



## ■ HIP

# Postoperative hypotension following acute hip fracture surgery is a predictor of 30-day mortality

## A PROSPECTIVE OBSERVATIONAL COHORT ANALYSIS

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### Aims

Hip fractures are some of the most common fractures encountered in orthopaedic practice. We aimed to identify whether perioperative hypotension is a predictor of 30-day mortality, and to stratify patient groups that would benefit from closer monitoring and early intervention. While there is literature on intraoperative blood pressure, there are limited studies examining pre- and postoperative blood pressure.

### Methods

We conducted a prospective observational cohort study over a one-year period from December 2021 to December 2022. Patient demographic details, biochemical results, and haemodynamic observations were taken from electronic medical records. Statistical analysis was conducted with the Cox proportional hazards model, and the effects of independent variables estimated with the Wald statistic. Kaplan-Meier survival curves were estimated with the log-rank test.

### Results

A total of 528 patients were identified as suitable for inclusion. On multivariate analysis, postoperative hypotension of a systolic blood pressure (SBP) < 90 mmHg two to 24 hours after surgery showed an increased hazard ratio (HR) for 30-day mortality (HR 4.6 (95% confidence interval (CI) 2.3 to 8.9);  $p < 0.001$ ) and was an independent risk factor accounting for sex (HR 2.7 (95% CI 1.4 to 5.2);  $p = 0.003$ ), age (HR 1.1 (95% CI 1.0 to 1.1);  $p = 0.016$ ), American Society of Anesthesiologists grade (HR 2.7 (95% CI 1.5 to 4.6);  $p < 0.001$ ), time to theatre > 24 hours (HR 2.1 (95% CI 1.1 to 4.2);  $p = 0.025$ ), and preoperative anaemia (HR 2.3 (95% CI 1.0 to 5.2);  $p = 0.043$ ). A preoperative SBP of < 120 mmHg was close to achieving significance (HR 1.9 (95% CI 0.99 to 3.6);  $p = 0.052$ ).

### Conclusion

Our study is the first to demonstrate that postoperative hypotension within the first 24 hours is an independent risk factor for 30-day mortality after hip fracture surgery. Clinicians should recognize patients who have a SBP of < 90 mmHg in the early postoperative period, and be aware of the increased mortality risk in this specific cohort who may benefit from a closer level of monitoring and early intervention.

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### Introduction

Hip fractures are one of the most common types of fractures encountered in orthopaedic practice, with a substantial disease burden. In the UK there are approximately 70,000 to 75,000 hospital admissions with hip fractures annually, with 72,160 in 2022, and an associated 30-day mortality of 6% to 7% according to the National Hip Fracture

Database.<sup>1</sup> It is estimated that hip fractures will affect 18% of females and 6% of males globally. Due to the consequences of an ageing population the number of hip fractures will reach an incidence of 4.5 million a year by 2050, despite hip fracture prevention measures.<sup>2,3</sup>

There are large societal and economic burdens for patients and healthcare systems in relation to

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**Table I.** Summary of patient characteristics.

Variable	Alive	Deceased	p-value
<b>Sex, n (%) (n = 528)</b>			0.021*
Male	130 (24.6)	19 (3.6)	
Female	355 (67.2)	24 (4.5)	
Mean age, yrs (SD) (n = 528)	81.3 (9.1)	87.5 (11.7)	< 0.001†
<b>ASA grade, n (%) (n = 522)</b>			< 0.001‡
I	8 (1.5)	0 (0)	
II	129 (24.7)	3 (0.6)	
III	284 (54.4)	22 (4.2)	
IV	58 (11.1)	18 (3.4)	
V	0 (0)	0 (0)	
Median time to theatre, hrs (IQR) (n = 518)	20.3 (13.5 to 30.8)	25.3 (14.3 to 40.3)	0.056§
Median preop Hb, g/l (IQR) (n = 528)	123 (112 to 133)	114 (104 to 125.5)	0.002§
Median last preop systolic BP, mmHg (IQR) (n = 523)	138 (124 to 155)	136 (115.5 to 147)	0.051§
<b>Anaesthetic, n (%) (n = 521)</b>			0.603*
GA	332 (63.7)	31 (5.6)	
Spinal	147 (28.2)	11 (2.1)	
<b>Inotropes, n (%) (n = 516)</b>			1.000*
Used	261 (50.6)	23 (4.5)	
Not used	214 (41.5)	18 (3.5)	
Median lowest systolic intraoperative BP, mmHg (IQR) (n = 381)	91 (77 to 111)	86.5 (72 to 97)	0.280§
Median intraoperative MAP, mmHg (IQR) (n = 450)	58 (49 to 68)	57 (51 to 66)	0.976§
Median lowest systolic BP 2 to 24 hrs postoperatively, mmHg (IQR) (n = 505)	102 (94 to 111)	93 (84 to 107)	0.004§

\*Fisher's exact test.

†Welch's t-test.

‡Chi-squared test.

§Mann-Whitney U test.

ASA, American Society of Anesthesiologists; BP, blood pressure; GA, general anaesthetic; IQR, interquartile range; MAP, mean arterial pressure; SD, standard deviation.

patients who suffer an acute hip fracture.<sup>2,4</sup> Efforts to identify at-risk patients could help to reduce mortality rates.

Previous literature, such as a meta-analysis by Welford et al<sup>5</sup> in 2021, showed reduced mortality if operated upon within 24 hours.<sup>6</sup> A recent study from the Norwegian Hip Fracture Register, and the development of the UK Nottingham Hip Fracture Score, have revealed other risk factors including advanced age, sex, comorbid status, and anaemia to be related to increased mortality.<sup>7,8</sup>

Hypotension with a systolic blood pressure (SBP) < 90 mmHg after non-cardiac surgery has previously been suggested to increase myocardial infarction and 30-day mortality as a subset of the POISE-2 trial, and this value has been suggested to occur in 30% of patients on postoperative day 1.<sup>9</sup> Similarly, the Perioperative Quality Initiative consensus statement suggested harm with postoperative SBP < 90 mm Hg.<sup>10</sup>

Specifically investigating hypotension within 24 hours following hip fracture surgery, a study of 168 patients in China found no mortality difference at one year, although they were unable to explore 30-day mortality. They were however able to conclude that hypotension increased length of stay, and cardiac and brain dysfunction.<sup>11</sup>

Intraoperative hypotension during hip fracture surgery has been well studied before, with Pressman et al<sup>12</sup> finding a relationship between lowest mean arterial pressure (MAP) and in-hospital mortality. Similarly, the ASAP-2 trial concluded that reduction in systolic and MAP led to an increased 30-day mortality.<sup>13</sup> Kluger et al<sup>14</sup> found no impact on mortality of the lowest MAP on multivariable analysis.

Preoperative hypotension defined as a SBP < 120 mmHg has been shown to increase 30-day mortality in elderly patients undergoing elective non-cardiac surgery.<sup>15</sup> A value of SBP < 90 mmHg has also been shown to be an independent risk factor in patients undergoing emergency colorectal surgery.<sup>16</sup>

However, to our knowledge, there are no studies as yet examining immediate pre- and postoperative hypotension in acute hip fracture patients and its effects on 30-day mortality; research in this area in general is limited. Due to hypotension previously being identified as a risk factor in other patient cohorts, our aim was to ascertain whether perioperative hypotension is an independent risk factor that could contribute to 30-day mortality in hip fracture patients within our centre. This would ensure at-risk patient cohorts are promptly identified with appropriate considerations made to their management, such as closer levels of monitoring or early escalation to higher levels of care, with the potential to reduce 30-day mortality through early identification and intervention.

## Methods

We collected data prospectively over a one-year period for patients who were operated on for an acute hip fracture including intracapsular, trochanteric, and subtrocantalic fractures from December 2021 to December 2022. Patients eligible for inclusion were patients aged over 18 years, presenting as an acute trauma. Patients who had a periprosthetic, pathological fracture or were already on an end-of-life pathway were removed from the analysis. Known risk factors from previous publications were identified, and information including patient

**Table II.** Univariate analysis on known risk factors and blood pressures.

Variable	HR (95% CI)	p-value
Male:female	2.1 (1.1 to 3.8)	0.019
Each additional year of age	1.1 (1 to 1.1)	< 0.001
Increasing ASA grade	3.5 (2.1 to 5.8)	< 0.001
Preoperative anaemia*	3.3 (1.7 to 6.6)	< 0.001
Admitted to theatre > 24 hrs from time seen	1.9 (1 to 3.5)	0.035
Preoperative SBP < 120 mmHg	1.9 (0.99 to 3.6)	0.052
Intraoperative SBP < 80 mmHg	0.92 (0.42 to 2)	0.827
Intraoperative MAP < 55 mmHg	1.1 (0.56 to 2.2)	0.737
SBP < 90 mmHg 2 to 24 hrs postoperative	3.5 (1.8 to 6.8)	< 0.001

\*Male < 130 g/l; female < 120 g/l.

ASA, American Society of Anesthesiologists; CI, confidence interval; HR, hazard ratio; MAP, mean arterial pressure; SBP, systolic blood pressure.

demographic details, comorbidities, observations, operation details, and biochemistry results were extracted from the hospital's electronic medical record system. Descriptive data were gathered and stored on Excel (Microsoft, USA). The study was conducted in line with the STROBE statement.<sup>17</sup>

In our study, a postoperative hypotension value was subsequently defined, at the conclusion of data collection and prior to data analysis, as a SBP of less than 90 mmHg, as this is the cut-off value most frequently used and recognized within the literature.<sup>18,19</sup> Upon analysis at this cut-off value for preoperative blood pressure, due to insufficient numbers of deceased patients at this value and the increased risk of statistical errors, a value of a SBP < 120 mmHg was used, which has been shown to be linked to increased mortality.<sup>15</sup> Any exposure to a MAP of < 55 has been shown previously by Wesselink et al<sup>20</sup> to increase risks and was therefore selected as a cut-off.<sup>20,21</sup> Similarly, a SBP < 80 mmHg intraoperatively has been associated with increased adverse outcomes.<sup>22</sup> Anaemia was defined as per the World Health Organization definition of 120 g/l for females and 130 g/l for males.<sup>23</sup> Both pre- and postoperative timepoints were determined by National Early Warning Score 2 advised frequency of observations.<sup>24</sup>

**Ethical statement.** Ethics guidance was not required for this study in accordance with NHS Health Research Authority guidance.<sup>25</sup> All information within this study was collected and approved through governance checks by West Hertfordshire Teaching Hospitals NHS Trust. The project was initially registered with the trust clinical audit team to proceed with data collection. Use of the data for external publication was approved by the trust research and development department and trust information governance and data protection team on 12 June 2023.

**Statistical analysis.** Statistical analysis was conducted on R v. 3.6.3 (R Foundation for Statistical Computing, Austria) and the Cox proportional hazards regression model was used on the Survival package v. 3.5-5.<sup>26</sup> Categorical variables were assessed with Fisher's exact test or chi-squared tests. Continuous variables were evaluated for normality with the Shapiro-Wilk test. Normally distributed data was assessed for differences with the Welch's unequal variances *t*-test and non-normally distributed data with the Mann-Whitney U test. Univariate analysis was conducted on perioperative blood pressure and known risk factors. Factors found to be positively associated with mortality were then analyzed using multivariate regression. The

**Table III.** Multivariate Cox regression hazard ratios.

Variable	HR (95% CI)	Z	p-value
BP < 90 mmHg 2 to 24 hrs postoperative	4.554 (2.323 to 8.927)	4.415	< 0.001
Sex	2.683 (1.388 to 5.189)	2.933	0.003
Increasing age (each additional year)	1.053 (1.009 to 1.098)	2.399	0.016
Increasing ASA grade	2.711 (1.535 to 4.787)	3.437	< 0.001
Time to theatre > 24 hrs	2.141 (1.101 to 4.163)	2.244	0.025
Preoperative anaemia	2.316 (1.025 to 5.232)	2.021	0.043

ASA, American Society of Anesthesiologists; BP, blood pressure; CI, confidence interval; HR, hazard ratio.

number of variables analyzed in multivariate analysis were limited to avoid potential errors with overfitting data and introducing bias.<sup>27,28</sup> Proportional hazards (PH) assumption was checked using statistical tests and graphical diagnostics based on the scaled Schoenfeld residuals, and multicollinearity was detected using variance inflation factors.<sup>29,30</sup> The Wald test was applied for magnitude of effect of each individual factor.<sup>31</sup> Further analysis of postoperative hypotension was conducted using Kaplan-Meier survival curves and the log-rank test for proportional hazards to demonstrate significant differences.<sup>32</sup>

## Results

A total of 533 patients were identified over the study period. Two patients were excluded for being on an end-of-life pathway prior to surgery, and three for a pathological fracture, resulting in 528 suitable for inclusion. Follow-up for the primary outcome of 30-day mortality was possible for all 528 patients. During this time there were 43 deaths (8.1%). Of these, ten occurred after discharge from the orthopaedic team (1.9%).

Our findings suggested a significant 9 mmHg difference in median postoperative blood pressures (2 to 24 hours postoperatively) between alive and deceased groups ( $p = 0.004$ , Mann-Whitney U test). We also found differences between the alive and deceased cohorts in age ( $p < 0.001$ , Welch's *t*-test), American Society of Anesthesiologists (ASA) grade ( $p < 0.001$ , chi-squared test),<sup>33</sup> median preoperative haemoglobin levels ( $p = 0.002$ , Mann-Whitney U test), and sex ( $p = 0.021$ , Fisher's exact test). There was no significant difference between the median last preoperative SBP prior to theatre ( $p = 0.051$ , Mann-Whitney U test), with the difference between the groups also being minimal at 2 mmHg (138 mmHg (95% confidence interval (CI) 136 to 141) vs 136 mmHg (95% CI 121 to 145)). A summary of patient characteristics can be found in Table I.

In our study of 505 patients with a postoperative BP available for analysis, 88 (17.4%) experienced a hypotensive episode postoperatively, and 417 (82.6%) were normotensive. Within the hypotensive cohort 15 patients died (17.0%), compared to 22 in the normotensive cohort (5.1%).

Fisher's exact test was used to compare patients who were hypotensive (SBP < 90 mmHg) two to 24 hours postoperatively between alive and deceased groups, and reached significance ( $p < 0.001$ ). The value for a preoperative SBP < 120 mmHg was not significant between groups ( $p = 0.075$ ).

Univariate analyses were conducted on known risk factors together with multiple timepoints of blood pressure during the perioperative period (Table II). The results

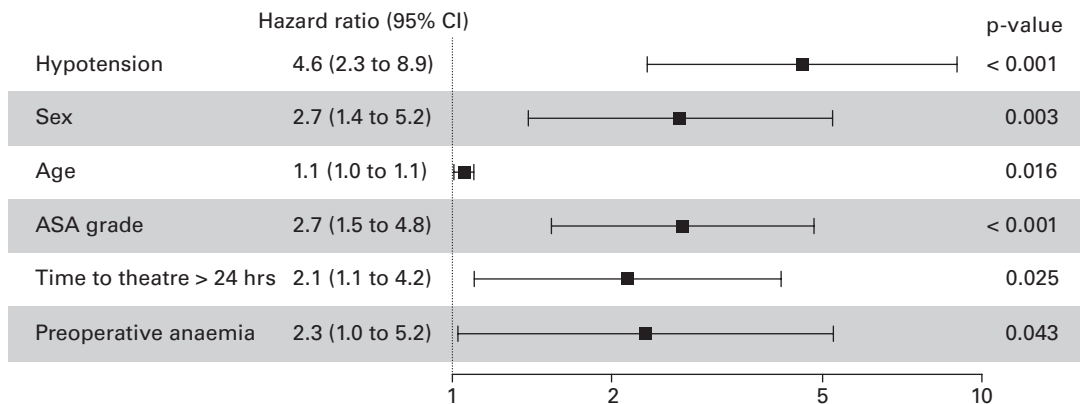


Fig. 1

Forest plot of Cox regression hazard ratios. ASA, American Society of Anesthesiologists; CI, confidence interval.

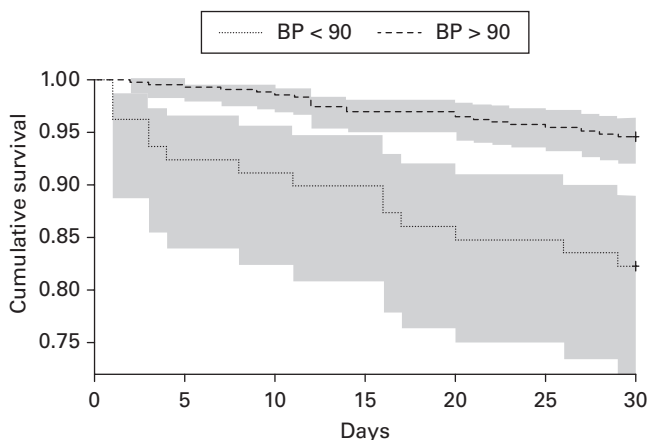


Fig. 2

Kaplan-Meier survival curve of lowest systolic blood pressure two to 24 hours postoperatively, and 30-day survival. BP, blood pressure.

of the univariate analysis revealed increased risks of known risk factors: increasing age, male sex, increasing ASA grade, preoperative anaemia, and a prolonged time to theatre of over 24 hours. A postoperative lowest SBP of less than 90 mmHg two to 24 hours after leaving theatre was a risk factor for 30-day mortality ( $p < 0.001$ ). Preoperative SBP of less than 120 mmHg showed no difference in mortality. Similarly, intraoperatively neither SBP nor MAP were significant.

Multivariate analysis was conducted with Cox regression analysis for postoperative hypotension accounting for known risk factors of sex, age, ASA grade, time to theatre over 24 hours, and preoperative anaemia. This was possible for 490 patients including 37 deaths; 38 patients were excluded due to missing data. The proportional hazards assumption was checked with scaled Schoenfeld residuals, which found no statistically significant results. Therefore, the proportional hazards assumption was found to be true, and is depicted in Supplementary Figure a. Variance inflation factors did not show any relations between variables; the results are shown in Supplementary Figure b.

The outcome of our multivariate analysis demonstrates that postoperative hypotension, in our study defined as the lowest SBP  $< 90$  mmHg within two to 24 hours of leaving theatre, is an independent risk factor when accounting for other known variables. In our study the Wald score is also greatest for postoperative hypotension over any other variable included in our multivariate analysis. Results are displayed in Table III; a visual representation of the Cox regression analysis via a forest plot is in Figure 1.

**Kaplan-Meier analysis.** Kaplan-Meier analysis was conducted on our data for postoperative hypotension of a SBP less than 90 mmHg via the log-rank test. The log-rank test was significant for differences between the two groups ( $p < 0.001$ ). The outcome of the Kaplan-Meier survival curve is shown in Figure 2.

Three of 15 patients in the hypotensive group and one patient in the normotensive group died within 48 hours postoperatively. However, even allowing for this, and removing these patients, 30-day mortality results remained significant via the log-rank test ( $p = 0.002$ ). This suggests that, even allowing for the initial insult of surgery, immediate postoperative hypotension has the potential for prolonged effects in the subsequent days and weeks. The Kaplan-Meier survival curve for mortality starting after 48 hours up to 30 days is shown in Supplementary Figure c.

**Discussion**

Our results are the first to demonstrate that immediate postoperative hypotension is a strong risk factor when predicting 30-day mortality in hip fracture patients. In our study we have shown that this is an independent risk factor when taking into account the previously known risk factors of sex, age, ASA grade, time to theatre, and preoperative anaemia.

Our results follow on from Yang et al,<sup>11</sup> who suggested postoperative hypotension was associated with increased 30-day morbidity, but were unable to assess mortality.

We also examined preoperative SBP prior to transfer to theatre, and were unable to demonstrate a difference between alive and deceased groups ( $p = 0.051$ , Mann-Whitney U test). Preoperative hypotension (SBP  $< 120$  mmHg) did not meet significance on univariate analysis for mortality ( $p = 0.052$ ). While this has previously been shown to be a factor in elective

non-cardiac surgery, further research into this area is needed to clarify any possible relationship in acute hip fractures. Our intraoperative blood pressure figures did not reach significance, contradicting other literature, which has suggested a relationship. Another limitation of our study was that we were not able to comment on duration of intraoperative hypotension, where other studies have shown a graded increase in mortality with an increased duration of intraoperative hypotension.<sup>20,21</sup>

Our study was in keeping with other literature of known independent risk factors on mortality, such as male sex, increasing age, increasing comorbidity status, anaemia, and increased time from presentation to operation.

Postoperative hypotension is most likely to be multifactorial. Hypovolaemia has been suggested to play a role in the development of postoperative hypotension.<sup>34,35</sup> Frail and comorbid patients, with higher ASA grades, have previously been shown to be at particular risk of increased hidden blood losses.<sup>36</sup> In this patient demographic, however, despite adequate fluid resuscitation, hypotension has been shown to persist.<sup>34</sup> It has been suggested that a systemic inflammatory response syndrome state postoperatively, with associated increases in inflammatory markers and vasodilation, can play a role in the development of postoperative hypotension.<sup>37</sup>

The results of our study provide an additional parameter for surgeons and clinicians to promptly identify and highlight patients most at risk of increased mortality in the immediate postoperative period, and therefore will be able to personalize and monitor their care during their inpatient stay. This further highlights the requirement for individualized circulatory management with early intervention, such as inotropic or vasopressor support, for this modifiable risk factor in order to improve morbidity and mortality. It has previously been shown that when patients with refractory hypotension immediately post hip fracture surgery have been transferred to a high-dependency unit (HDU) for a higher level of monitoring, this reduced the incidence of hypotension developing without impacting critical care capacity.<sup>38</sup>

We suggest an area of investigation for future studies would be to evaluate mortality longer than 30 days.<sup>11</sup> It would be of interest to further investigate, in larger studies, whether this increased risk of hypotension remains following the initial event of surgery and illness in the following weeks and months.

The main strength of the study is that it was a prospective study with a large sample size of 528 patients with no losses to follow-up within the one-month time period. It is also, to our knowledge, the first to examine the effect on mortality of immediate postoperative hypotension. The limitations of our study are the small number of patients in our deceased group, and that this limited the number of variables we were able to include in our multivariate analysis. For some patients there was incomplete data collection due to missing values on the electronic medical record (EMR) system. For the 13 patients admitted to higher levels of care (HDU/intensive treatment unit), blood pressure values are not stored on the EMR and were therefore unavailable. We had some data points that were missing and not available, though these were a small number and we have judged that the impact of this is minimal. Our data were

also limited to a single centre; further multicentre data would be valuable.

This is the first study to suggest that postoperative hypotension is an important risk factor for predicting 30-day mortality in hip fracture patients. The results should further help clinicians to promptly identify patients with an increased risk of mortality, and provide additional interventions or closer monitoring of patients with postoperative hypotension in the immediate postoperative period.



### Take home message

- Immediate postoperative hypotension within 24 hours is a significant independent risk factor associated with 30-day mortality.

- Clinicians should be aware of the increased risk of mortality in this cohort and promptly identify patients falling into this category, allowing for improved individualization of care through either preventative measures or closer monitoring.

### Supplementary material



Plots of scaled Schoenfeld residuals for variables within the multivariate analysis, variance inflation factors of analyzed variables within the multivariate analysis, and Kaplan-Meier survival curve of lowest systolic blood pressure at two to 24 hours postoperative and day two to 30 postoperative survival.

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 G. Eniola: Investigation, Writing – review & editing.  
 K. Deierl: Conceptualization, Methodology, Writing – review & editing.

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