

## Cognitive and physical performance are well preserved following standard blood donation: A noninferiority, randomized clinical trial

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**BACKGROUND:** A walking blood bank (WBB) refers to the use of fellow combatants for battlefield blood donation. This requires pretesting combatants for infectious diseases and blood type. A fundamental prerequisite for this technique is that the donating soldier will suffer minimal physiological and mental impact. The purpose of the current study is to assess the effect of blood shedding on battlefield performance.

**METHODS:** This is a double-blind randomized control trial. Forty Israel Defense Forces combatants volunteered for the study. Participants underwent baseline evaluation, including repeated measurement of vital signs, cognitive evaluation, physical evaluation, and a strenuous shooting test. Three weeks after the baseline evaluation, subjects were randomized to either blood donation or the control group. For blinding purposes, all subjects underwent venous catheterization for the duration of a blood donation. Repeated vital signs and function evaluation were then performed.

**RESULTS:** Thirty-six patients were available for randomization. Baseline measurements were similar for both groups. Mean strenuous shooting score was  $80.5 \pm 9.5$  for the control group and  $82 \pm 6.6$  for the test group ( $p = 0.58$ ). No clinically or statistically significant differences were found in tests designed to evaluate cognitive performance or physical functions. Vital signs taken multiple times were also similar between the test and control groups.

**CONCLUSIONS:** Executive, cognitive, and physical functions were well preserved after blood donation. This study supports the hypothesis that a WBB does not decrease donor combat performance. The categorical prohibition of physical exercise following blood donation might need to be reconsidered in both military and civilian populations.

**E**xsanguination is the most frequent etiology of preventable death in military as well as civilian trauma.<sup>1</sup> Once hemorrhage is controlled, resuscitation and volume replacement are used when needed.

An increasing number of studies support balanced resuscitation with blood products at ratios of 1:1:1 between red blood cells, plasma, and platelets in an attempt to mimic whole blood.<sup>2-5</sup> Transfusion of whole blood allows for balanced resuscitation, while transfusing less solution volume and possibly providing superior results compared to component therapy.<sup>6</sup> The Israel Defense Forces Medical Corps (IDF-MC) currently uses refrigerated low-titer type O whole blood as a resuscitation fluid during aeromedical evacuation, while freeze-dried plasma remains the resuscitation fluid of choice at the point of injury where no refrigeration is available.<sup>7</sup> The logistics of providing cold-stored components on the battlefield are challenging; establishing a walking blood bank (WBB) would relieve this burden.

**ABBREVIATIONS:** CRM = compensatory reserve measurement; IDF = Israel Defense Forces; IDF-MC = Israel Defense Forces Medical Corps; RT = reaction time; WBB = walking blood bank.

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The terms *WBB* and *buddy transfusion* refer to performing emergency blood donations at remote locations, occasionally at the location of the injury.<sup>8</sup> The collected blood is then transfused to the patient. Implementation of WBBs requires a program of pretesting combatants for infectious diseases and blood type, identifying those with type O blood and low titer of immunoglobulin M anti-A and anti-B, and educating both medical providers in transfusion medicine and enrolled donors about blood delivery safety issues. WBBs can also be regarded as part of a safety net both when logistical limitations hamper use of component therapy and in situations where the number of casualties exceeds available resources. However, it is not without risks.

A fundamental prerequisite for use of a WBB in the military setting is that the donating soldier will suffer minimal physiologic derangement. Establishing a WBB in a military setting raises several concerns. If a soldier who just donated blood gets injured, he or she has a unit of blood less to bleed. There is also conflicting literature on the effects of physical performance after donation, and scarce literature on cognitive performance after donation.

Most available data on patient function following blood donation are derived from nonrandomized, noncontrolled studies, and none report a noninferiority design.<sup>9</sup> While these studies provide valuable information, they are subject to errors, limiting their applicability. Several of these studies report a decline in maximal oxygen uptake following a 450 cc blood donation,<sup>10,11</sup> while others report no significant effect of blood donation on several performance-focused indices.<sup>12</sup> In addition, most of these studies focus on aerobic performance, while data on anaerobic performance are lacking.

The purpose of the current study is to assess the effect of blood donation on battlefield performance among combat soldiers. Our randomized, double-blind trial allows for comparisons between subjects donating and subjects not donating blood under similar environmental conditions. We chose a noninferiority design because we are evaluating whether, under simulated battlefield conditions, the performance of soldiers after blood donation may be inferior to that of soldiers who have not donated blood.

## METHODS

This study is a double-blind, randomized controlled trial. The trial was designed and analyzed with a noninferiority approach. The study was approved by the IDF-MC institutional review board (ID-IRB #1865). All participants provided written informed consent. The manuscript was written and edited according to the Consolidated Standards of Reporting Trials statement. No changes to trial design and methods were made following trial commencement.

### Study design

Infantry combatants from the IDF School for Infantry and Command course received an oral and written explanation

concerning the study and, if they expressed a wish to participate in the study, provided informed consent. Inclusion criteria, exclusion criteria, and criteria for discontinuation of the study are provided in Table 1.

Subjects were divided into groups of six. All participants underwent baseline performance assessment including repeated measurements of vital signs, cognitive assessment (three tests), physical assessment (five tests), and strenuous marksmanship performance. Adverse reactions were recorded for all participants.

Three weeks after baseline testing, subjects were randomized to either blood donation or the control group. In each group, three subjects were randomized to blood donation using a random numbers generator (<https://www.randomizer.org/>). After completion of a medical questionnaire as part of routine blood donation under the auspices of the Israeli National Blood Service, all participants underwent venous catheterization and had blood samples drawn for hemoglobin concentration; 450 mL of blood were collected from test subjects, while control subjects were not bled. The control subjects had their catheters remain in place for the duration of a standard blood donation. Airline sleep masks were used as blindfolds to prevent subjects from learning their assigned group and were removed from both the test and control subjects only after blood donation was completed for the three test subjects in each enrollment group. Following this, all volunteers were offered a 500-mL bottle water, an energy bar, and 1 hour of rest, after which performance testing began.

All performance assessments were conducted by certified IDF fitness trainers. Only the study coordinator knew

**TABLE 1. Inclusion criteria, exclusion criteria, and criteria for discontinuation of the study**

Inclusion criteria	<ul style="list-style-type: none"> <li>• Volunteering combat soldier</li> <li>• Over 6 months of military service</li> <li>• Basic training graduate</li> <li>• Meets blood donation criteria (according to MDA's criteria for blood donation)</li> </ul>
Exclusion criteria	<ul style="list-style-type: none"> <li>• Does not meet blood donation criteria</li> <li>• Donated blood in the past 3 months</li> <li>• Treated with any medication in the past week</li> <li>• Any fever in the past week</li> </ul>
Discontinuation criteria	<ul style="list-style-type: none"> <li>• Any test subject who wishes to drop out for any reason</li> <li>• Abnormal vital sign measurements at any point of the testing following 30 minutes of rest:                             <ul style="list-style-type: none"> <li>○ Heart rate &gt; 100 bpm</li> <li>○ Temperature &gt; 38°C (PO)</li> <li>○ Systolic blood pressure &lt; 90 mm Hg</li> <li>○ 15% drop in systolic blood pressure from base measurement</li> </ul> </li> <li>• Any other medical condition that arises during testing deemed unfit by supervising medical team</li> </ul>

Israeli national blood services.

which subjects had donated blood; the field researchers who collected the data and the fitness trainers were not aware of the subjects' donation status.

### Outcomes

As the main study objective was to assess combat performance, marksmanship performance after physical exertion, measured on a scale of 0 to 100, was defined as the primary outcome. Vital signs and cognitive and physical performances other than marksmanship performance were considered secondary outcomes.

### Vital signs

Measurements of heart rate and blood pressure (Omron Healthcare, Inc.) were collected four times during the trials. Measurements were performed before blood donation, before the physical exercise, before the shooting range, and after completion of all tests. All measurements were taken in a sitting position following a 5-minute rest. Compensatory reserve measurement (CRM, Flashback Technologies) was recorded with the vital signs. The CRM is a novel, continuous, and noninvasive monitoring technology with the ability to assess compensatory reserve via feature extraction of real-time continuous arterial pulse waveforms.<sup>13-15</sup> This dynamic analysis provides an output reading from 0 to 1, where 1 represents a "full tank" and 0 represents the point where decompensation occurs.

### Marksmanship assessment

Subjects completed a target sprint exercise at the shooting range using their personal, sighted M4 assault rifles: Following a 100-meter sprint, subjects fired five rounds kneeling and five rounds prone at a 50-meter target, all in under 60 seconds. Scores were calculated using a scored accuracy target board and ranged from 0 to 100.

### Physical exercise

Physical performance was evaluated by a test battery comprising the following:

**Long jump from standing:** Subjects jumped from a standing position. The best of two attempts, measured in centimeters, was considered the final score.

**Weighted pull-ups:** Subjects were instructed to wear a standard 7-kg vest and performed as many pull-ups as possible. The number of repetitions was considered the final score.

**Deadlifts:** Subjects performed as many repetitions as possible with a 60-kg trap bar; total number of repetitions was considered the final score.

**Walking lunges:** Subjects completed a 50-meter course with a 60-kg trap bar as rapidly as possible. Time to completion, in seconds, was considered the final score.

**200-meter sprint:** Subjects completed a 200-meter sprint; time, in seconds, was considered the final score.

### Cognitive and subjective evaluations

**Serial sevens subtraction test:** subjects performed as many subtractions as possible in 1 minute. Number of correct answers was considered the final score.<sup>16</sup>

**Reaction time (RT):** During RT clinical testing, participants sat with their dominant forearm resting on a flat horizontal table surface, with their open hand at the edge of the surface. The examiner suspended a ruler vertically so that the top of the ruler was aligned with the top of the participant's open hand. At predetermined random time intervals ranging from 4 to 15 seconds, the examiner released the ruler and the participant caught it as quickly as possible. The distance the ruler fell was recorded, in centimeters, by measuring from the top of the table to the most superior aspect of the participant's hand. Each participant was tested 20 times, with the average of the results from trials 5 through 15 used to produce the final score.<sup>17,18</sup>

**Fatigue assessment:** Subjects were asked a single question regarding subjective fatigue on a scale of 1 to 10 at the start and at the end of the testing day.

**Perceived exertion:** Subjects were asked a single question regarding subjective exertion on a scale of 6 to 20 (Borg scale) at the start and at the end of the testing day.<sup>19</sup>

Both scales, the 6 to 20 (the original Borg scale) and the 0 to 10 (the revised category-ratio Borg scale) are commonly used in clinical practice to measure perceived exertion, while neither surpasses the other. In our study, both scales were used following one another in an attempt keep the subjects' answers as objective as possible, with no influence of the fatigue assessment's questionnaire on the perceived exertion's questionnaire and vice versa.

### Statistical analysis

This study was designed as a noninferiority study. We could not find any published data on the tactical significance of scoring intervals to support the choice of a specific noninferiority margin. In our experience, interpretation of the numerical score is done in 10-point intervals, and practically, up to a 10-point difference is not seen as substantially different. Accordingly, we set the noninferiority margin as -10 points. Thus, the null hypothesis is that participant performance after donating blood is at least 10 points worse than performance after not donating blood. This hypothesis would be rejected if the blood donation group were no worse than 10 points lower than the non-blood donation group.

For sample size calculation, a preliminary analysis of the marksmanship score revealed a standard deviation of 10 points. Using the R package *TrialSize*,<sup>20</sup> given an alpha of 0.025 and 80% power, we calculated that we would need a sample size of 32 subjects for the detection of performance not worse than 10 points lower in the donation group versus the control group. To ensure 32 subjects would complete the trial, we enrolled 40 subjects for the study.

Continuous data are presented as mean  $\pm$  standard deviation. To assess differences in the primary outcome

between the test and control groups, analysis of covariance was used to adjust for baseline performance<sup>21,22</sup> and a 95% confidence interval (CI) was calculated for the difference in means between the study group and the control group. A lower limit of the CI not less than -10 would lead to rejection of the null hypothesis. To calculate the p value, a one-sided t test with a confidence level of 97.5% was used to assess whether the difference in means (i.e., test minus control) was less than -10.<sup>23</sup>

For the secondary outcomes, we report the 95% CIs for the differences in means. For those outcomes where a higher result is better, a more negative CI reflects worse performance in the donation group as compared to the nondonation group. Conversely, for those outcomes where a lower result is better, a more positive CI reflects worse performance in the donation group as compared to the nondonation group.

In addition, we provide standard two-sided t tests, without correcting for baseline measurements, to compare the test and control groups. While these tests are assessing a null hypothesis that differs from our study goal (specifically, equivalence vs. noninferiority), they provide some additional understanding of the magnitude of the differences between the test and control groups given our sample size. No correction was made for multiple comparisons.

The effect of blood donation on vital sign changes was further assessed using a linear model.

Statistical analysis was performed using R version 3.6.<sup>24</sup>

We planned to present both intention to treat and per-protocol analyses if any dropouts or treatment crossovers were to occur after randomization.

## RESULTS

Forty subjects were enrolled in the study and completed baseline measurements. Four subjects suffered fever in the week before randomization and were thus excluded from the study. Overall, 36 patients were available for randomization. All subjects who were randomized completed the study protocol. No adverse reaction were recorded, and there were no crossovers (Fig. 1). Baseline measurements for both groups were similar and are presented in Table 2. All tests were completed in a similar duration for the control and study group, with 238.3 (19.8) minutes and 239 (17.7) minutes, respectively (p = 0.92).

### Marksmanship scores

Baseline marksmanship scores were similar between the control and study groups (77.4 ± 10.8 and 78.3 ± 7.5, respectively, p = 0.76). Mean marksmanship score following donation was 80.5 ± 9.5 for the control group and 82 ± 6.6 for the donation group. The CI for the difference using analysis of covariance was (-3.7, 5.9). As the lower limit of the

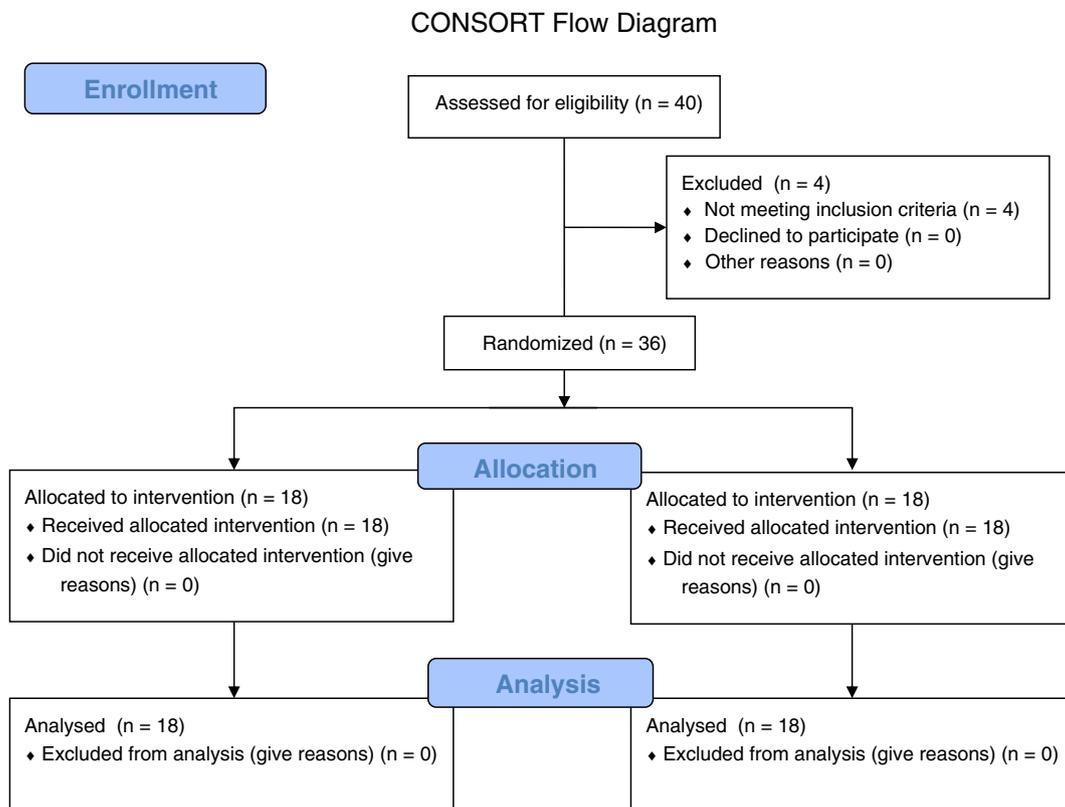


Fig. 1. Consolidated Standards of Reporting Trials flow diagram.

**TABLE 2. Baseline measurements**

		Control	Study	p
Demographics	Age	20.4 (0.73)	20.3 (0.49)	0.65
	BMI	23.48 (2.07)	22.5 (1.71)	0.13
Vital signs and hemoglobin	Initial HR (b/m)	72 (13.82)	76.11 (16.83)	0.43
	Initial systolic BP (mm Hg)	119.33 (8.17)	119.28 (10.79)	0.99
	Initial CRM	0.83 (0.12)	0.76 (0.15)	0.18
	Prefunctional HR (b/p)	68.56 (10.39)	69.72 (12.01)	0.76
	Prefunctional systolic BP (mm Hg)	116.72 (9.22)	118.56 (10.08)	0.57
	Prefunctional CRM	0.83 (0.09)	0.82 (0.12)	0.76
	Presprint HR (b/m)	92.11 (12.37)	91.67 (12.68)	0.92
	Presprint systolic BP (mm Hg)	122.39 (10.92)	123.67 (10.71)	0.73
	Presprint CRM	0.81 (0.2)	0.79 (0.19)	0.75
	Final HR (b/p)	92.11 (12.37)	91.67 (12.68)	0.34
	Final systolic BP (mm Hg)	130.72 (11.7)	128.67 (15.25)	0.65
	Final CRM	0.73 (0.22)	0.76 (0.17)	0.6
	Cognitive and subjective assessment	Hemoglobin	15.56 (1.2)	15.14 (0.73)
Reaction time		0.17 (0.02)	0.16 (0.02)	0.24
Fatigue (start)		4.67 (1.64)	4.89 (2.05)	0.72
Fatigue (end)		5.89 (1.91)	5.28 (1.84)	0.33
Exertion (start)		6.78 (1.56)	7.22 (1.63)	0.41
Exertion (end)		13.06 (2.53)	12 (2.33)	0.2
Physical performance measurements	Serial sevens	11.28 (5.05)	9.94 (3.75)	0.38
	Standing long jump	2.05 (0.15)	2.18 (0.17)	0.02
	Deadlifts	53.33 (25.09)	48.5 (23.93)	0.56
	Weighted pull-ups	12 (4.83)	14.06 (5.53)	0.24
	Walking lunges	94.89 (25.65)	97.89 (35.52)	0.77
Marksmanship performance	20-meter sprint	27 (27)	26.11 (26.11)	0.18
	Shooting score	77.39 (10.8)	78.33 (7.46)	0.76

Values are mean (standard deviation).

BMI = body mass index; BP =blood pressure; CRM = compensatory reserve measurement; HR = heart rate.

CI is not less than -10, the null hypothesis is rejected, and the donation group's performance is not considered inferior to the control group's performance. With use of the one-sided t test, the p value for the hypothesis that the difference in means is lower than -10 (i.e., farther from 0 than -10, the noninferiority margin) is less than 0.001 and is thus strongly rejected.

**Physical exercise**

Five tests were used to assess physical performance. For all five tests, baseline measurements in the test and control group were similar (Table 2). Following blood donation, no substantial differences were detected between the control and donation group for jump distances (1.79 ± 0.2 meters and 1.88 ± 0.2 meters, respectively; 95% CI, -0.03 to 0.22), deadlifts

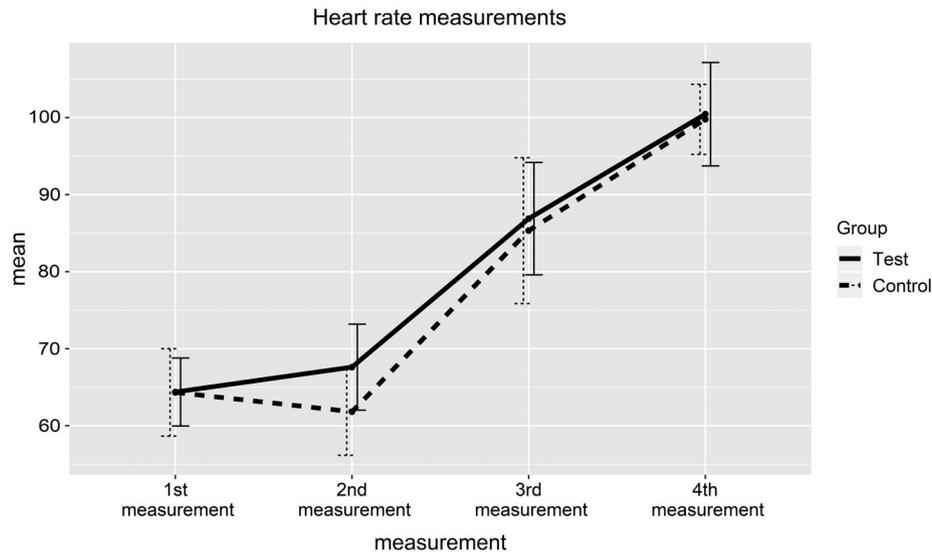
**TABLE 3. Experiment day measurements**

		Control	Study	p t test	95% CI for differences in means
Cognitive and subjective assessment	Reaction time	0.16 (0.02)	0.15 (0.01)	0.6	-0.01 to 0.01*
	Fatigue (start)	5.06 (1.95)	4.89 (1.94)	0.8	-1.48 to 1.15*
	Fatigue (end)	6.61 (1.5)	6.56 (1.42)	0.91	-1.05 to 0.94*
	Fatigue (change)	1.56 (2.2)	1.67 (2)	0.88	-1.31 to 1.54
	Exertion (start)	8.22 (3.02)	8.22 (2.37)	1	-1.84 to 1.84*
	Exertion (end)	14.94 (2.53)	15.67 (2.2)	0.37	-0.88 to 2.33*
	Exertion (change)	6.72 (3.58)	7.44 (3.13)	0.52	-1.56 to 3
Physical performance measurements	Serial sevens	12.78 (5.05)	10.78 (3.75)	0.22	-5.28 to 1.28†
	Standing long jump	1.79 (0.2)	1.88 (0.17)	0.15	-0.03 to 0.22†
	Deadlifts	40.44 (17.03)	36.72 (15.49)	0.5	-14.75 to 7.31†
	Weighted pull-ups	11.22 (4.51)	12.78 (4.8)	0.32	-1.6 to 4.71†
	Walking lunges	79.5 (29.06)	74 (32.12)	0.59	-26.25 to 15.25*
Marksmanship performance	20-meter sprint	35.23 (2.81)	34.13 (1.9)	0.18	-2.73 to 0.54*
	Shooting score	80.47 (9.54)	82 (6.58)	0.58	-4.05 to 7.1†

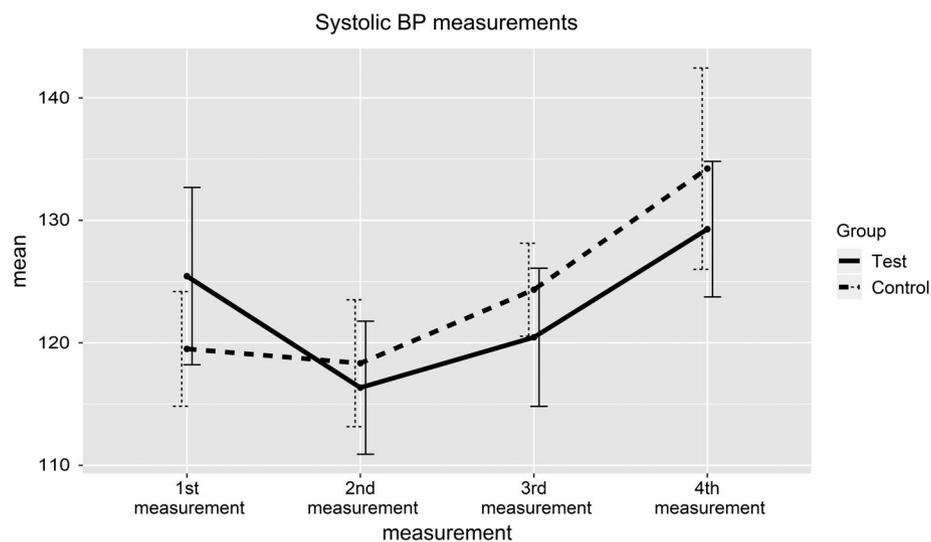
Values are mean (standard deviation).

\* Lower (more negative) value represents a favorable result.

† Higher (more positive) value represents a favorable result.



**Fig. 2.** Mean heart rate measurements (beats/min) for the control and test group throughout the experiment day.



**Fig. 3.** Mean systolic blood pressure measurements (mm Hg) for the control and test group throughout the experiment day.

repeats ( $40.4 \pm 17$  repeats and  $36.7 \pm 15$  repeats, respectively; 95% CI, 14.8-7.3) weighted pull-up repeats ( $11.2 \pm 4.5$  repeats and  $12.8 \pm 4.8$  repeats, respectively; 95% CI, -1.6 to 4.7), walking lunges ( $79.5 \pm 29.1$  sec and  $74.0 \pm 32.1$ , sec, respectively; 95% CI, -26.2 to 15.2) and sprint time ( $35.2 \pm 2.8$  sec and  $34.1 \pm 1.9$  sec, respectively; 95% CI, -2.7 to 0.5). Explicit p values for the differences in means are presented in Table 3.

**Cognitive and subjective evaluations**

Baseline measurements were similar for the control and donation groups in all four cognitive and subjective evaluations (Table 2).

During the test day, reported fatigue rose by  $1.6 \pm 2.2$  points for the control group and  $1.7 \pm 2.0$  for the donation

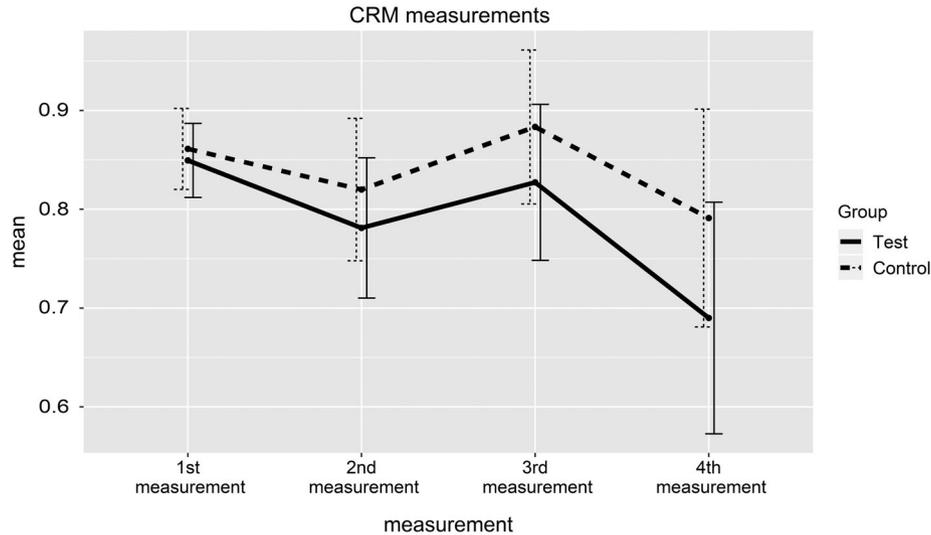
group (95% CI, -1.3 to 1.5). Similarly, reported exertion rose by  $6.7 \pm 3.6$  for the control group and  $7.4 \pm 3.1$  for the donation group (95% CI, -1.6 to 3.0).

Response time score was similar for the control and donation groups ( $0.16 \pm 0.02$  and  $0.15 \pm 0.01$ , respectively; 95% CI, -0.01 to 0.01).

Subtraction scores were also similar between the control and donation groups ( $12.8 \pm 5.0$  and  $10.8 \pm 3.8$ , respectively; 95% CI, -5.3 to 1.3). Explicit p values for the differences in means are presented in Table 3.

**Vital signs**

Vital signs were taken multiple times throughout the experiment. Vital sign trends throughout the test day are shown in



**Fig. 4.** Mean compensatory reserve measurements (CRMs) for the control and test group throughout the experiment day.

Figs. 2 through 4. Using a linear model, heart rate was found to be significant ( $F[4, 139], 51.25; p < 0.001$ ), with no significant effect of blood donation (estimated change, 2; 95% CI,  $-2.2$  to  $6.2$ ). A significant model was found for systolic blood pressure ( $F[4, 139], 7.0; p < 0.001$ ), with blood donation having no significant effect (estimated change,  $-1.2$ , 95% CI,  $-5.1$  to  $2.7$ ). Similarly, a significant model was found for CRM ( $F[4, 139], 4.1; p < 0.001$ ). Blood donation did have a borderline effect on CRM (estimated change,  $-0.05$ ; 95% CI,  $-0.1$  to  $0$ ).

No adverse events occurred during either testing day, and all subjects who began a testing day completed all tests.

## DISCUSSION

The current study suggests that soldiers remain combat effective following blood donation.

The outcomes tested in this study were selected to indicate alterations in clinically relevant performance, specifically battlefield performance, after blood donation. Marksmanship, rarely assessed, represents a vital function for combatants, and was chosen accordingly as the primary outcome. Moreover, as the influence of blood donation on aerobic performance was previously reported,<sup>10-12</sup> we chose to focus on anaerobic function due to the lack of evidence in the scientific literature. Anaerobic metabolism is based on carbohydrate breakdown in the absence of oxygen and is characterized by short bursts of activity, such as sprinting and battlefield assaults and thus allows for the high-intensity, short reactions commonly required in austere military scenarios. Our comparisons of anaerobic performance found no substantial differences, suggesting that donation of a single blood unit does not have a clinically relevant effect on these outcomes. Our study results are supported

by the findings of several studies in which no effect of blood donation was evident on anaerobic performance. Hill et al.<sup>25</sup> did not find differences in blood lactate concentrations nor in the maximal accumulated oxygen deficit after 450-cc blood donation among 19 young men and women after cycle ergometer tests. The authors stated that there was no evidence of any effect on anaerobic capacity, despite the possible bicarbonate and hemoglobin loss because of the blood donation. Similarly, Christensen and Christensen<sup>26</sup> found no changes in maximal lactate up to 2 days after blood withdrawal in a study conducted on seven males for 53 days after a loss of 1000 cc of blood. In the current study, no significant effect on subjects' anaerobic glycolysis process was detected following the 450-cc blood donation. Importantly, compensatory mechanisms may be attenuated in the severely dehydrated patient; thus, results cannot necessarily be applied to combatants injured during combat.

Heart rate rose following exertion during the test day. Blood donation did not affect changes in heart rate or systolic blood pressure and did not vary between the groups. Similar patterns were reported in a recent randomized, blinded controlled trial.<sup>9</sup> These findings are not surprising as the loss of 450 cc of blood is equivalent to what is known as Class 1 shock, which is not expected to affect heart rate or blood pressure.<sup>27</sup> Other studies evaluating the physiologic consequence of blood donation also failed to demonstrate recognizable changes in heart rate or systolic blood pressure.<sup>28</sup> In the current study, vital signs changed as a result of the strenuous physical exercise performed; however, these changes were similar whether subjects donated blood or not, suggesting a limited effect of donation on physiologic reserve. The CRM, designed to measure physiologic reserve, was the only parameter to demonstrate a difference between the groups. Previous reports also support

the capability of CRM measurements to detect low volumes of blood loss.<sup>28-31</sup> Despite the decline in CRM values throughout the testing day, the CRM nadir, reached at the end of the testing day, was  $0.69 \pm 0.24$ , well above the manufacturer's cutoff for moderate compromise.<sup>15</sup> This finding further supports the hypothesis that preserved compensatory mechanisms exist despite a loss of 450 mL of blood.

While data on the long-term cognitive effects of blood donation exist,<sup>32</sup> few data discuss the short-term or immediate effects. Eliassen et al.<sup>9</sup> assessed cognitive function following blood donation in a randomized controlled trial and did not detect any effect after blood donation. This current evaluation included three different tools designed to measure processing speed, executive functions, short-term memory, delayed memory, and attention capacity. The tests chosen for the current study, while not designed directly to measure cognitive functions, were selected to reflect combat-relevant performance. RT, a highly relevant function in combat performance, was similar in the test and the control group both at baseline and following donation. Subjective measures of exhaustion following physical exercise, not usually addressed, were similar for the test and control group, both at baseline and following donation. The serial sevens subtraction test is a simple and rapid test used to assess attention, and while a significant difference between the test and the control group was not found, it is important to appreciate that since this test is not usually used in the context of acute cognitive assessment, the applicability of these results is limited.

Several studies discuss the effect of blood donation on physiologic and laboratory parameters. Ziegler et al.<sup>10</sup> reported a decline in peak oxygen uptake and longer times to complete a self-paced 3-km treadmill time trial 3 days after blood donation. Measurements recovered within days following donation. A similar study design by Burnley et al.<sup>11</sup> reported several components of oxygen uptake to decrease 24 hours after donating 450 cc of blood, while other components of oxygen uptake remained unchanged. Similar results were reported for women.<sup>33</sup> In a meta-analysis published by Remoortel et al.,<sup>34</sup> blood donation resulted in lower hemoglobin levels, lower oxygen maximal uptake, and lower maximal exercise capacity in the first 2 days following blood donation. In a randomized controlled trial published by Eliassen et al.<sup>9</sup> a decline in maximal oxygen consumption was detected following blood donation in the test group. These changes were not demonstrated in the control group. Similarly, differences were detected in hemoglobin and lactate levels, but the clinical significance of these changes is unclear. While published data on battlefield-relevant performance following blood donation does exist, most share several limitations. Strandenes et al.<sup>35</sup> tested donor performance following blood donation in a pilot study of a unique group of elite combatants and found no significant differences in marksmanship skills and aerobic and anaerobic performance

following blood donation. However, being a pilot study, power analysis was not performed, tests were performed based on subject availability, and a control group was not assigned. Similarly, measurements taken from a group of elite combatants, who can be regarded as elite athletes, cannot necessarily be applied to all combatants. Evaluating the performance of combatants from an enlisted infantry brigade can be better used to extrapolate to a wider population. The implications of the current study are not necessarily limited to blood donation on the battlefield. Current guidelines in the IDF mandate at least 6 hours of complete rest following standard blood donation. Following the results of the current study, these guidelines are reevaluated to allow for a shorter rest period.

### Limitations

The current study has several limitations. The first limitation is related to the relatively small sample size, possibly limiting the applicability of the results to the general population. The second limitation concerns the correlation between the selected tests and corresponding combat function. While an attempt was made to select tests that will reflect on relevant performance, there are few data to validate this assumption. Furthermore, as only short-term outcomes were measured, long-term effects of blood donation cannot be made. The third limitation relates to the homogeneity of the study group. As is apparent from the study design and from baseline measurements, the study included subjects of similar age and physical fitness. While this is the relevant population for military scenarios, the results cannot necessarily be applied to other populations, such as reserve duty soldiers. Nevertheless, the results of the current study can potentially help in the development of civilian postdonation management protocols, especially in similar communities such as the sporting community.

Finally, this study was conducted in a controlled scenario, which does not reflect all aspects of combat physiology such as stress, fatigue, and dehydration. Safety consideration mandated rehydration, nutrition, and rest following blood donation, further limiting the similarity to combat scenarios.

### CONCLUSION

This study, performed as part of the efforts to establish an IDF-MC WBB program, provides a preliminary indication that the donation of one unit of blood does not significantly compromise combat performance. While the main objective of the study was to assess combat performance, a wider application of the results may be considered. Further studies are required; however, it seems that the policy of categorical prohibition for limited physical exercise following blood donation needs to be reconsidered, at least in young, healthy populations.

**CONFLICT OF INTEREST**

The authors have disclosed no conflicts of interest.

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