be considered when evaluating the age-related transfusion criteria in the future.

Recognizing patients that are potentially in need of PHBT by the medical dispatcher is also challenging. The nontrauma patients suffering from hemorrhagic shock seem to be indistinguishable from the mass of medical emergencies. Thus, in the current study, the majority of the HEMS dispatch decisions for nontrauma patients in need of PHBT were made by prehospital personnel on the scene or the HEMS unit itself following a consultation call. The prompt recognition of major bleeding is fundamental to get PHBT therapy to nontrauma patients in a reasonable time frame.

We reported relatively high primary survival rate in patients suffering cardiac arrest and receiving PHBT. We were unable to obtain the precise timing of PHBT in relation to the cardiac arrest. However, the clinical practice in the unit favors initiating PHBT during resuscitation only in patients with



cardiac arrest witnessed by the prehospital staff, preferably the HEMS unit. If the patient is encountered during cardiac arrest, first-line intervention is advanced life support including a bolus of crystalloid fluid followed by PHBT only in case of return on spontaneous circulation. No transfusion-related adverse events occurred in the study population. This finding is in line with the earlier literature showing prehospital transfusion complication rate of 1% (4). The main limitation of the current study is that data were gathered from only one HEMS unit. Thus, these findings may not apply to different prehospital systems. Because the study was designed as a single center study, it has a relatively small number of patients. This unit is characterized by a mixed and relatively high caseload consisting only of primary missions and staffed by a specialized team, including a senior physician who is fully focused on prehospital work. This may increase the consistency of treatment and data collection. On the other hand, this may limit the generalizability of the results. However, the etiologies and profiles of non-trauma patients resembled the previously reported ones (7, 13). Some of the data from hospital records were collected retrospectively, which might cause unintentional bias. Besides the serious limitation of the study, it also has some considerable strengths. First, we used a prospectively collected PHBT quality registry with a uniform prehospital dataset. Second, the protocol used was implemented and monitored carefully in the HEMS unit, leading to high awareness of the therapy and high compliance with the PHBT protocol.

We conclude that nontrauma patients receiving the PHBT with same triggers than trauma patients are a significant group consisting mainly of patients with gastrointestinal bleeding, vascular catastrophes, postoperative complications and obstetrical emergencies. This heterogeneous group seems to be critically ill and have mortality rate similar to trauma patients. PHBT protocols must be assessed from a nontrauma perspective and the therapy components and treatment targets must be tailored to each patient group.

## References

- Spahn DR, Bouillon B, Cerny V, Duranteau J, Filipescu D, Hunt BJ, Komadina R, Maegele M, Nardi G, Riddez L, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. *Crit Care*. 2019;23(1):98. doi:10.1186/s13054-019-2347-3.
- Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, Junco DJ, Brasel K, Bulger EM, Callcut RA, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015; 313(5):471–82. doi:10.1001/jama.2015.12.
- Kushimoto S, Kudo D, Kawazoe Y. Acute traumatic coagulopathy and trauma-induced coagulopathy: an overview. *J Intensive Care*. 2017;5(1):6. doi:10.1186/s40560-016-0196-6.
- Rijnhout TW, Wever KE, Marinus RH, Hoogerwerf N, Geeraedts LM, Tan EC. Is prehospital blood transfusion effective and safe in hemorrhagic trauma patients? A systematic review and meta-analysis. *Injury*. 2019;50(5):1017–27. doi: 10.1016/j.injury.2019.03.033.
- Guyette FX, Sperry JL, Peitzman AB, Billiar TR, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Putnam T, Duane TM, Phelan HA, Brown JB. Prehospital blood product and crystalloid resuscitation in the severely injured patient: A Secondary Analysis of the Prehospital Air Medical Plasma Trial. *Ann Surg*. 2021;273(2):358–64. doi: 10.1097/SLA.0000000000003324.
- Zhu CS, Pokorny DM, Eastridge BJ, Nicholson SE, Epley E, Forcum J, Long T, Miramontes D, Schaefer R, Shiels M, et al. Give the trauma patient what they bleed, when and where they need it: establishing a comprehensive regional system of resuscitation based on patient need utilizing cold-stored, low-titer O+ whole blood. *Transfusion*. 2019;59(S2):1429–38. doi:10.1111/trf.15264.
- Thiels CA, Aho JM, Fahy AS, Parker ME, Glasgow AE, Berns KS, Habermann EB, Zietlow SP, Zielinski MD. Prehospital blood transfusion in non-trauma patients. *World J Surg*. 2016;40(10):2297–304. doi:10.1007/s00268-016-3572-4.
- Sunde GA, Vikenes B, Strandenes G, Flo KC, Hervig TA, Kristoffersen EK, Heltne JK. Freeze dried plasma and fresh red blood cells for civilian prehospital hemorrhagic shock resuscitation. *J Trauma Acute Care Surg*. 2015;78(6 Suppl 1): S26–S30. doi:10.1097/TA.0000000000000633.
- Fahy AS, Thiels CA, Polites SF, Parker M, Ishitani MB, Moir CR, Berns K, Stubbs JR, Jenkins DH, Zietlow S, et al. Prehospital blood transfusions in pediatric trauma and non-trauma patients: a single-center review of safety and outcomes. *Pediatr Surg Int*. 2017;33(7):787–92. doi:10.1007/s00383-017-4092-5.
- Parker ME, Khasawneh MA, Thiels CA, Berns KS, Stubbs JR, Jenkins DH, Zietlow SP, Zielinski MD. Prehospital transfusion for gastrointestinal bleeding. *Air Med J*. 2017;36(6): 315–9. doi:10.1016/j.amj.2017.06.002.
- Butwick AJ, Goodnough LT. Transfusion and coagulation management in major obstetric hemorrhage. *Curr Opin Anaesthesiol*. 2015;28(3):275–84. doi:10.1097/ACO.0000000000000180.
- Shand S, Curtis K, Dinh M, Burns B. Prehospital blood transfusion in New South Wales, Australia: a retrospective cohort study. *Prehosp Emerg Care* 2020;15:1–11. doi: 10.1080/10903127.2020.1769781.
- Mapp JG, Bank EA, Osborn LA, Stringfellow ML, Reininger DW, Winckler CJ, Prehospital Research and Innovation in Military and Expeditionary Environments (PRIME) Group. Epidemiological and accounting analysis of ground ambulance whole blood transfusion. *Prehosp Disaster Med*. 2020; 35(1):98–103. doi:10.1017/S1049023X1900517X.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624): 806–8. doi:10.1136/bmj.39335.541782.AD.
- Beesems SG, Wittebrood KM, de Haan RJ, Koster RW. Cognitive function and quality of life after successful resuscitation from cardiac arrest. *Resuscitation*. 2014;85(9):1269–74. doi:10.1016/j.resuscitation.2014.05.027.

16. Shackelford SA, Del Junco DJ, Powell-Dunford N, Mazuchowski EL, Howard JT, Kotwal RS, Gurney J, Butler FK, Gross K, Stockinger ZT. Association of prehospital blood product transfusion during medical evacuation of combat casualties in Afghanistan with acute and 30-day survival. *JAMA*. 2017;318(16):1581–91. doi:10.1001/jama.2017.15097.
17. Thiebaud PC, Yordanov Y, Galimard JE, Raynal PA, Beaune S, Jacquin L, Ageron FX, Pateron D. Management of upper gastrointestinal bleeding in emergency departments, from bleeding symptoms to diagnosis: a prospective, multicenter, observational study. *Scand J Trauma Emerg Med*. 2017;25:78. doi:10.1186/s13049-017-0425-6.
18. Villanueva C, Colomo A, Bosch A, Concepcion M, Hernandez-Gea V, Aracil C, Graupera I, Poca M, Alvarez-Urturi C, Gordillo J, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*. 2013;368(1):11–21. doi:10.1056/NEJMoa1211801.
19. Donovan K, Stanworth S, Jairath V. The optimal use of blood components in the management of gastrointestinal bleeding. *Best Pract Res Clin Gastroenterol*. 2019;42–43. doi:10.1016/j.bpg.2019.02.002.
20. Wanhainen A, Verzini F, Herzelee I, Arraire E, Bown M, Cohnert T, Dick F, Herwaarden J, Karkos C, Koelemay M, et al. European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57:8–93. doi:10.1016/j.ejvs.2018.09.020.
21. Walker A, Brenchley J, Sloan JP, Lalanda M, Venables H. Ultrasound by emergency physicians to detect abdominal aortic aneurysms: a UK case series. *Emerg Med J*. 2004;21(2):257–9. doi:10.1136/emj.2002.002121.
22. Laukontaus SJ, Aho PS, Pettila V, Albäck A, Kantonen I, Railo M, Hynninen M, Lepäntalo M. Decrease of mortality of ruptured abdominal aortic aneurysm after centralization and in-hospital quality improvement of vascular service. *Ann Vasc Surg*. 2007;21(5):580–5. doi:10.1016/j.avsg.2007.03.019.
23. Pirneskoski J, Peräjoki K, Nuutila M, Kuisma M. Urgent EMS managed out-of-hospital delivery dispatches in Helsinki. *Scand J Trauma Resusc Emerg Med*. 2016;24:94. doi:10.1186/s13049-016-0285-5.
24. Thurn L, Wikman A, Westgren M, Lindqvist PG. Massive blood transfusion in relation to delivery: incidence, trends and risk factors: a population-based cohort study. *BJOG Int J Obstet Gynaecol*. 2019;126(13):1577–86. doi:10.1111/1471-0528.15927.
25. Abraham NS, Castillo DL. Novel anticoagulants: bleeding risk and management strategies. *Curr Opin Gastroenterol*. 2013;29(6):676–83. doi:10.1097/mog.0b013e328365d415.
26. Cannon JW. Hemorrhagic shock. *N Engl J Med*. 2018;378(4):370–9. doi:10.1056/NEJMra1705649.
27. Pottecher J, Ageron F-X, Fauché C, Chemla D, Noll E, Duranteau J, Chapiteau L, Payen J-F, Bouzat P. Prehospital shock index and pulse pressure/heart rate ratio to predict massive transfusion after severe trauma: retrospective analysis of a large regional trauma database. *J Trauma Acute Care Surg*. 2016;81(4):713–22. doi:10.1097/TA.0000000000001191.
28. Vandromme MJ, Griffin RL, Kerby JD, McGwin G, Rue LW, Weinberg JA. Identifying risk for massive transfusion in the relatively normotensive patient: utility of the prehospital shock index. *J Trauma*. 2011;70(2):384–8. doi:10.1097/TA.0b013e3182095a0a.
29. Torabi M, Mirafzal A, Rastegari A, Sadeghkhan N. Association of triage time shock index, modified shock index, and age shock index with mortality in emergency severity index level 2 patients. *Am J Emerg Med*. 2016;34(1):63–8. doi:10.1016/j.ajem.2015.09.014.
30. Guyette FX, Meier EN, Newgard C, McKnight B, Daya M, Eileen MB, Powell JL, Brasel KJ, Kerby JD, Egan D, et al. A comparison of prehospital lactate and systolic blood pressure for predicting the need for resuscitative care in trauma transported by ground. *J Trauma Acute Care Surg*. 2015;78:600–6. doi:10.1097/TA.0000000000000549.