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Risk stratification in emergency medicine: towards improved age and sex adjusted risk assessment

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THE DIFFERENCE BETWEEN THE PATIENTS' INITIAL AND PREVIOUSLY MEASURED SYSTOLIC BLOOD PRESSURE AS PREDICTOR OF MORTALITY IN OLDER EMERGENCY DEPARTMENT PATIENTS

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ABSTRACT

Purpose To assess how often baseline systolic blood pressure (SBP) could be retrieved from the Electronic Health Record (EHR) in older Emergency Department (ED) patients. Secondly, to assess whether the difference between baseline SBP and initial SBP in the ED (Δ SBP) was associated with mortality.

Methods A multicenter hypothesis-generating cohort-study including patients ≥ 70 years. EHRs were searched for baseline SBPs. The association between Δ SBP and 30-day mortality was investigated.

Results. Baseline SBP was found in 220 out of 300 patients (73.3%; 95%CI 68.1-78.0%). In 72 patients with normal initial SBPs (133-166 mmHg) in the ED, fifteen (20.8%) had a negative Δ SBP with 20.0% mortality. A negative Δ SBP was associated with 30-day mortality (AHR 4.7; 1.7-12.7).

Conclusions. Baseline SBPs are often available in older ED patients. The Δ SBP may have prognostic value and may be used as an extra variable to recognize hypotension. Future studies should clarify whether the Δ SBP improves risk stratification in the ED.

INTRODUCTION

Due to higher prevalence of hypertension in older patients,^{79, 80} a seemingly normal blood pressure in older Emergency Department (ED) patients may in fact be relative hypotension and may not be recognized as such, possibly leading to under-treatment and higher mortality.

Therefore, knowledge of an individual ED patient's baseline systolic blood pressure (SBP) may be essential to assess whether the initial SBP reflects hypotension or normotension. Unfortunately, baseline SBP may often not be available in the ED as Electronic Health Record (EHR) are not routinely shared among general practitioners and hospitals,⁸¹ due to privacy laws and under registration.

Therefore, the aim of the present hypothesis-generating study is two-fold: First, to assess how often individual baseline SBPs are available in older ED patients, and secondly, to evaluate whether the absolute reduction of SBP compared to the patients' baseline SBP value (Δ SBP) is associated with 30-day mortality. The prognostic value of Δ SBP has not been studied before using the patients' individual baseline SBP values. If baseline SBPs are often available and the Δ SBP is associated with 30-day mortality, this variable may contribute to better risk stratification leading to better recognition of vital threads in ED patients.

METHODS

Study design and setting

This multicenter retrospective cohort study was conducted in two EDs in the Netherlands: a tertiary care center with approximately 25,000 ED visits annually and an urban care center with approximately 20,000 ED visits annually. Data were collected from 1 to 27 January 2018. The study was approved by the medical ethics committee of the MMC. The study was registered in the Netherlands Trials Register: NL9029.

Patient selection

During the study period, all consecutive ED patients ≥ 70 years who were subsequently hospitalized were included (the prevalence of hypertension increases above this age, according to Statistics Netherlands (www.cbs.nl)). Patients were excluded if non-urgently triaged according to the Manchester or Dutch Triage System or transferred to another hospital.

Outcomes

The primary outcome was the number (N) (%) of patients with an SBP documented (objective 1) or 30-day mortality (objective 2). If patients were discharged alive and 30-day mortality was not known, they were considered alive after 30 days.

Sample size

See supplementary file 1.

Data collection

Data were collected from the EHR. One researcher in each hospital (IvI, IvD) extracted the data. No clear definition exists in the literature of a baseline SBP. In our study, the baseline SBP was defined as the mean of a maximum of the three most recent SBP values from the General Practitioner (GP) referral letters and the three most recent SBP values from the outpatient clinical records. SBP values were not considered as a baseline value if the notes or records described signs for acute illness (i.e., pneumonia, urinary tract infection or fever) or acute pain (i.e., trauma, acute abdominal pain), or if patients were referred to the ED on the same day. The Δ SBP was calculated by subtracting the baseline SBP from the initial SBP in the ED. Thus, a negative Δ SBP indicated that the SBP in the ED was lower than the patients' baseline SBP.

Statistical analyses

Patient characteristics were described for survivors and non-survivors as mean (standard deviation (SD)), median (interquartile range (IQR)) or number (N, (%)) as appropriate. Paired Student's t-tests, Wilcoxon Signed rank test and Pearson χ^2 tests were used to compare patient characteristics. The Δ SBP and initial SBP in the ED were categorized in tertiles based on their distribution. The categorized Δ SBP could be negative, normal, and positive. The categorized initial SBP in the ED was considered low, normal, and high. A cox regression analysis was used to assess the crude and adjusted association between Δ SBP, the initial SBP in the ED, and 30-day mortality, adjusted for age, sex, and triage category (urgent or very urgent/immediate) as a measure of disease severity. The Kaplan-Meier method was employed to generate survival plots, using the log-rank test, for 30-day mortality.

A sensitivity analysis was performed limited to patients who had baseline SBP values documented within 5 years prior to ED-presentation, to limit the chance that antihypertensive drugs were prescribed and because individual baseline values may have changed by ageing.¹²

Adjusted Hazard Ratio's (AHRs) are presented with 95% confidence intervals (95% CIs).

An α of 0.05 was considered as statistically significant. Data were analyzed using SPSS (version 25.0, IBM, New York, USA).

RESULTS

During the study period, 3102 patients presented to the ED of which 300 patients met the inclusion criteria (figure 1). Baseline SBP values were found in 220 patients (73.3%; 95% CI 68.1-78.0%). In the urban care center, a baseline SBP was found in 117 out of 141 patients (83.0%; 75.7-88.8%) compared to 103 out of 159 patients (64.8%; 56.8-72.2%) in the tertiary care center (difference: 18.2%; 8.5-27.9%). 30-day mortality was 14.3% (10.3-19.6%). Differences in patient characteristics existed between survivors and non-survivors (see table 1).

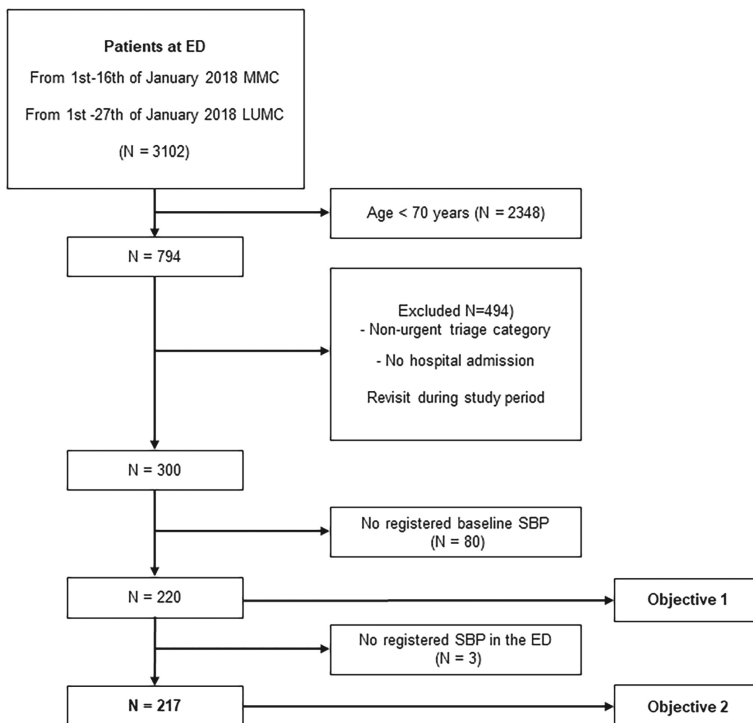


Figure 1 Patient flow and inclusion through the study. The Electronical Patient Records were used to retrospectively include patients in two hospitals starting at 1st January 2018.

Table 1 Patients characteristics

	Total cohort N=217 (100%)	Survivors N = 196 (90.3%)	Non-survivors N = 21 (9.7%)	P value
Demographics				
Age, years, mean (SD)	79 (6.6)	79 (6.4)	82 (7.6)	0.04
Females, N (%)	108 (49.8)	100 (51.0)	8 (38.1)	0.36
Tertiary care center, N (%)	100 (46.1)	90 (45.9)	10 (47.6)	1.0
Baseline SBP †				
Baseline SBP, mmHg, mean (SD)	142 (16.8)	142 (16.4)	143 (20.9)	0.74
Months till ED visit, median [IQR]	33 [16 – 56]	32 [16 – 53]	40 [18 – 77]	0.27
Δ SBP, N (%), ‡				
Negative (< -6.5 mmHg)	73 (33.6)	59 (30.1)	13 (61.9)	0.01
Normal (6.5 – 21.7mmHg)	72 (33.2)	70 (35.7)	3 (14.3)	
Positive (>21.7mmHg)	72 (33.2)	67 (34.2)	5 (23.8)	
Comorbidity				
CCI, mean (SD)	5 (3.1)	5 (3.1)	5 (2.9)	0.87
Use of antihypertensive agents, N (%)	161 (74.2)	145 (74.0)	16 (76.2)	0.88
Arrival by ambulance, N (%)	127 (58.5)	112 (57.1)	15 (71.4)	0.26
Triage category				
Urgent, N (%)	128 (59.0)	121 (61.7)	7 (33.3)	<0.01
Very-urgent, N (%)	76 (35.0)	67 (34.2)	9 (42.9)	
Immediate, N (%)	9 (4.1)	4 (2.0)	5 (23.8)	

Table 1 Patients characteristics (continued)

Specialty	Total cohort N=217 (100%)	Survivors N = 196 (90.3%)	Non-survivors N = 21 (9.7%)	P value
Internal medicine, N (%)	78 (35.9)	68 (34.7)	10 (47.6)	0.48
Pulmonary medicine, N (%)	53 (24.4)	49 (25.0)	4 (19.0)	
Neurology, N(%)	40 (18.4)	39 (19.9)	1 (4.8)	
Cardiology, N (%)	16 (7.4)	13 (6.6)	3 (14.3)	
Other, N (%)	29 (13.4)	26 (13.3)	3 (14.3)	
Top three chief complaints				0.87
Feeling unwell, N (%)	55 (25.3)	51 (26.0)	4 (19.0)	
Dyspnea, N (%)	50 (23.0)	41 (20.9)	9 (42.9)	
Abdominal pain, N (%)	14 (6.5)	13 (6.6)	1 (4.8)	
Other, N (%)	54 (24.9)	50 (25.5)	4 (19.0)	
Initial vital signs in the ED				
SBP, mmHg, mean (SD)	150 (35.4)	151 (34.8)	137 (39.8)	0.07
SBP, categorized, mmHg, N (%)				0.03
Low (< 133 mmHg)	76 (35.0)	63 (32.1)	13 (61.9)	
Normal (133-166 mmHg)	71 (32.7)	67 (34.2)	4 (19.0)	
High (>166 mmHg)	70 (32.3)	66 (33.7)	4 (19.0)	
HR bpm, median [IQR]	86 [75-104]	85 [75-103]	98 [72-107]	0.27
RR /min, median [IQR]	20 [16-28]	18 [16-25]	28 [22 - 32]	<0.01
SPO2, %, median [IQR]	96 [94-97]	96 [94-97]	94 [90-97]	0.03

Table 1 Patients characteristics (continued)

	Total cohort N=217 (100%)	Survivors N = 196 (90.3%)	Non-survivors N = 21 (9.7%)	P value
O2 administration, N (%)	102 (47.0)	83 (42.3)	19 (90.5)	<0.01
O2, L/min, median [IQR]	0.0 [0.0 – 4.0]	0.0 [0.0-3.0]	4.0 [0.0-6.0]	<0.01
Body temperature, °C, median, [IQR] (26)	37.3 [36.6-38.4]	37.2 [36.7-38.4]	37.5 [36.0-38.4]	0.89
NRS 1-10, median [IQR]	1 [0-3]	1 [0 -3]	0 [0-2]	0.07
Administered fluid in ED, N (%)	75 (34.6)	64 (32.7)	11 (52.4)	0.08
Disposition				<0.01
Admission to a ward, N (%)	171 (78.8)	158 (80.6)	13 (61.9)	
Admission to MCU, N (%)	5 (2.3)	5 (2.6)	0 (0)	
Admission to ICU, N (%)	10 (4.6)	4 (2.0)	6 (28.6)	
Admission to CCU, N (%)	9 (4.1)	8 (4.1)	1 (4.8)	
Admission to Neurocare, N (%)	22 (10.1)	21 (10.7)	1 (4.8)	

Table 1 Patients characteristics (continued)

	Total cohort N=217 (100%)	Survivors N = 196 (90.3%)	Non-survivors N = 21 (9.7%)	P value
Length of hospital stay days, median [IQR]	5 [2-9]	5 [2-9]	3 [2-9]	0.44

Abbreviations: N = number, SD = Standard deviation, IQR = Interquartile range, CCI = Charlson Comorbidity Index, ED = emergency department, SBP = systolic blood pressure, mmHg = millimetre mercury, Δ = delta, DBP = diastolic blood pressure, HR = heart rate, RR = respiratory rate, SPO2 = peripheral oxygen saturation, O2 = oxygen, °C = degree Celsius, NRS (0-10) = numeric rating scale for pain, MCU = medium care unit, ICU = intensive care unit, CCU = cardiac care unit, Neurocare = high dependency care unit for neurology patients.

†The baseline SBP was defined as a mean of SBP values which included a maximum of the three most recent SBP values from referral letters of the General Practitioner and the three most recent SBP values from the outpatient clinical records. SBP values were not considered as a baseline value if the letters or records described signs for acute illness (i.e. pneumonia, urinary tract infection or fever) or acute pain (i.e. trauma, acute abdominal pain), or if patients were referred to the ED at the same day. The mean time from the measured baseline SBP till ED visit is presented.

‡The Δ SBP was calculated by subtracting the baseline SBP from the first measured SBP in the ED. A negative Δ SBP therefore indicated that the SBP in the ED was lower than the patients' baseline SBP. the Δ SBP was categorized in tertiles based on distribution. Missing values (survivors; non-survivors) = Use of antihypertensive agents (2;0), Arrival by ambulance (5;0), Triage category (4;0), responsible specialism (1;0), Presenting complaints (41;3), HR (8;1), RR (34;2), SPO2 (16;2), O2 administration (59;6), Body temperature (23;3), NRS (51;7), Administered fluid in Ed (4;0), Admission to (3;1).

A cross table between the categorized Δ SBP and the initial SBP in the ED showed that 15 out of 72 patients (20.8%; 13.1-31.6%) with a negative Δ SBP had a normal (mid tertile) initial SBP in the ED (see table 2). Mortality was highest if the Δ SBP was negative and the initial SBP in the ED was low, with 15 out of 57 deceased patients (%26.3).

Table 3 shows the crude and adjusted association for the Δ SBP and the initial SBP in the ED and 30-day mortality. Kaplan Meier survival curves confirm the prognostic role of Δ SBP in ED patients ≥ 70 years (figure 2).

The sensitivity analysis showed similar results (supplementary file 2).

Table 2. A cross table of categorized Δ SBP and the initial SBP in the ED with numbers of 30-day mortality

	Initial SBP in the ED			Total (N)
	Low, <133mmHg, (N)	Normal, 133-166mmHg, (N)	High, >166mmHg, (N)	
Δ SBP (categorized)	57	15	0	72
Negative (< -6.5 mmHg)	† 15 (26.3%)	† 3 (20.0%)	† 0 (0.0%)	
Normal (-6.5 – 21.7mmHg)	18	43	12	73
	† 2 (11.1%)	† 2 (4.7%)	† 1 (8.3%)	
Positive (>21.7mmHg)	1	13	58	72
	† 0 (0.0%)	† 2 (15.4%)	† 6 (10.3%)	
Total (N)	76	71	70	217

SBP = Systolic Blood Pressure, ED = Emergency Department, Δ = delta. The Δ SBP and the initial SBP in the ED were categorized in tertiles based on their distribution. † number of patients who died in 30days, with percentages in that group.

Table 3. The association between a delta systolic blood pressure and 30-day30-day mortality in hospitalized Emergency Department patients ≥ 70 years.

	30-day mortality			
	Univariable HR (95% CI)	P-value	Multivariable AHR (95% CI)	P-value
ΔSBP (categorized)				
Negative (< -6.5 mmHg)	4.2 (1.5-11.2)	0.01	4.7 (1.7-12.7)	<0.01
Normal (-6.5 – 21.7mmHg)	1.0		1.0	
Positive (>21.7mmHg)	1.7 (0.55-5.1)	0.37	2.0 (0.63-6.1)	0.25
Initial SBP in the ED (categorized)				
Low (<133mmHg)	2.5 (1.0-5.9)	0.05	2.5 (1.0-6.0)	0.04
Normal (133-166mmHg)	1.0		1.0	
High (>166mmHg)	1.0 (0.35-2.9)	0.99	1.1 (0.38-3.1)	0.90

Abbreviations: HR = Hazard Ratio, AHR = Adjusted Hazard Ratio, 95% CI = 95% Confidence Interval, SBP = Systolic Blood Pressure, ED = Emergency Department, Δ = delta.

The association between Δ SBP and 30-day mortality, and initial SBP in the ED and 30-day mortality, were both adjusted for age, sex, and triage category (urgent, or very urgent/immediate). Because of multi-collinearity, we did not include the initial SBP in the model with delta SBP and mortality.

The Δ SBP was calculated by subtracting the baseline SBP from the first measured SBP in the ED. A negative Δ SBP, therefore, indicated that the SBP in the ED was lower than the patients' baseline SBP. The Δ SBP and the initial SBP in the ED were categorized in tertiles based on their distribution.

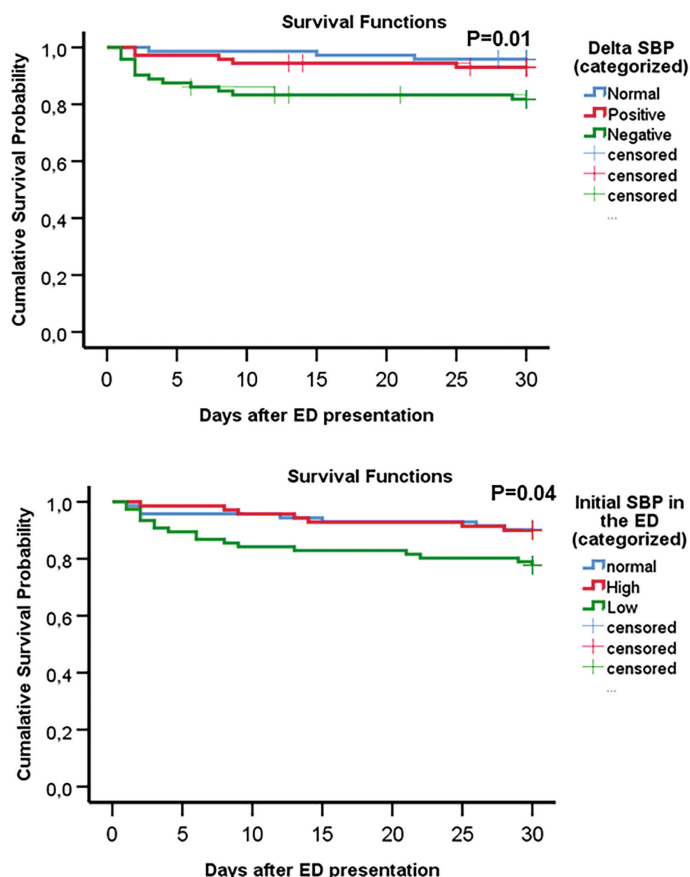


Figure 2 A Kaplan-Meier curve is shown for categorized delta systolic blood pressure and 30-day mortality, and for the initial systolic blood pressure in the Emergency Department and 30-day mortality.

DISCUSSION

In this hypothesis-generating study a baseline SBP value could be retrieved from the EHR in most hospitalized ED patients ≥ 70 years. In addition, 21% of patients with a normal SBP at ED presentation had a negative Δ SBP and these patients had an increased risk for 30-day mortality.

Low SBP is a well-known risk factor for mortality in older ED patients.^{11,66} Due to the high prevalence of hypertension in the elderly,^{79,82} a seemingly normal SBP may, in fact, be relative hypotension. Consequently, this may lead to an underestimation of the risk and a lower urgency to initiate treatment. Thus,

the deviation from a patients' normal SBP may be relevant. This hypothesis is supported by a study in patients undergoing abdominal surgery, in which an individualized, targeted SBP reduced the risk of postoperative organ dysfunction compared to standard management.⁸³ This study suggests that individualized treatment using the baseline SBP as a target may improve outcomes. In another study in patients with septic shock, a higher target mean arterial pressure resulted in minor kidney injury among patients known with chronic hypertension.⁸⁴

We are not aware of earlier studies on the association between the difference in SBP between baseline values and SBP at presentation in the ED and outcome in acutely ill patients. However, using another definition, Δ SBP showed prognostic value in trauma patients in the ED.⁸⁵⁻⁸⁷ In these studies, the Δ SBP was calculated as the difference between the initial SBP in the ED and the prehospital SBP on the same day. A declining SBP in the hours before ED admission was associated with increased mortality, as was also shown for hospitalized patients.^{88,89} In our study, we did not attempt to study short-term SBP trends, but we assessed whether a lower SBP in the ED compared to a baseline SBP was associated with 30-day mortality in older patients. Although baseline SBP in our study could have been measured years before the ED visit, we hypothesized that this SBP would provide important information about the patients' normal value.

Our study was not designed to study whether the Δ SBP was a better predictor for mortality than the initial SBP in the ED. Nonetheless, our study may have implications for clinical practice. We found that even if SBP at admission is normal (> 133 mmHg), some patients had relative hypotension. Future studies should assess whether using the Δ SBP in risk stratification tools like, i.e., the National Early Warning Score has added value to the SBP alone. Also, many challenges are reported regarding health information exchange among hospitals and primary care centers.^{81,90} Because baseline SBPs may have significant prognostic value, our findings argue in favor of promoting health information exchange among hospitals and primary care centers to have baseline vital signs available in the ED.

Our study has several limitations. First, the baseline SBP was defined as a mean of values found in referral letters of GPs and outpatient clinical records. No information existed on how these SBPs were measured. Also, the median time of the measured baseline SBP till ED visit was substantial. Furthermore, antihypertensive agents could have been prescribed in the meantime, or baseline SBPs could have been changed by (patho)physiological changes.¹² We tried to overcome this with a sensitivity analysis using only baseline

SBPs measured <5 years from ED visit, which showed similar results. In addition, baseline SBP should be unaffected by pain, psychological stress, or acute illness. We cannot rule out the possibility that this was not always documented in the files, which could have influenced baseline SBP. Secondly, 30-day mortality was missing in seven patients who were discharged alive. However, five of these patients had a negative Δ SBP and therefore we do not expect this would have affected our results. Lastly, the limited sample size of this study and the two-center design limit the generalizability of our findings and may lead to overestimation of the effect size. Nonetheless, we believe that the Δ SBP needs further investigation in larger prospective studies because it may improve recognition of hypotension.

SUPPLEMENTARY FILE 1

Sample size estimation: In this hypothesis-generating study, we wanted to include 200 patients for objective 2 in both hospitals. We expected that baseline SBP values would be available in approximately 70% of the patients. For objective 1 we therefore expected to include approximately 285 patients in total. Based on a previous study, the mortality in our patient selection would be approximately 8-10 percent, which would result in 16-20 deceased patients.⁹¹ We could therefore adjust for three potential confounders in the multivariable logistic regression analyses according to the existing rule of thumb.⁴⁴

SUPPLEMENTARY FILE 2

Sensitivity analysis, including hospitalized Emergency Department patients ≥ 70 years, who had baseline SBP values < 5 years old till the ED visit.

In-hospital mortality				
	Univariable OR (95% CI)	P-value	Multivariable AOR (95% CI)	P-value
ΔSBP (categorized)				
Negative (< -6.5 mmHg)	3.8 (1.0-14.6)	0.06	4.2 (1.0-17.1)	0.05
Normal ($-6.5 - 21.7$ mmHg)	1.00		1.00	
Positive (> 21.7 mmHg)	1.3 (0.3-6.1)	0.73	1.6 (0.3-7.6)	0.58
Initial SBP in the ED (categorized)				
Low (< 133 mmHg)	3.5 (0.9-13.2)	0.07	3.2 (0.83-12.7)	0.04
Normal (133-166 mmHg)	1.00		1.00	
High (> 166 mmHg)	0.99 (0.19-5.1)	0.99	1.1 (0.2-5.9)	0.90

Abbreviations: OR = Odds Ratio, AOR = Adjusted Odds Ratio, 95% CI = 95% Confidence Interval, SBP = Systolic Blood Pressure, ED = Emergency Department, Δ = delta.

The sensitivity included 185 patients in total, including 16 non-survivors.

The multivariable regression analysis was adjusted for age, sex and triage category (urgent, or very urgent/immediate).

The baseline SBP contained one SBP value closest to the ED visit and < 5 years. The Δ SBP was calculated by subtracting the baseline SBP from the first measured SBP in the ED. A negative Δ SBP therefore indicated that the SBP in the ED was lower than the patients' baseline SBP. The Δ SBP and the initial SBP in the ED were categorized in tertiles based on their distribution.

