Pulse Pressure as an Early Warning of Hemorrhage in Trauma Patients

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BACKGROUND: Hypotension based on low systolic blood pressure (SBP) is a well-documented indicator of ongoing blood loss. However, the utility of pulse pressure (PP) for detection of hemorrhage has not been well studied. The purpose of this study was to determine whether a narrowed PP in nonhypotensive patients is an independent predictor of critical administration threshold (CAT+) hemorrhage requiring surgical or endovascular control.

STUDY DESIGN: We performed a retrospective single-center study (January 2010 to October 2014), including trauma patients $\geq$16 years old with SBP $\geq$ 90 mmHg upon emergency department (ED) admission. We identified patients who were both CAT+ and required either surgical or interventional radiology for definitive hemorrhage control as the active hemorrhage (AH) group. Analyses were then performed to elucidate the association between PP and hemorrhage.

RESULTS: Of the total 18,015 patients identified, 283 (1.6%) met the criteria for clinically significant hemorrhage. Mean PP was significantly lower in the AH group compared with the non-AH group (39 $\pm$ 18 mmHg vs 53 $\pm$ 19 mmHg, $p < 0.0001$). Multivariate analysis revealed that narrowed initial ED PP is an independent predictor of AH (adjusted odds ratio [AOR] 0.975) along with age (AOR 1.01), penetrating mechanism (AOR 9.476), field SBP (AOR 0.985), ED heart rate (AOR 1.024), and Injury Severity Score (AOR 1.126). Cutoff analysis of PP values identified a significantly higher risk of AH at a PP cutoff of 55 mmHg (AOR 3.44, $p = 0.005$, AUC 0.955) in patients 61 years or older vs 40 mmHg (AOR 2.73, $p < 0.0001$, AUC 0.940) for patients 16 to 60 years old. The predicted probability of AH increases as PP narrows.

CONCLUSIONS: In patients who are nonhypotensive, a narrowed PP is an independent early predictor of active hemorrhage requiring blood product transfusion and intervention for hemorrhage control. (J Am Coll Surg 2019;229:184−191. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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Hemorrhage is the most common cause of preventable death in the injured patient. Rapid identification of those who are bleeding is critical so that the bleeding can be stopped and lost volume replaced. While external bleeding can easily be seen, identification of internal cavitary bleeding can be a challenge. Hypotension, as determined by low systolic blood pressure (SBP), is a well-documented indicator of ongoing blood loss requiring emergent therapeutic intervention.[1] Although pulse pressure has been used for determining fluid responsiveness,[2] or as a predictor of cardiovascular disease[3,4] in the nontrauma setting, a gap currently exists in the literature regarding its utility as an early detector of hemorrhage in a trauma patient who is not hypotensive.

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Abbreviations and Acronyms

AH = active hemorrhage
AOR = adjusted odds ratio
CAT = critical administration threshold
ED = emergency department
IR = interventional radiology
ISS = Injury Severity Score
LAC+USC = Los Angeles County + University of Southern California Medical Center
PP = pulse pressure
SBP = systolic blood pressure

Pulse pressure (PP) is defined as the difference between the diastolic and systolic blood pressure. The difference between the 2 values can either become wider or narrower. In a bleeding patient, pulse pressure narrows as an early response to decreased intravascular volume. As the venous capacitance decreases, the measured diastolic blood pressure increases, before any change to the systolic blood pressure is seen. What is considered a narrowed pulse pressure can also vary depending on age; older patients tend to have wider pulse pressures due to a combination of decreased diastolic pressure and an increased systolic pressure secondary to stiffness of large arteries.[5] Older patients who have sustained volume loss may also fail to mount a normal physiologic compensatory response, and the pulse pressure narrowing may not be as pronounced.[6] The purpose of this study was to determine whether a narrowed PP in a nonhypotensive patient is an independent predictor of bleeding. Practical cut-off values for pulse pressure indicating hemorrhage for various age groups were also explored.

METHODS

After institutional review board approval, all nonhypotensive (systolic blood pressure $\geq$ 90 mmHg) patients who sustained penetrating or blunt trauma, presenting to the Los Angeles County + University of Southern California Medical Center (LAC+USC) between January 2010 and October 2014, were identified for this retrospective review. Patients were excluded if they died in the emergency department, were pregnant, were younger than16 years old, or if they were transferred from an outside facility.

Patients were initially identified and extracted from the LAC+USC Trauma Registry. Admission systolic and diastolic blood pressure were used to calculate pulse pressure by subtracting the diastolic from systolic blood pressure. ICD-9 codes were used to identify patients who had either undergone an interventional radiologic (IR) or surgical procedure for hemorrhage control. A review of the LAC+USC blood bank database was completed to identify those patients who had received blood products and to further determine the amount and types of products received within their first 24 hours of admission. Patients were defined as having active hemorrhage (AH) if they were identified as CAT+ (3 units of packed red blood cells [pBRC] in any 60-minute period within 24 hours of admission)[7] and required interventional radiology or surgery for definitive hemorrhage control. If patients did not meet these criteria they were considered to be nonactive hemorrhage (non-AH).

The following data on patient demographics, injury severity, blood product received, IR procedures, operative procedures, and outcomes were collected for analysis: date and time of arrival to the emergency department, age, sex, mechanism and description of injury and Injury Severity Score (ISS), field and admission vital signs (Glasgow Coma Scale, heart rate [HR], blood pressure), amounts of blood products received in 24 hours (pRBC, fresh frozen plasma [FFP], platelets [plt] and cryoprecipitate [cryo]), IR findings and procedure completed, surgical intervention, intraoperative findings, ventilator days, hospital length of stay, ICU length of stay, and mortality. With regard to IR and surgical interventions, procedure and/or operative reports were reviewed to verify that a therapeutic procedure to control hemorrhage was performed. Data were recorded into a computerized spreadsheet and analyzed therein (Microsoft Excel 2007; Microsoft Corporation).

All patients defined as AH and those who were determined to be non-AH were compared using univariate analyses to compare demographic data, clinical interventions, and in-hospital outcomes. Variables with values of $p < 0.2$ were further analyzed with multivariate analysis. Values of $p < 0.05$ were considered statistically significant. Adjusted odds ratios (AOR) with 95% confidence interval (CI) were derived from the logistic regression. Statistical analysis was performed using SPSS for Mac, version 23 (IBM Corporation).

Stepwise logistical regression was then completed to identify independent predictors of active hemorrhage, and further regression using cut-off analysis at 5-mmHg increments was performed to identify pulse pressure values predictive of hemorrhage, after adjusting for covariates. We looked at ages 16 to 60 separately from ages 61+ to account for possible differences in age-specific physiology.

RESULTS

From January 2010 to October 2014, 18,015 patients sustained either penetrating or blunt trauma and were not hypotensive (systolic blood pressure ≥ 90 mmHg), making up our study cohort. These patients were predominantly male (74.4%) and the majority were Hispanic (55.7%). The overwhelming mechanism of injury was blunt injury (84.8%), with the most common injuries resulting from ground level falls (29.5%), motor vehicle crashes (18.7%), and auto vs pedestrian incidents (13.4%). A minority of patients (12.5%) sustained penetrating injuries including gunshot wounds (5.9%), stab wounds (5.6%), and other penetrating wounds (1.0%). Of the total study population, 283 (1.6%) met the definition of AH and were considered to have a clinically significant bleed. Overall, 47.7% of the AH patients sustained blunt trauma; the most common mechanisms were auto vs pedestrian (18.4%) and motor vehicle collisions (13.8%). All AH patients with penetrating trauma either sustained a gunshot wound (32.2%) or a stab wound (19.8%).

When compared with those who did not have active hemorrhage, the AH patients were younger (median age 34 years [range 24 to 48 years] vs 40 years [range 26 to 59 years], $p < 0.0001$) and more predominantly male (86.2% vs 74.2%, $p < 0.0001$). Additionally, the AH patients had a higher ISS (25 vs 5, $p < 0.0001$), lower emergency department (ED) systolic blood pressure (median 124 mmHg [106.5 to 140 mmHg] vs 135 mmHg [121 to 150 mmHg]), $p < 0.0001$), a lower field pulse pressure (42 ± 20 mmHg vs 54 ± 20 mmHg, $p < 0.0001$) and a significantly lower ED pulse pressure (39 ± 18 mmHg vs 53 ± 19 mmHg, $p < 0.0001$). The AH patients more frequently had an ED pulse pressure of <25 mmHg (14.4% vs 4.7%, $p < 0.0001$) compared with non-AH patients (Table 1). Comparison of interventions performed and in-hospital outcomes revealed further differences between the AH and non-AH patients. All AH patients required a blood transfusion, while only 13.3% of the non-AH patient received transfusion. The AH group required significantly more blood products in the first 24 hours (packed RBCs: 15.6 units ± 18.1 units vs 0.3 units ± 1.8 units, $p < 0.0001$; fresh frozen plasma: 9.8 units ± 6.8 units vs 0.2 units ± 1.4 units, $p < 0.0001$; platelets: 1.8 units ± 2.6 units vs 0.1 units ± 0.4 units, $p < 0.0001$; cryoprecipitate: 3.1 units ± 6.8 units vs 0 units ± 0.7 units, $p < 0.0001$), than the non-AH patients.

When comparing operative and surgical interventions between these 2 groups again, the AH patients required either operative or IR intervention compared with only 0.4% (IR) and 3.1% (OR) in the non-AH group (Table 2). When the non-AH patients did undergo these interventions, they had statistically fewer positive findings of hemorrhage during IR interrogation (0.3% vs 4.9%, $p < 0.0001$) and lower rates of hemoperitoneum (1.2% vs 69.3%, $p < 0.0001$), solid organ injury (0.8% vs 50.2%, $p < 0.0001$), bowel injury with bleed (0.3% vs 7.8%, $p < 0.0001$), and vascular injury (0.1% vs 15.2%, $p < 0.0001$) during operative exploration (Table 2). Regarding in-hospital outcomes, the AH patients had a greater number of ventilator days (6 ± 12.5 days vs 0.77 ± 4.1 days, $p < 0.0001$), longer hospital length of stay (22.2 ± 30.8 days vs 7.3 ± 12.3 days, $p < 0.0001$), longer ICU length of stay (11.3 ± 17.3 days vs 2 ± 5.7 days, $p < 0.001$), and a higher rate of in-hospital mortality (31.1% vs 2.4%, $p < 0.0001$) compared with non-AH patients.

To assess independent predictors of a clinically significant bleed in AH patients, a step-wise logistical regression was performed. Increased age (adjusted odds ratio [AOR] 1.01, $p < 0.0001$), penetrating mechanism of injury (AOR 9.476, $p < 0.0001$), lower field systolic blood pressure (AOR 0.985, $p < 0.0001$), increased ED heart rate (AOR 1.024, $p < 0.0001$), increased ISS (AOR 1.136, $p < 0.0001$), and narrowed ED pulse pressure (AOR 0.975, $p < 0.0001$) were all found to be independent predictors of active hemorrhage (Table 3). Adjusted PP means were 61 ± 10 mmHg in patients over age 61 years vs 51 ± 11 mmHg in younger patients after adjusting for covariates of sex, age, race, and weight, $p < 0.0001$. Further regression analysis identified a significantly higher risk of AH at a PP cutoff of 55 mmHg (AOR 3.44, $p = 0.005$, AUC 0.955) in patients 61 years or older and 40 mmHg (AOR 2.73, $p < 0.0001$, AUC 0.940) for patients 16 to 60 years old (Table 4). The predicted probability of AH increases as the PP narrows (Fig. 1).

DISCUSSION

Bleeding is the number 1 cause of preventable death in the trauma patient, and all efforts should be directed at detecting the source of bleeding, stopping the bleeding, and replacing lost volume. There has been a vast array of studies examining the utility of clinical vital signs as a marker that the patient is bleeding. Heart rate has been proposed as a potential early indicator, with a compensatory increase in heart rate in response to volume loss.[8] However, several studies have shown that although tachycardia is independently associated with hypotension, its sensitivity and specificity limits its usefulness in the initial evaluation of trauma victims.[9] Furthermore, heart rate alone, specifically tachycardia, is not sufficient to indicate hypovolemia or the need for hemorrhage control.[10,11] Heart rate varies widely and can be altered by many variables after injury, including stress and pain. The phenomenon of relative bradycardia (defined as systolic blood pressure ≤ 90mmHg and heart rate ≤ 90 bpm) has also been documented as a fairly common hemodynamic finding, seen in upwards of one-third of patients, during which time the heart is unable to respond to hypovolemic shock.[12] Therefore, heart rate alone is unreliable in identifying patients who are bleeding and require immediate intervention.

Hypotension, often defined as a SBP < 90 mmHg and further redefined at differing thresholds such as a SBP < 110 mmHg,[13] can be a strong predictor of mortality as well as the need for surgical intervention. A single SBP < 105 mmHg during the trauma resuscitation has been shown to suggest the presence of more severe injuries requiring intervention.[14] Additionally, when compared with trauma score and capillary refill, a SBP < 90 mmHg was the most sensitive parameter found to detect uncontrolled hemorrhage, but identified only 50% of blunt trauma patients with bleeding.[15] Pre-hospital and ED hypotension have also been shown to be strong predictors of both internal injuries and mortality.[16-18] However, the literature also indicates that by the time SBP

Table 1. Demographics of Trauma Patients, January 2010 to October 2014 (n = 18,015)

Variable	Total (n = 18,015)	AH (n = 283)	Non−AH (n = 17,732)	p Value
Age, y, median (IQR)	40 (26−56)	34 (24−48)	40 (26−56)	<0.0001
Male sex, n (%)	13,398 (74.4)	244 (86.2)	13,154 (74.2)	<0.0001
Race, n (%)	18,015	283	17,732	0.0590
Hispanic	10,028 (55.7)	178 (62.9)	9,850 (55.5)	
White	4,230 (23.5)	48 (17.0)	4,182 (23.6)	
Black	1,643 (9.1)	21 (7.4)	1,622 (9.1)	
Asian	1,615 (9.0)	28 (9.9)	1,587 (8.9)	
Other/unknown	499 (2.8)	8 (2.8)	491 (2.8)	
Weight, kg, mean ± SD	71.3 ± 30.4	78.8 ± 24.9	71.2 ± 30.4	<0.0001
Mechanism, n (%)	18,015	283	17,731	<0.0001
Blunt	15,271 (84.8)	135 (47.7)	15,136 (85.4)	
GLF	5,316 (29.5)	7 (2.5)	5,309 (29.9)	
MVC	3,369 (18.7)	39 (13.8)	3,330 (18.8)	
AVP	2,418 (13.4)	52 (18.4)	2,366 (13.3)	
Other	1,787 (9.9)	4 (1.4)	1,783 (10.1)	
Assault	1,319 (7.3)	2 (0.7)	1,317 (7.4)	
MCC	806 (4.5)	23 (8.1)	783 (4.4)	
Fall from height	256 (1.4)	8 (2.8)	248 (1.4)	
Penetrating	2,255 (12.5)	147 (51.9)	2,108 (11.9)	
GSW	1,065 (5.9)	91 (32.2)	974 (5.5)	
SW	1,008 (5.6)	56 (19.8)	952 (5.4)	
Other	182 (1.0)	0 (0.0)	182 (1.0)	
Unknown	489 (2.7)	1 (0.4)	265 (1.5)	
ISS, median (IQR)	5 (2−10)	25 (16−34)	5 (2−10)	<0.0001
Field GCS, median (IQR)	15 (14−15)	15 (9−15)	15 (14−15)	<0.0001
Admission GCS, median (IQR)	15 (15−15)	14 (8−15)	15 (15−15)	<0.0001
Field SBP, median (IQR)	134 (118−150)	108 (92−136)	135 (119−150)	<0.0001
Admission SBP, median (IQR)	135 (121−150)	124 (106.5−140)	135 (121−150)	<0.0001
Field hypotension, SBP <90, n (%)	442 (3.4)	44 (18.0)	398 (3.2)	<0.0001
Field HR, mean ± SD	96 ± 20	104 ± 24	96 ± 20	<0.0001
Admission HR, mean ± SD	91 ± 20	110 ± 30	91 ± 20	<0.0001
Field tachycardia, n (%)	5,779 (45.3)	160 (61.1)	5,619 (45.0)	<0.0001
Tachycardia, n (%)	5,754 (32.0)	176 (62.6)	5,578 (31.5)	<0.0001
Field pulse pressure, mean ± SD	54 ± 20	42 ± 20	54 ± 20	<0.0001
Pulse pressure, mean ± SD	53 ± 20	39 ± 18	53 ± 19	<0.0001
Field pulse pressure < 25 mmHg, n (%)	399 (0.5)	27 (13.0)	372 (3.3)	<0.0001
ED pulse pressure < 25 mmHg, n (%)	897 (2.2)	55 (14.4)	842 (4.7)	<0.0001

Bleed defined as CAT+ (3U within 1 h in the first 24-h period) and procedure (OR or IR) for bleeding.
AH, active hemorrhage; AVP, auto vs pedestrian; CAT+, critical administration threshold hemorrhage; ED, emergency department; GCS, Glasgow Coma Score; GLF, ground level fall; GSW, gunshot wound; HR, heart rate; IQR, interquartile range; IR, interventional radiology; ISS, Injury Severity Score; MCC, motorcycle crash; MVC, motor vehicle collision; Non-AH, non-active hemorrhage; OR, operating room; SBP, systolic blood pressure; SW, stab wound.

Table 2. Interventions of Trauma Patients January 2010 to October 2014 (n = 18,015)

Variable	Total (n = 18,015)	AH (n = 283)	Non-AH (n = 17,732)	p Value
Field intubation, n (%)	55 (0.4)	13 (4.9)	42 (0.3)	<0.0001
IVF, mean ± SD	1,323 ± 1096	1,511 ± 1026	1,319 ± 1,097	0.0280
pRBC, median (IQR)				
24 h	0 (0–0)	10 (5–20)	0 (0–0)	<0.0001
Total	0 (0–0)	12 (6.5–23)	0 (0–0)	<0.0001
FFP, median (IQR)				
24 h	0 (0–0)	5 (2–12)	0 (0–0)	<0.0001
Total	0 (0–0)	6 (2–16)	0 (0–0)	<0.0001
Plt, median (IQR)				
24 h	0 (0–0)	1 (0–3)	0 (0–0)	<0.0001
Total	0 (0–0)	1 (0–3)	0 (0–0)	<0.0001
Cryo, median (IQR)				
24 h	0 (0–0)	0 (0–0)	0 (0–0)	<0.0001
Total	0 (0–0)	0 (0–0)	0 (0–0)	<0.0001
Transfusion given, n (%)	2,650 (14.7)	283 (100.0)	2,367 (13.3)	<0.0001
Interventional radiology, n (%)	82 (0.5)	16 (5.7)	66 (0.4)	<0.0001
IR positive	73 (0.4)	14 (4.9)	59 (0.3)	<0.0001
Bilateral int iliac artery	24 (0.1)	8 (2.8)	16 (0.1)	<0.0001
Other IR	23 (0.1)	6 (2.1)	17 (0.1)	<0.0001
Splenic artery	13 (0.1)	0 (0.0)	13 (0.1)	0.8410
Hepatic artery	8 (0.0)	1 (0.4)	7 (0.0)	0.1190
Pelvis	7 (0.0)	2 (0.7)	5 (0.0)	0.0050
Renal artery	2 (0.0)	0 (0.0)	2 (0.0)	0.9690
IR negative	9 (0.0)	2 (0.7)	7 (0.0)	0.0080
Operative intervention, n (%)	815 (4.5)	267 (94.3)	548 (3.1)	<0.0001
With bleeding	528 (2.9)	267 (94.3)	261 (1.5)	<0.0001
No bleed on laparotomy	309 (1.7)	13 (4.6)	296 (1.67)	
Vessel ligation	10 (0.1)	5 (1.8)	5 (0.0)	<0.0001
Vessel repair	5 (0.0)	4 (1.4)	1 (0.0)	<0.0001
Thoracotomy, n (%)	120 (0.7)	85 (30.0)	35 (0.2)	<0.0001
Sternotomy, n (%)	32 (0.2)	16 (5.7)	16 (0.1)	<0.0001
Laparotomy, n (%)	719 (4.0)	209 (73.9)	510 (2.9)	<0.0001
Hemoperitoneum, n (%)	410 (2.3)	196 (69.3)	214 (1.2)	<0.0001
Solid organ injury	278 (1.5)	142 (50.2)	136 (0.8)	<0.0001
Bowel injury with bleed	75 (0.4)	22 (7.8)	53 (0.3)	<0.0001
Vascular injury	67 (0.4)	43 (15.2)	24 (0.1)	<0.0001
Other hemostasis pack	6 (0.0)	2 (0.7)	4 (0.0)	0.0040
No hemoperitoneum, n (%)	309 (1.7)	13 (4.6)	296 (1.7)	<0.0001
Bowel injury no bleed	120 (0.7)	6 (2.1)	114 (0.6)	0.0020
Negative laparotomy	114 (0.6)	14 (4.9)	100 (0.6)	<0.0001
Mesenteric injury	64 (0.4)	8 (2.8)	56 (0.3)	<0.0001
Diaphragm injury	63 (0.3)	9 (3.2)	54 (0.3)	<0.0001
Bladder injury	36 (0.2)	3 (1.1)	33 (0.2)	0.0190
Stomach injury	33 (0.2)	2 (0.7)	31 (0.2)	0.0950
Other laparoscopic finding	24 (0.1)	1 (0.4)	23 (0.1)	0.3160

AH, active hemorrhage; Cryo, cryoprecipitate; FFP, fresh frozen plasma; IQR, interquartile range; IR, interventional radiology; IVF, intravenous fluids; Non-AH, nonactive hemorrhage; Plt, platelets; pRBC, packed red blood cells.

begins to decline, the patient has already begun the onset of cardiovascular collapse.[19]

Moving beyond individual vital signs, scoring systems have also been developed in hopes of identifying life-threatening hemorrhage. Several of these have been tested, but have sensitivities of only 50% to 60%.[20,21] The pulse rate over pressure evaluation index, which is calculated by heart rate over pulse pressure, was found to have a sensitivity of 55%, with a specificity of 79%, in its ability to identify those who will decompensate in the emergency department.[22] Similarly, the Shock Index, which is calculated as heart rate over SBP, was found to be associated with bleeding, but again, had a sensitivity of only 54.5%. Several contemporary studies have found that the utility of the Shock Index deteriorates further if the patient has underlying diabetes, hypertension, or coronary artery disease.[23] Last, a Reverse Shock Index (SBP/HR) cut off of <1 was found to be a sign of poor outcome in adult trauma patients, even when normotensive;[24] however, this study noted that due to fluctuations in vital signs, a patient's true reverse shock index value was difficult to assign.

In this study, pulse pressure correlated well with patients requiring transfusion and further intervention for hemorrhage control. Although only 1.6% of the study population met the definition of active hemorrhage, these patients had a statistically significant narrowing of pulse pressure that was greater than that in the non-AH group and were found to have more significant injuries during IR and operative exploration. Furthermore, narrowed ED pulse pressure was shown not only to be an independent predictor of active hemorrhage, but as it narrows, the predicted probability of active hemorrhage increases. Pulse pressure is a stand alone early warning that bleeding is occurring and can easily be obtained and repeated in the resuscitation area with standard monitoring. Although previous studies have discussed its utility in combination with other clinical data, we now know that pulse pressure on its own can be a critical early data point in assessing the trauma patient, especially in the setting of normal systolic blood pressure. The presence of a narrowed pulse pressure should raise suspicion that there is occult, ongoing blood loss and a search for the source is warranted. The pulse pressure response also varies by age. Older patients are unable to physiologically compensate in the same manner as younger patients. As such, and not surprisingly, for patients more than 60 years old, the PP cut off was 15 mmHg higher than that seen in younger patients. Regardless of age, the pulse pressure can be quickly calculated in the resuscitation bay. Therefore, even in the nonhypotensive patient, if pulse pressure is narrowed, a search for potential sources is warranted due to the strong association with active hemorrhage.

This is a single-center retrospective study based on trauma registry data and is therefore inherently limited by the study design. The study subjects' hemodynamic status was determined by a single static blood pressure when they arrived in the ED. Additionally, comorbidities of the study subjects that may affect pulse pressure were not available for analysis.

Table 3. Multivariate Analysis Regarding the Association Between Variables and Active Hemorrhage

	Clinically significant bleed			
Forward conditional regression, variable	**p Value**	**Adjusted p value**	**AOR**	**CI**
Age	<0.0001	.044	1.01	1.000, 1.020
Penetrating	<0.0001	<.0001	9.476	6.493, 13.826
Field SBP	<0.0001	<.0001	0.985	0.980, 0.990
ED HR	<0.0001	<.0001	1.024	1.018, 1.031
ISS	<0.0001	<.0001	1.136	1.121, 1.152
ED pulse pressure	<0.0001	<.0001	0.975	0.965, 0.984
ED GCS	<0.0001	.599		
Race	<0.0001	.138		
Weight	<0.0001	.272		
Field GCS	<0.0001	.401		
Field HR	<0.0001	.959		
Field pulse pressure	<0.0001	.286		
Sex	<0.0001	.428		

Cox & Snell R Square 0.069. Nagelkerke R square 0.410. Multicollinearity test was checked before doing multivariate analysis. Logistical regression performed with variables which were significant in the univariate analysis.

AH, active hemorrhage defined as CAT+ and OR or IR to control bleed; AOR, adjusted odds ratio; CAT+, critical administration threshold hemorrhage; ED, emergency department; GCS, Glasgow Coma Scale; HR, heart rate; IR, interventional radiology; ISS, Injury Severity Score; OR, operating room; SBP, systolic blood pressure.

Table 4. Cutoff Analysis of Pulse Pressure Values Corresponding with Bleed in Patients Aged 16 to 60 Years vs Patients 61 Years or Older

Pulse pressure	AOR (95% CI)	Adjusted p value	R2	AUC (95% CI)
Age 16 to 60 y				
<10 or ≥10	2.30 (1.32–4.03)	.003	0.399	0.935 (0.918–0.952)
<15 or ≥15	3.146 (1.42–6.95)	<.0001	0.399	0.935 (0.918–0.952)
<20 or ≥20	1.85 (1.07–3.20)	.028	0.397	0.935 (0.918–0.952)
<25 or ≥25	1.91 (1.27–2.87)	.002	0.400	0.936 (0.919–0.953)
<30 or ≥30	2.24 (1.58–3.16)	<.0001	0.405	0.936 (0.919–0.953)
<35 or ≥35	2.73 (1.98–3.77)	<.0001	0.414	0.939 (0.923–0.955)
<40 or ≥40*	2.73 (1.98–3.75)*	<.0001*	0.414*	0.940 (0.925–0.955)*
<45 or ≥45	2.35 (1.69–3.27)	<.0001	0.409	0.939 (0.924–0.955)
<50 or ≥50	2.18 (1.53–2.11)	<.0001	0.405	0.938 (0.922–0.954)
<55 or ≥55	2.30 (1.53–3.45)	<.0001	0.404	0.937 (0.921–0.954)
<60 or ≥60	2.66 (1.61–4.38)	<.0001	0.404	0.938 (0.922–0.954)
<65 or ≥65	2.81 (1.53–5.16)	<.0001	0.402	0.937 (0.921–0.953)
Age 61 y or older				
<50 or ≥50		0.258		
<55 or ≥55*	3.438 (1.440–8.205)*	0.005*	0.377*	0.955 (0.929–0.981)*
<60 or ≥60	4.544 (1.650–12.510)	0.003	0.383	0.951 (0.919–0.983)
<65 or ≥65	4.796 (1.579–14.564)	0.006	0.381	0.954 (0.924–0.985)
<70 or ≥70	4.797 (1.388–16.574)	0.013	0.376	0.951 (0.917–0.984)
<75 or ≥75		0.227		

Covariates: age, injury severity score, penetrating, field systolic blood pressure, emergency department heart rate. Outcome: CAT+ and procedure (OR or IR) in 24 h.
*Significant.
AOR, adjusted odds ratio; AUC, area under curve; CAT+, critical administration threshold hemorrhage; IR, interventional radiology; OR, operating room.

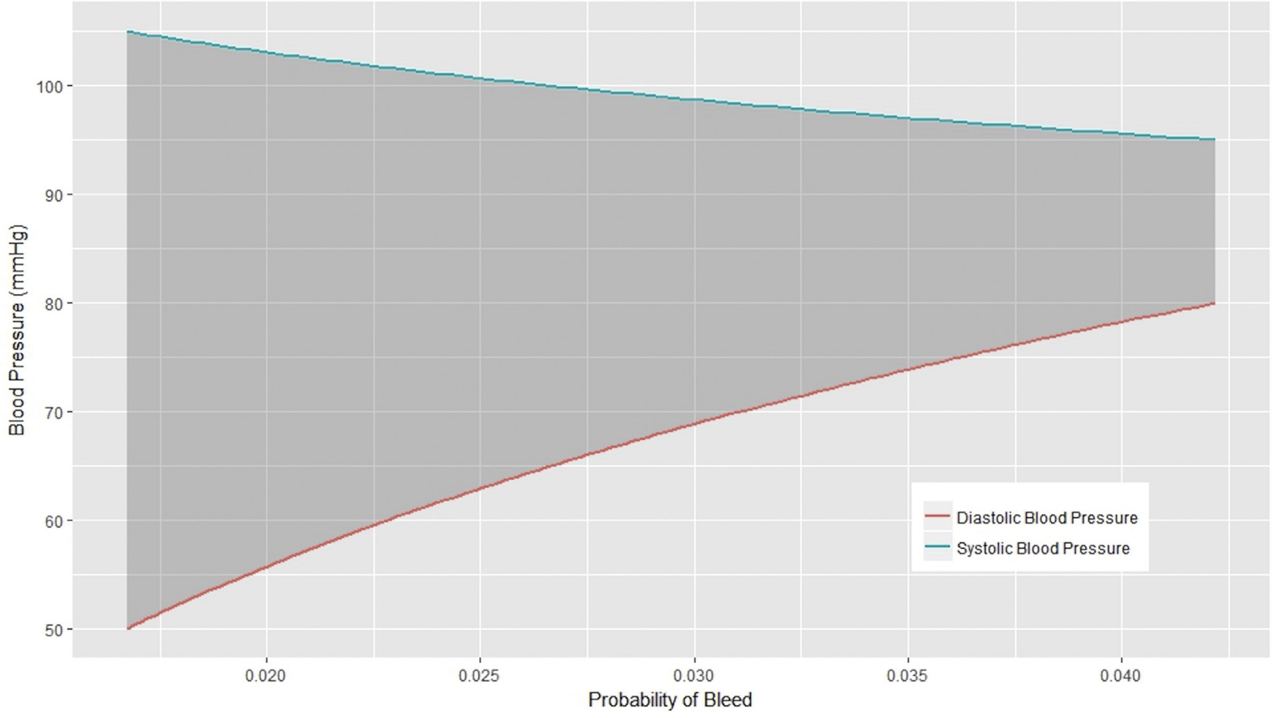

Figure 1. Predicted probability of bleeding as a function of pulse pressure in all patients.

CONCLUSIONS

The utility of pulse pressure as an independent predictor of hemorrhage has not previously been established. In this study, a narrowed pulse pressure, even without hypotension, was associated with active hemorrhage requiring blood product transfusion and intervention for hemorrhage control. The cut-off value depends on the age of the patient, with $\geq$55 mmHg in patients 61 years or older and <40 mmHg for those 16 to 60 years old. As the pulse pressure narrows, the predicted probability of active hemorrhage also increases. Pulse pressure is a simple and rapidly calculated variable that can be used early in the resuscitation period to help guide the treatment of injured patients.

Author Contributions

Study conception and design: Inaba, Priestley, Byerly
Acquisition of data: Priestley, Byerly, Wong
Analysis and interpretation of data: Byerly, Biswas
Drafting of manuscript: Inaba, Priestley, Byerly
Critical revision: Inaba, Lam, Benjamin, Demetriades

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