# Emergency sternal intraosseous access for warm fresh whole blood transfusion in damage control resuscitation

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**BACKGROUND:** Intraosseous (IO) vascular access is increasingly used as an emergency tool for achieving access to the systemic circulation in critically ill patients. The role of IO transfusion of blood in damage control resuscitation is however questionable due to possible inadequate flow rate and hemolysis. Some experts claim that IO transfusion is contraindicated. In this study, we have challenged this statement by looking at flow rates of autologous fresh whole blood reinfusion and hemolysis using two of the commonly used Food and Drug Administration–approved and Conformité Européenne (CE)-marked sternal needles. Additionally, the success rate of sternal access between the two devices is evaluated.

**METHODS:** Volunteer professional military personnel, were enrolled prospectively in a nonrandomized observational study design. We collected 450 mL of autologous whole blood from each participant. Participants were divided into the following three groups of 10: Tactically Advanced Lifesaving IO Needle (T.A.L.O.N.) IO, FAST1 IO, and intravenous group. The reinfusion was done by gravity only. Blood sampling was performed before blood collection and 30 minutes after reinfusion. Investigation of hemolysis was performed by measurements of haptoglobin and lactate dehydrogenase. Success rate was evaluated by correct aspiration of bone marrow.

**RESULTS:** Median reinfusion rate was 46.2 mL/min in the FAST1 group, 32.4 mL/min in the T.A.L.O.N. group, and 74.1 mL/min in the intravenous group. Blood samples from all participants were within normal ranges. There was no statistically significant difference in haptoglobin and lactate dehydrogenase between the groups. In the FAST1 group, 1 (9%) of 11 procedures failed. In the T.A.L.O.N. group, 4 (29%) of 14 procedures failed.

**CONCLUSION:** Although preferable, achieving peripheral venous access in the bleeding patient is a major problem. Our findings suggest that fresh whole-blood transfusion through the IO route is safe, reliable, and provide sufficient flow for resuscitation. (*J Trauma Acute Care Surg.* 2018;84: S120–S124. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)

**LEVEL OF EVIDENCE:** Therapeutic/Care management study, level III.

**KEY WORDS:** Intraosseous access; sternal intraosseous needle; intraosseous needle; remote damage control resuscitation; damage control resuscitation; hemostatic resuscitation; emergency transfusion; hemorrhagic shock.

Intraosseous (IO) vascular access is an old technique for entering the noncollapsible venous plexuses in the bone marrow cavity that connects with the systemic circulation.[1,2] Access to the vascular system of the critically ill, injured adult, or pediatric patient is essential for lifesaving resuscitation and medication. Whether due to trauma or disease, vascular collapse may delay or preclude even experienced medical providers from obtaining standard peripheral or central intravenous (IV) access in time-sensitive emergencies. First responders may lack the experience, skill, and technical capacity to achieve IV access successfully in these situations. Several articles have described the implementation of IO access techniques in civilian and military rescue scenarios where rapid access may be crucial.[3–7] Today, IO access is standard of care in Pediatric Advanced Life Support, Advanced Trauma Life Support, Infusion Nurse Society, and Advanced Cardiac Life Support.

The most common access sites used are long bones, preferably tibia or humerus. Because of reported superior flowrates using the humeral access, this has over the past years become the preferable access point especially in the trauma patient in need of fluid resuscitation.[8] The sternum is another option that has gained increased use especially in combat casualty care.[9]

Publications on the use of sternal access for blood transfusion date back as far as 1941.[10] Modern damage control resuscitation (DCR) principles include the strategy of early transfusion of blood and blood products in resuscitation of patients with traumatic hemorrhagic shock.[11–13]

In a recent publication, the IO route used for transfusion of blood products has been questioned.[14] Based on Darcy law which describes flow of a viscous fluid through porous media and the resulting low flow rates, the authors state that the maximal flow rates attainable for transfusing blood products used in DCR via the IO route are inadequate for successful resuscitation,

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and that "nothing of substance can be achieved by transfusing blood via the IO route in Damage Control Resuscitation." Further, the authors state that the application of pressure to obtain sufficient flow may cause shearing forces in the fluid that may cause hemolysis and subsequent acute renal injury, indicating that the IO route in DCR is contraindicated.

The critical points highlighted in the above-mentioned article are in contrast to recent experience with the prehospital blood product transfusion through sternal and humeral IOs in recent conflicts in Afghanistan and Iraq.[15] However, the clinical and scientific evidence for the safe use of IO access in DCR and hemostatic resuscitation is limited. To our knowledge, there are only three animal studies that address the concerns of transfusing blood via the IO route.[16–18] No prospective human clinical trials exist.

The Norwegian Naval Special Operation Commando has many years of experience with using sternal IO needles as a tool in emergencies. In 2010, the unit implemented a warm fresh whole blood (WFWB) protocol using a prescreened, preselected walking donor pool for far forward hemorrhagic shock resuscitation.[19] The concept of blood donation in the field is trained on a regular basis with "real life" blood donation and subsequent autologous reinfusion of WFWB through a sternal IO device or an 18G IV catheter.

In this setting, we have studied the performance of two Food and Drug Administration–approved and CE-marked sternal needles in autologous reinfusion of whole blood on hemolysis and flow rate. Our primary objectives were to compare flow rate using the sternal IO route with two different devices when transfusing WFWB, and to measure posttransfusion hemolysis using s-haptoglobin and lactate dehydrogenase (LD) as markers of hemolysis. Our secondary objective was to compare the success rate of sternal access between the two devices. Our hypothesis is that the sternal IO access is a feasible method of transfusing WFWB in DCR, when IV access is unattainable—and that the procedure does not give rise to any significant hemolysis when WFWB is transfused by gravity only.

## METHODS

### Subjects

This is a prospective comparative nonrandomized study, which enrolled volunteer professional military personnel who attended Norwegian Naval Special Operation Commando training in remote DCR (RDCR) and provided written informed consent.[11] The study is approved by the Regional Ethics Committee for medical research ethics (REK 2014/691), and registered in Clinicaltrials. gov (NCT02924792).

Warm fresh whole blood was reinfused using two different sternal devices EZ-IO Tactically Advanced Lifesaving IO Needle (T.A.L.O.N.) (Teleflex Inc., Reading, PA) and FAST1 (Pyng Medical Corp., Richmond, BC, Canada). The results were compared with reinfusion through a standard 18G IV line (BD Venflon 18G 1.3 × 45 mm, Franklin Lakes, NJ).

### Sample Size

We have not identified published articles comparing IO with IV infusion of WFWB with flowrate and hemolysis as outcomes to use for power calculations. One study by Leidel et al,[20] however, compared the success rate and procedure time in IO and central venous catheterization in adult patients under resuscitation in the emergency department. In this study, 10 consecutive patients were included. Later, the same group performed a study comparing two different IO devices in regard of technical success rate and complications.[21] This study included a total of 40 consecutive adult patients under resuscitation, 20 patients in each arm. As we perform our study on healthy volunteers, we have chosen to start with an inclusion of 10 volunteer participants in each arm, a total of 30 patients. The number of participants in the IO group will be a total of 20.

The study participants were divided into the following three groups: T.A.L.O.N. IO group, FAST1 IO group, and the IV group.

### Blood Collection Procedure

The subjects were given theoretical and practical lessons before the procedure. Five hundred milligram of Ciprofloxacin was given 30 minutes before the procedure as infection prophylaxis. Baseline blood sampling was performed before blood donation. The blood collection bags (CPDA-1 blood bag, Terumo Penpol; Puliyarakonam, Thiruvananthapuram, India) were marked with participants' names and social security numbers. Whole blood (WB) was then collected from either left or right antecubital vein. During the procedure, the collection bag was placed on a blood collection mixer (Docon; Macopharma, Mouvaux, France) and filled to a total of 513 mL representing a mix of 63 mL of CPDA-1 and 450 mL of WB.

The bags were stored in room temperature for up to 20 minutes awaiting reinfusion.

### IO Procedure

Participants in both IO groups were offered infiltration anesthesia at the injection site with 5 mL of Lidocaine 20 mg/mL before placement of the IO device. The participants performed the procedure on each other under supervision as a part of the training. The IO needles were placed in the manubrium of sternum according to the manufacturer's instructions. In the IO groups, bone marrow was aspirated and discarded, followed by a flushing procedure with 2 mL of 0.9% sodium chloride solution before starting the WFWB reinfusion. In the IV group, participants received an 18G 1.2 × 45 mm IV cannula placed in the left or right antecubital vein.

### Reinfusion Procedure

Reinfusion of WB was done through a standard blood administration set with 180-cm tubing (Sangofix Air Vented; B. Braun Melsungen AG, Melsungen Germany), connected to a three-way stopcock with 10-cm connection tube (Discofix C 3-way Stopcock connection tubing; B. Braun Melsungen AG).

The reinfusion was done by gravity only, without additional pressure on bags, with subjects lying on their backs, and the collection bag and tubing fully extended above participants' chests (IO) or arms (IV).

In the IO groups, rapid flushing with 2 mL of 0.9% sodium chloride solution was repeated if the provider considered flow inadequate. Thirty minutes after reinfusion, the post–reinfusion

blood samples were collected. Number of failed IO insertions, total reinfusion time, number of flushing procedures, and pain associated with the procedure (Visual analogue scale 0–10) were noted.

## Blood Samples

Blood sampling was performed by venipuncture according to procedures at Haukeland University Hospital before blood collection and 30 minutes after completed reinfusion of blood. Investigation of hemolysis was performed by measurements of haptoglobin and LD (Cobas 800 c702; Roche Diagnostics GmbH, Mannheim, Germany). Hemoglobin (Hb) and platelet (Plt) count were also obtained (Cell-Dyn Sapphire; Abbott Diagnostics, Abbott Park, IL). The 30-minute time point was selected because previous studies have demonstrated that haptoglobin levels can drop rapidly in response to hemolysis.[22–24]

## Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp, Armonk, NY). Tests of distribution of variables were performed by use of Shapiro-Wilk tests. Due to the fact that many variables did not show normal distribution, descriptive data are reported as median (quartiles), and comparisons performed by use of Kruskal-Wallis nonparametric test (for three groups), Wilcoxon signed rank test for related samples, and Mann-Whitney *U* test for two independent samples. *p* Values less than 0.05 were considered statistically significant.

# RESULTS

A total of 36 participants provided informed consent. Two participants were excluded due to failure in the blood collection procedure. Four participants were excluded due to IO procedure failure as described below. In the T.A.L.O.N. group, 4 (29%) of the 14 IO procedures failed (n = 10). In two cases, the needle was flushed out during the flushing procedure. One participant in the T.A.L.O.N. group was moved to the IV group after failed insertion. In one case, the provider was not able to confirm correct placement with aspiration of bone marrow, and in the last case, we observed subcutaneous hematoma suggesting displacement. In the T.A.L.O.N group, 9 of the 14 providers had never attempted the procedure before, 2 of the 14 providers had done it once, and three providers had done it more than five times. In the FAST1 group, 1 (9%) of 11 IO insertions failed (n = 10). The device did not enter perpendicular to the manubrium of sternum causing no flow without pressure. In this group, 8 of the 11 providers had never attempted the procedure before. Three of the 11 providers had done it once.

Descriptive data of the three groups are provided in Table 1. There was a significant difference in age between all groups, but no significant difference in height, weight, body mass index, or blood collection time. All participants were male except one female included in the IV arm. Baseline Hb, haptoglobin, Plt count, and LD values were within normal ranges in all subjects.

Median reinfusion rate was 46.2 mL/min (39.3–51.2 mL/min) in the FAST1 group, 32.4 mL/min (26.3–39.3 mL/min) in the T.A.L.O.N. group and 74.1 (72.0–84.8) ml/min in the IV group. There were statistically significant differences between all groups ($p < 0.05$). Note that the flow rate in the T.A.L.O.N group was slower compared with the FAST1.

**TABLE 1.** Descriptive Data for the Participants in All Three Study Groups

| | FAST1 | T.A.L.O.N. | IV |
|---|---|---|---|
| Age* | 27 (26–36) | 25 (22–31) | 34 (32–37) |
| Height, cm | 185 (180–192) | 184 (178–188) | 181 (175–186) |
| Weight, kg | 88 (82–94) | 85 (84–95) | 84 (79–91) |
| BMI | 25.5 (24.3–27.0) | 26.2 (25.1–26.8) | 26.6 (23.0–27.8) |
| Collection time, s | 409 (352–498) | 389 (324–448) | 469 (366–510) |

Results reported as medians (quartiles). Groups were compared using Kruskal-Wallis nonparametric test. There was a statistical significant difference in age between all three groups.
* *p* Value < 0.05.

In the FAST1 group, median number of flushing procedures was 1.[1,2,25] In the T.A.L.O.N. group, 2.[2,3] Pain associated with the reinfusion was registered as follows: in the FAST1 group, the median VAS was 4,[2–6] in the T.A.L.O.N. group, 3.[1–4]

Blood samples from all participants were within normal ranges (Fig. 1.) Between-group comparison of median change in Hb, haptoglobin, and LD before and after reinfusion showed no statistically significant differences.

Within-group analysis of hemolysis and change in Hb before and after reinfusion showed significant elevation of LD in the FAST1 group 174 (155–216) to 176 (156–242) U/L, $p < 0.05$). However, no significant decrease in haptoglobin was observed, and no significant changes were observed in Hb. For the T.A.L.O.N. group, only the change in Hb (15.8 g/dL [15.1–16.3 g/dL] to 15.45 g/dL [14.9–16.2 g/dL]) was significant ($p < 0.05$). In the IV group, haptoglobin decreased from 0.88 g/L (0.70–1.34 g/L) to 0.86 g/L (0.68–1.31 g/L) ($p < 0.05$).

# DISCUSSION

Although the flow rates are lower compared with the standard peripheral IV line, IO infusion rates are sufficient to maintain flow rates needed to fulfill criteria for massive transfusion.[25] In this study, no pressure other than gravity (180 cm) was placed on the blood bags, tubing system, and device. Higher flow rates are probably achievable using additional pressure on the bags. However, high-volume transfusion with blood products in the initial prehospital setting of hemorrhagic shock is neither achievable due to the logistical restraints in such circumstances, nor medically sensible in the event of noncompressible hemorrhage.[26] Our findings suggest that it is possible to administer one unit of WFWB in about 11 minutes without the use of pressure, which in most cases is sufficient for the initial resuscitation. In the present study, the FAST1 device delivered higher flow rates and more consistent results, compared with the T.A.L.O.N. device.

We did not find any strong evidence of hemolysis (Fig. 1). There was a tendency toward elevation of LD in all groups, however, only significant in the FAST1 group. The elevation was subtle and within normal analytical reference standards. Further, we did not find significant change in haptoglobin that should be

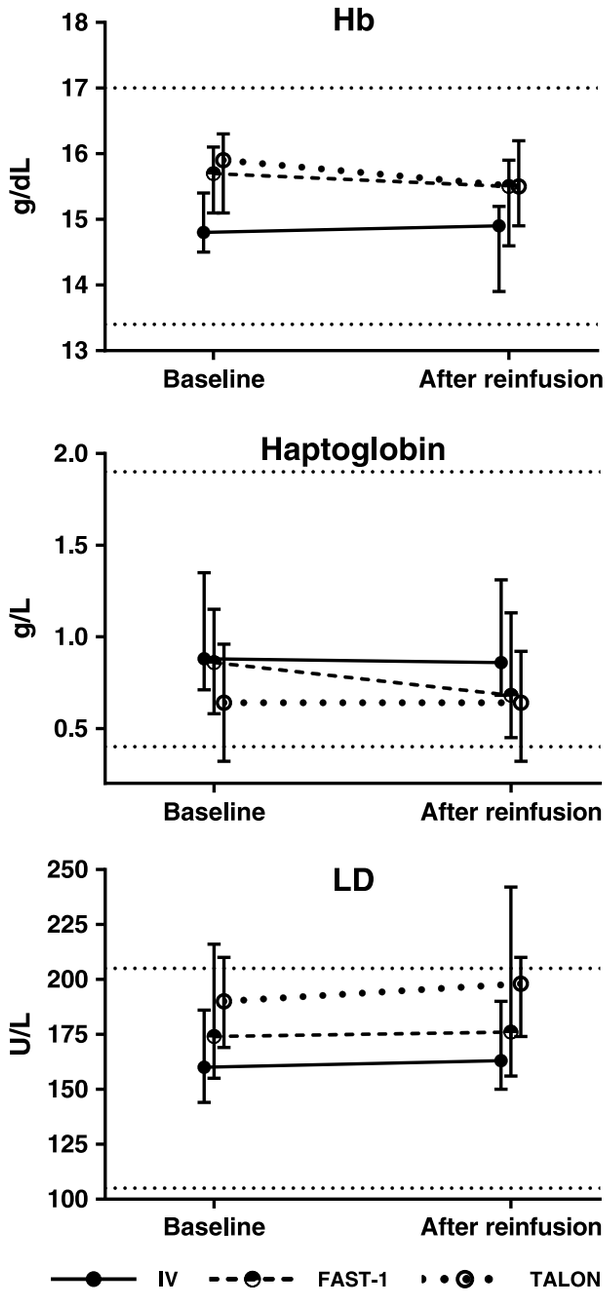


**Figure 1.** Show the medians (quartiles) change in Hb, Plt count, haptoglobin, and LD, before and after reinfusion in the three groups. *Dotted lines* show normal laboratory reference range. In the FAST1 group, the change in LD was statistically significant. In the T.A.L.O.N. group, the change in Hb was significant. In the IV group, the change in Haptoglobin was significant ($p < 0.05$).

expected in the case of hemolysis. Because of a small sample size, we choose to perform between-group comparisons of the median change in the aforementioned parameters.

We did not find significant differences between the groups indicating that the tendency of elevation in LD is similar in the IV and IO groups, supporting our hypothesis that there is no significant hemolysis in the IO group compared with the IV group.

In this study, we found that the T.A.L.O.N. device was displaced in 4 of 14 cases. In emergency scenarios, the success rate and the stability of the device during patient transfer are important factors, especially in prehospital care. Our experience with the T.A.L.O.N. device indicates that it is easily dislodged during patient movement or accidental drag in the tubing. The FAST1 sternal device seems to be more reliable in terms of success rate and resilience to displacement. In the present study, only 1 of the 11 devices was displaced. These data correspond to the high success rates found in earlier reports.[27]

In our experience, the initial verification of placement with aspiration of bone marrow, followed by a low-volume, high-pressure, flushing procedure (1–2 mL of saline in a 1- to 2.5-mL syringe), is an important step to obtain patent flow. Further, we advocate the use of a three-way stopcock at the connection to the IO device to be able to repeat the flushing procedure without having to disconnect the administration set, if the flow rate deteriorates during infusion.

Many services have abandoned the FAST1 device for live training and even in clinical practice due to reports of tip retention in the sternum after removal attempts of the device.[28]

Since 2013, we have performed live training annually with no tip retention after introducing a self-made stylet that is inserted into the IO tubing. The tip of the stylet is custom-made to fit the interior of the metal tip. A careful rotation maneuver of the stylet during direct pull of the tubing and stylet ensure high removal success rate.

## Limitations

WFWB has a lower hematocrit than cold stored packed red blood cells. Higher hematocrit and lower temperature may lead to lower flow rates due to elevated viscosity and subsequently the need for pressure to obtain adequate flow. Second, this study has been conducted without the use of pressure in the system. As stated in the aforementioned article, high pressure may cause shearing forces and subsequently hemolysis.[14] Also, the short duration of our study limits our ability to rule out possible delayed hemolysis or more rapid clearance of red blood cells following IO transfusion. However, it is unlikely that any significant immediate, mechanical hemolysis caused by the infusion procedure occurred, as reflected by lack of clinical signs or symptoms of hemolysis or changes in laboratory parameters, such as haptoglobin and LD. Further investigations on these matters are warranted. On the other hand, we found sufficient flow rates without the use of positive pressure with WFWB. Flow rates may also be influenced by hypoxia, hypercarbia, and acidosis (often present in the critically ill), leading to local vasodilation and increased IO blood flow.

Further, we acknowledge that this study does not reflect the events following massive transfusion through an IO device, hence, we cannot rule out significant hemolysis following transfusion of more than one unit of WFWB. However, the utility of the IO device is in the context of initial resuscitation awaiting large bore peripheral or central IV cannulas in higher echelons of care. Lastly, many services use other IO sites of insertion. We suggest that larger studies should be performed transfusing more than one unit should be performed. Further prospective evidence is also warranted for both the tibial and humeral access used in clinical practice worldwide.

## CONCLUSION

These findings suggest that sternal IO access is suitable for the immediate resuscitation of hemorrhagic shock with WFWB. Flow rates seem to be sufficient, and no clinical relevant significant hemolysis was observed. Given the relatively high insertion success rate, sternal IO devices, such as the FAST1, are valuable tools for front-line providers in early hemostatic resuscitation with WFWB for the critically ill in DCR. In this material, there was a high frequency of displacement of the T.A.L.O.N needle.

### AUTHORSHIP

C.B. was lead investigator and contributed in all aspects of the study. T.K.F. contributed in all aspects of the study. T.O.A. contributed in the development of study design, data analysis, data interpretation, and critical revision. J.S., H.E., and H.B. contributed in data collection and data analysis. A.B.G. and A.C. contributed in critical revision. G.S. contributed in all aspects of the study. All authors contributed in writing and revisions of the final article.

### DISCLOSURE

No conflicts of interest.

## REFERENCES

1. Drinker CK, Drinker KR, Lund CC. The circulation in the mammalian bone marrow. *Am J Physiol*. 1922;62:1–92.
2. Burgert JM. A primer on intraosseous access: history, clinical considerations, and current devices. *Am J Disaster Med*. 2016;11(3):167–173.
3. Byars DV, Tsuchitani SN, Erwin E, Anglemyer B, Eastman J. Evaluation of success rate and access time for an adult sternal intraosseous device deployed in the prehospital setting. *Prehosp Disaster Med*. 2011;26(2):127–129.
4. Helm M, Haunstein B, Schlechtriemen T, Ruppert M, Lampl L, Gäßler M. EZ-IO(®) intraosseous device implementation in German Helicopter Emergency Medical Service. *Resuscitation*. 2015;88:43–47.
5. Vassallo J, Horne S, Smith JE. Intraosseous access in the military operational setting. *J R Nav Med Serv.* 2014;100(1):34–37.
6. Lewis P, Wright C. Saving the critically injured trauma patient: a retrospective analysis of 1000 uses of intraosseous access. *Emerg Med J*. 2015;32(6):463–467.
7. Rush S, D'Amore J, Boccio E. A review of the evolution of intraosseous access in tactical settings and a feasibility study of a human cadaver model for a humeral head approach. *Mil Med*. 2014;179(8 Suppl):24–28.
8. Engels PT, Erdogan M, Widder SL, Butler MB, Kureshi N, Martin K, Green RS. Use of intraosseous devices in trauma: a survey of trauma practitioners in Canada, Australia and New Zealand. *Can J Surg*. 2016;59(6):374–382.
9. Butler FK. TCCC updates: two decades of saving lives on the battlefield: Tactical Combat Casualty Care Turns 20. *J Spec Oper Med*. 2017;17(2):166–172.
10. Tocantins LM, O'Neill JF, Price AH. Infusions of blood and other fluids via the bone marrow in traumatic shock and other forms of peripheral circulatory failure. *Ann Surg*. 1941;114(6):1085–1092.
11. Jenkins DH, Rappold JF, Badloe JF, Berséus O, Blackbourne L, Brohi KH, Butler FK, Cap AP, Cohen MJ, Davenport R, et al. Trauma hemostasis and oxygenation research position paper on remote damage control resuscitation: definitions, current practice, and knowledge gaps. *Shock*. 2014;41 Suppl 1:3–12.
12. Holcomb JB. Damage control resuscitation. *J Trauma*. 2007;62(6 Suppl):S36–S37.
13. American College of Surgeons Committee on T. Advanced Trauma Life Support For Doctors (Student Course Manual) 8th edition. Advanced Trauma Life Support For Doctors (Student Course Manual) 8th edition. 2008: 87.
14. Harris M, Balog R, Devries G. What is the evidence of utility for intraosseous blood transfusion in damage-control resuscitation? *J Trauma Acute Care Surg*. 2013;75(5):904–906.
15. Savell S, Mora AG, Perez CA, Bebarta VS, Maddry MJ. En route intraosseous access performed in the combat setting. *Am J Disaster Med*. 2016;11(4):225–231.
16. Plewa MC, King RW, Fenn-Buderer N, Gretzinger K, Renuart D, Cruz R. Hematologic safety of intraosseous blood transfusion in a swine model of pediatric hemorrhagic hypovolemia. *Acad Emerg Med*. 1995;2(9):799–809.
17. Bell MC, Olshaker JS, Brown CK, McNamee GA Jr, Fauver GM. Intraosseous transfusion in an anesthetized swine model using 51Cr-labeled autologous red blood cells. *J Trauma*. 1991;31(11):1487–1489.
18. Burgert JM, Mozer J, Williams T, Gegel BT, Johnson S, Bentley M, Johnson A. Effects of intraosseous transfusion of whole blood on hemolysis and transfusion time in a swine model of hemorrhagic shock: a pilot study. *AANA J*. 2014;82(3):198–202.
19. Strandenes G, De Pasquale M, Cap AP, Hervig TA, Kristoffersen EK, Hickey M, Cordova C, Berseus O, Eliassen HS, Fisher L, et al. Emergency whole-blood use in the field: a simplified protocol for collection and transfusion. *Shock*. 2014;41 Suppl 1:76–83.
20. Leidel BA, Kirchhoff C, Bogner V, Stegmaier J, Mutschler W, Kanz KG, Braunstein V. Is the intraosseous access route fast and efficacious compared to conventional central venous catheterization in adult patients under resuscitation in the emergency department? A prospective observational pilot study. *Patient Saf Surg*. 2009;3(1):24.
21. Leidel BA, Kirchhoff C, Braunstein V, Bogner V, Biberthaler P, Kanz KG. Comparison of two intraosseous access devices in adult patients under resuscitation in the emergency department: a prospective, randomized study. *Resuscitation*. 2010;81(8):994–999.
22. Graw JA, Yu B, Rezoagli E, Warren HS, Buys ES, Bloch DB, Zapol WM. Endothelial dysfunction inhibits the ability of haptoglobin to prevent hemoglobin-induced hypertension. *Am J Physiol Heart Circ Physiol*. 2017;312(6):H1120–H1127.
23. Dale J, Myhre E, Rasmussen K. Elimination of hemoglobin and lactate dehydrogenase from plasma in normals and patients with intravascular hemolysis. *Scand J Clin Lab Invest*. 1972;29(4):389–395.
24. Zagorski J, Marchick MR, Kline JA. Rapid clearance of circulating haptoglobin from plasma during acute pulmonary embolism in rats results in HMOX1 up-regulation in peripheral blood leukocytes. *J Thromb Haemost*. 2010;8(2):389–396.
25. Savage SA, Sumislawski JJ, Zarzaur BL, Dutton WP, Croce MA, Fabian TC. The new metric to define large-volume hemorrhage: results of a prospective study of the critical administration threshold. *J Trauma Acute Care Surg*. 2015;78(2):224–229; discussion 229–30.
26. Nevin DG, Brohi K. Permissive hypotension for active haemorrhage in trauma. *Anaesthesia*. 2017;72(12):1443–1448.
27. Macnab A, Christenson J, Findlay J, Horwood B, Johnson D, Jones L, Phillips K, Pollack C Jr, Robinson DJ, Rumball C, et al. A new system for sternal intraosseous infusion in adults. *Prehosp Emerg Care*. 2000;4(2):173–177.
28. Hodgetts JM, Johnston A, Kendrew J. Long-term follow-up of two patients with retained intraosseous sternal needles. *J R Army Med Corps*. 2017;163(3):221–222.