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# Relationship between preoperative glucose level and all-cause mortality in patients with osteoporotic vertebral compression fracture who underwent percutaneous vertebroplasty

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**To investigate the relationship between preoperative blood glucose levels and long-term all-cause mortality in patients with osteoporotic vertebral compression fractures (OVCF) who underwent percutaneous vertebroplasty (VP). This single-center retrospective study involved a chart review of patients admitted for VP to treat OVCF between 2013 and 2020. Patients with pathological or multiple fractures or those who did not undergo bone mineral density assessment were excluded. All relevant information was collected from electronic medical records. The survival status of all patients was confirmed at the end of March 2021. Cox proportional hazard models with multivariate adjustments were used to examine the effects of blood glucose levels on all-cause mortality. Overall, 131 patients were retrospectively analyzed (mean age: 75.8 ± 9.3 years, male patients: 26.7%) with a median follow-up period of 2.1 years. Preoperative hyperglycemia (hazard ratio: 2.668, 95% confidence interval [CI] 1.064, 6.689; p = 0.036) and glucose levels (hazard ratio: 1.007, 95% CI 1.002–1.012; p = 0.006) were found to be independently associated with a higher risk of all-cause mortality. This correlation remained significant even after adjusting for age and sex, and other factors and comorbidities that might affect outcomes (hazard ratio: 2.708, 95% CI 1.047, 7.003, p = 0.040 and 1.007; 95% CI 1.001, 1.013, p = 0.016, respectively). Furthermore, a history of diabetes mellitus was not a significant factor influencing long-term all-cause mortality. Preoperative glucose levels were found to be independently associated with survival outcomes in patients with OVCF who underwent VP. Conversely, diabetes mellitus was not associated with long-term all-cause mortality. Our findings highlight that preoperative hyperglycemia is a risk factor for long-term mortality in this aging surgical population.**

**Keywords** Osteoporotic vertebral compression fracture, Percutaneous vertebroplasty, Blood glucose, DM, All-cause mortality

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Osteoporotic vertebral compression fractures (OVCFs), the most common type of osteoporotic fractures, are common in older adults[1,2]. The incidence rate of OVCFs was reported to be 10.5% among patients in the 70- to 79-year-old age group and up to 18% among patients aged > 80 years[3]. OVCFs can cause considerable morbidities, such as back pain, disabilities, prolonged bed rest, decreased quality of life, poor mental health, and even mortality[4]. The pathology of OVCFs is limited to the anterior half of the vertebral body and does not involve the posterior osseous components or ligamentous complex. Therefore, for painful OVCFs with intractable pain, vertebroplasty (VP) is an effective procedure for decreasing pain and complications related to being bedridden and preventing further kyphotic deformities[5–7].

However, the effect of VP on the overall long-term survival of patients with OVCFs remains unclear despite its demonstrated effectiveness in reducing fracture-related mortality[8]. These findings imply that there may be additional factors influencing the overall long-term survival of these patients. Diabetes mellitus (DM) and hyperglycemia are conditions characterized by impaired insulin secretion or peripheral-tissue insulin resistance, resulting in impaired oxygen delivery due to hemoglobin glycosylation and subsequent tissue ischemia. DM and hyperglycemia have been identified as independent risk factors for increased surgical complications[9–11]. However, their impact on long-term survival remains unclear. Therefore, this study aimed to investigate the association between preoperative glucose levels and all-cause mortality in patients with OVCFs receiving VP.

## Methods

We hypothesized that glucose levels at admission may affect all-cause mortality in patients with OVCF receiving VP. This retrospective study at a single tertiary referral center included all adult patients diagnosed with single-level OVEF who underwent VP between 2013 and 2020. An OVCF was defined as a low-energy trauma mechanism, including a simple fall or no obvious trauma history. Participants with a history of high-energy trauma, including falls from a height, traffic accidents, initial presentation of multiple traumas, or diagnosis of burst fracture, were excluded. Patients with pathological fractures and those with no data on bone mineral density were also excluded. Preoperative admission glucose levels and baseline demographics, including age, sex, and comorbidities, were collected from the electronic medical records of the patients. The survival status of the patients was confirmed by the end of March 2021 using information from the Ministry of Health and Welfare, R.O.C. De-identified data were used for the analyses. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of Taichung Veterans General Hospital, Taichung, Taiwan (approval number: CE22167A). Informed consent was waived due to the retrospective nature of the study design.

In this study, the guidelines of the American Diabetes Association[11] were followed, and the patients were divided into two groups based on preoperative glucose levels: < 110 mg/dl (normoglycemia) and ≥ 110 mg/dL (hyperglycemia). Subsequent analysis was conducted to investigate the influence of preoperative hyperglycemia and glucose level on long-term all-cause mortality. Confounding factors such as age, sex, body mass index, smoking, hypertension, cardiovascular disease, and osteoporosis were adjusted for before proceeding with further analysis.

### Statistical analysis

Categorical and continuous variables were examined for statistically significant between-group differences using the chi-square test and independent *t*-test, respectively. Kaplan–Meier survival curves were plotted for the study population according to their preoperative glucose levels (normoglycemia [< 110 mg/dL] vs. hyperglycemia [≥ 110 mg/dL]). Cox proportional hazard models were used to examine the effects of hyperglycemia (< 110 mg/dL vs. ≥ 110 mg/dL), preoperative glucose levels (as a continuous variable), and history of diabetes on all-cause mortality with adjustments for age, sex, and concomitant chronic diseases. A cubic spline analysis of preoperative glucose levels vs. risk of all-cause mortality per a Cox proportional hazards model was conducted as a sensitivity test. All statistical analyses were performed using Statistical Package for the Social Sciences (IBM SPSS version 22.0; International Business Machines Corp., NY, USA). Statistical significance was set at $p < 0.05$.

## Results

Overall, 131 patients were included in this study. The mean age of the patients was 75.8 ± 9.3 years, and 26.7% were male. Furthermore, 20.6% and 54.2% of the patients were diagnosed with diabetes and hypertension, respectively. A history of cardiovascular disease was noted in 8.4% of the participants, while 77.9% had osteoporosis.

Baseline characteristics categorized by preoperative fasting plasma glucose levels into two groups are presented in Table 1. Most baseline characteristics were not significantly different between the two groups. However, in the hyperglycemia group, there were fewer male patients (19.7% vs. 36.4%, $p = 0.034$), and the patients had higher body mass indexes (BMIs; 24.6 ± 4.5 vs. 23.1 ± 3.4, $p = 0.032$) and higher prevalence of diabetes (31.6% vs. 5.5%, $p < 0.001$).

This study employed a Cox proportional hazard model to analyze the impact of hyperglycemia on admission (≥ 110 mg/dL) relative to that of normoglycemia (< 110 mg/dL) on all-cause mortality (Table 2). The analysis revealed a significant correlation between hyperglycemia on admission (≥ 110 mg/dL) and all-cause mortality (hazard ratio, 2.668; 95% CI 1.064–6.689; $p = 0.036$). This correlation remained significant even after adjusting for age and sex (Model 2), as well as other factors and comorbidities that may affect the outcome, such as BMI, smoking, hypertension, cardiovascular disease, and osteoporosis (Model 3). Kaplan–Meier survival curves for both groups show a significantly lower survival rate in the hyperglycemia group during median follow-up of 2.1 years (log-rank test: $p = 0.029$; Fig. 1).

We further analyzed the impact of preoperative fasting glucose levels (as a continuous variable) on all-cause mortality using a Cox proportional hazard model (Table 2). The analysis revealed a significant correlation

| | Admission fasting plasma glucose | | P |
|---|---|---|---|
| | < 110 mg/dL | ≥ 110 mg/dL | |
| Number of patients | 55 | 76 | |
| Age, years | 75.1 ± 9.6 | 76.4 ± 9.0 | 0.398 |
| Male sex, n (%) | 20 (36.4) | 15 (19.7) | 0.034 |
| Body mass index, kg/m$^2$ | 23.1 ± 3.4 | 24.6 ± 4.5 | 0.032 |
| Smoking, n (%) | 4 (7.3) | 5 (6.6) | 0.877 |
| Diabetes, n (%) | 3 (5.5) | 24 (31.6) | < 0.001 |
| Hypertension, n (%) | 25 (45.5) | 46 (60.5) | 0.087 |
| Cardiovascular disease, n (%) | 4 (7.3) | 7 (9.2) | 0.693 |
| Osteoporosis, n (%) | 43 (78.2) | 59 (77.6) | 0.940 |
| Fasting plasma glucose, mg/dL | 97.8 ± 7.0 | 159.6 ± 65.1 | < 0.001 |
| Level of vertebroplasty, n (%) | | | 0.952 |
| T-spine | 22 (40.0) | 30 (39.5) | |
| L-spine | 33 (60.0) | 46 (60.5) | |

**Table 1.** Baseline characteristics of the study population. Values are mean ± SD or n (%).

| | Hazard ratio (95% CI) | P |
|---|---|---|
| Fasting plasma glucose (≥ 110 mg/dL vs. < 110 mg/dL) | | |
| Model 1 | 2.668 (1.064, 6.689) | 0.036 |
| Model 2 | 2.673 (1.047, 6.821) | 0.040 |
| Model 3 | 2.708 (1.047, 7.003) | 0.040 |
| Fasting plasma glucose (mg/dL) | | |
| Model 1 | 1.007 (1.002, 1.012) | 0.006 |
| Model 2 | 1.008 (1.003, 1.013) | 0.001 |
| Model 3 | 1.007 (1.001, 1.013) | 0.016 |
| History of diabetes (yes vs. no) | | |
| Model 1 | 1.579 (0.659, 3.783) | 0.306 |
| Model 2 | 1.596 (0.664, 3.834) | 0.296 |
| Model 3 | 2.781 (0.980, 7.890) | 0.055 |

**Table 2.** Association of preoperative hyperglycemia, glucose levels, and history of diabetes with all-cause mortality. Model 1, unadjusted. Model 2, adjusted for age and sex. Model 3 adjusted for variables in Model 2 plus body mass index, smoking, hypertension, cardiovascular disease, and osteoporosis.

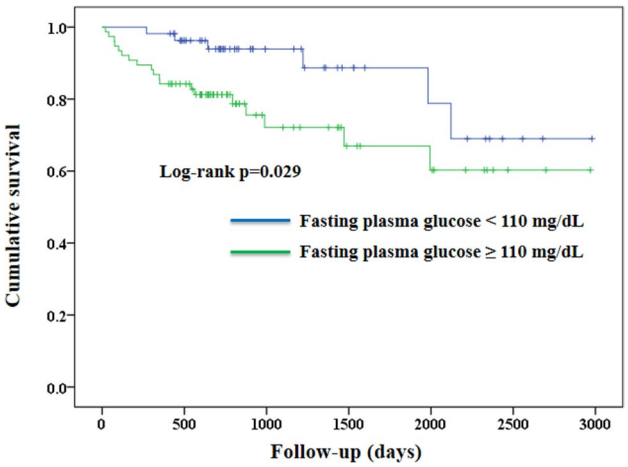


**Fig. 1.** Kaplan–Meier survival curves of the study population per preoperative glucose levels. Normoglycemia (< 110 mg/dL) vs. Hyperglycemia (≥ 110 mg/dL).

between preoperative fasting glucose level and all-cause mortality (hazard ratio, 1.007; 95% CI 1.002–1.012; p = 0.006). This correlation remained significant even after adjusting for age and sex (Model 2), as well as other factors and comorbidities that may affect the outcome, such as BMI, smoking, hypertension, cardiovascular disease, and osteoporosis (Model 3). A cubic spline plot analysis (Fig. 2) showed that the hazard ratio of all-cause mortality began to increase when the glucose levels on admission exceeded 130–150 mg/dL.

Finally, to investigate the impact of DM on all-cause mortality, a Cox proportional hazard model was employed for analysis (Table 2). Although the hazard ratio was 1.579, the 95% confidence interval and p-value did not reach statistical significance, indicating that the presence of DM was not a significant factor influencing long-term all-cause mortality.

To validate our findings, we examined the association of fasting plasma glucose with all-cause mortality in another cohort of 266 patients (mean age 76.0 ± 9.4 years, male 22.9%, mean body mass index 24.6 ± 4.0 kg/m$^2$) who underwent VP for compression fractures between 2013 and 2020 in our hospital. These patients did not have data on bone mineral density, and were not included in our initial analyses. After median follow-up of 4.2 years, we found a significant association between fasting plasma glucose (≥ 110 vs. < 110 mg/dl) and all-cause mortality after adjustment of age, sex, and body mass index (hazard ratio 1.625; 95% CI 1.038–2.545; p = 0.034; Table 3). Similar association was noted when fasting plasma glucose was examined as a continuous variable (mg/dl) (hazard ratio 1.625; 95% CI 1.038–2.545; p = 0.034).

## Discussion

In this study, higher preoperative glucose levels were found to be associated with increased long-term all-cause mortality, with a median follow-up period of > 2 years among patients with OVCFs who underwent VP. This correlation remained significant even after adjusting for other confounding factors using Cox proportional hazard models. Additionally, the presence of DM did not affect long-term all-cause mortality. These findings underscored the role of preoperative hyperglycemia as a risk factor for increased long-term mortality in patients with OVCFs undergoing VP.

The occurrence of OVCFs increased significantly with age[12]. Older age also led to higher morbidity and mortality rates[13,14]. VP is a common procedure for treating painful OVCFs, which can lower fracture-related

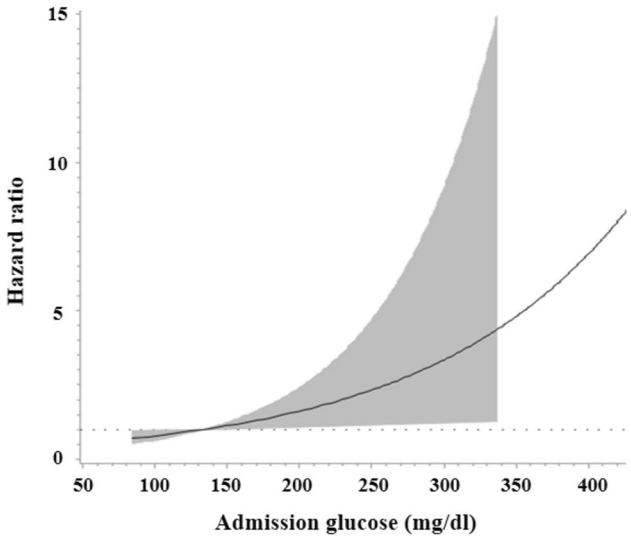


**Fig. 2.** Cubic spline analysis of preoperative glucose levels versus the risk of postoperative long-term all-cause mortality. Adjustments for age, sex, body mass index, smoking, diabetes, hypertension, cardiovascular disease, and osteoporosis (p = 0.034).

| | Hazard Ratio (95% CI) | P |
|---|---|---|
| Fasting plasma glucose (≥ 110 mg/dL vs. < 110 mg/dL) | | |
| Model 1 | 1.649 (1.056, 2.577) | 0.028 |
| Model 2 | 1.625 (1.038, 2.545) | 0.034 |
| Fasting plasma glucose (mg/dL) | | |
| Model 1 | 1.005 (1.001, 1.010) | 0.026 |
| Model 2 | 1.005 (1.000, 1.009) | 0.046 |

**Table 3.** Associations of fasting plasma glucose with all-cause mortality in another cohort of 266 patients who underwent vertebroplasty. Model 1, unadjusted. Model 2, adjusted for age, sex, and body mass index.

mortality[8], pain scores determined using the visual analog scale, opioid and non-steroidal anti-inflammatory drug use, and complications related to prolonged immobilization[5–7]. However, its impact in reducing long-term all-cause mortality rates remains unclear[15–18]. Identifying risk factors for mortality in elderly patients is therefore crucial.

Diabetes and hyperglycemia impair oxygen delivery to peripheral tissues through hemoglobin glycosylation, resulting in tissue ischemia and other downstream consequences. DM is a major risk factor for complications following various surgical procedures. Approximately 25% of patients who underwent spinal surgery had a history of diabetes[19–21]. Extensive research has demonstrated that diabetes and hyperglycemia are independent risk factors associated with increased surgical complications, such as surgical site infection and adverse cardiovascular events, following spine surgery[9,10]. Previous studies have also shown that long-term poor blood glucose control can lead to the accumulation of advanced glycation end products, which can inhibit osteoblast differentiation, promote osteoblast apoptosis and osteoclast formation, reduce bone mass, and worsen osteoporosis[22,23]. Additionally, patients with diabetes may have other comorbidities that influence their medical outcomes[9,24]. There is plenty of literature to support the notion that high preoperative glucose levels and DM lead to poorer outcomes and higher complication rates.

However, to our knowledge, there is no available literature examining the impact of preoperative blood glucose levels on the long-term survival of patients who underwent VP for OVCFs. Our study found that among patients who underwent VP for OVCFs, preoperative hyperglycemia emerged as an independent risk factor for long-term all-cause mortality. Conversely, DM was not associated with long-term all-cause mortality. Such results underscore the greater impact of hyperglycemia on long-term survival compared with DM, although this is not the first study with such findings.

Umpierrez et al.[25] analyzed 2030 consecutive adult patients admitted to the general ward. After adjusting for other relevant risk factors, newly discovered hyperglycemia was found to be associated with an 18.3-fold increased mortality rate compared with that in patients with normoglycemia, whereas in the known diabetes group, the increase was only 2.7-fold. Additionally, patients with newly discovered hyperglycemia during admission, compared with those having a history of DM or normoglycemia during admission, had longer hospital stays, higher admission rates to intensive care units, and were less likely to be discharged home.

Although the underlying mechanisms remain unclear, the study by Umpierrez et al. suggests that newly diagnosed hyperglycemia may be a marker of more severe illness rather than the primary cause of increased morbidity and mortality[25]. This is because the blood glucose levels of patients with newly diagnosed hyperglycemia were lower than those of the patients with known DM. Stress hyperglycemia, caused by physiological illness, results in a temporary increase in blood glucose levels and typically occurs in individuals with undiagnosed DM or impaired glucose intolerance or owing to severe stress leading to increased counterregulatory hormone levels[25].

Stress hyperglycemia may involve several potential mechanisms, including increased secretion of counterregulatory hormones (catecholamines, cortisol, and glucagon), leading to increased gluconeogenesis and decreased glycogenolysis[26,27]; lactate serving as a substrate for gluconeogenesis, with increased lactate resulting in increased gluconeogenesis[28,29]; and peripheral insulin resistance[25]. Conversely, hyperglycemia itself can create a toxic cellular milieu[30,31], leading to intracellular and extracellular dehydration, electrolyte abnormalities, and suppression of immune function[25].

In another recent study[32], an analysis of 174,671 hospitalized patients found that inpatient hyperglycemia was associated with a 2.18-fold increased risk of mortality compared with normoglycemia (odds ratio [OR]: 95% CI 2.08, 2.31). Furthermore, this study categorized baseline glycemic status into four groups: non-type 2 DM, pre-DM, unscreened status, and type 2 DM. The study found that compared to baseline type 2 DM status, the ORs for 30-day mortality were 1.41 (1.25–1.60), 1.32 (1.16–1.51), and 1.30 (1.04–1.62) in non-type 2 DM, pre-DM, and unscreened status groups, respectively. This study also confirmed the impact of hyperglycemia at the time of admission on mortality, which was even greater in patients without pre-existing DM than in those with DM. The study suggests that this could be because individuals in the type 2 DM or pre-DM status groups may have already undergone relevant lifestyle changes and received medications in a community setting, which could have a protective effect[33]. This finding is similar to those of our study, in which we found no association between isolated DM and all-cause mortality; instead, preoperative hyperglycemia remained associated with all-cause mortality even after eliminating other interfering factors.

When the preoperative glucose level was above 150 mg/dL, the hazard ratio for long-term mortality increased significantly (Fig. 2). This result indicates that maintaining a preoperative glucose level below 150 mg/dL is beneficial for elderly patients with OVCFs. Lastly, the current study emphasizes the association between preoperative glucose levels and long-term all-cause mortality after VP.

Despite the novelty of this study, it has some limitations. First, the retrospective nature of this study introduced a potential risk of selection bias, and the sample size of our patient cohort was relatively small. Second, although other related comorbidities and risk factors were controlled for, the severity of comorbidities (such as blood pressure control status, glycosylated hemoglobin [HbA1c] levels in patients with DM, severity of cardiovascular disease, and T-score for osteoporosis) was not accounted for, which could have influenced the results. Finally, HbA1c, which reflects the 3-month control status of diabetes, has been shown to be associated with infection rate and postoperative outcomes of elective spine surgery[34]; however, there was no data regarding its association with long-term mortality after an orthopedic surgery. Given that this study focused on patients who required VP for painful OVCFs, which is often an urgent or emergent surgery rather than an elective one, the modifiable variable of interest was the preoperative glucose level instead of HbA1c. However, as mentioned earlier, long-term blood glucose control also affects postoperative outcomes; therefore, including HbA1c levels in the analysis could be considered in a larger prospective study in the future.

## Conclusion

Preoperative hyperglycemia was independently associated with survival outcomes in patients with OVCFs who underwent VP. Conversely, DM was not associated with long-term all-cause mortality. Our findings highlight that preoperative hyperglycemia is a risk factor for long-term mortality in an aging surgical population.

## Data availability

The data that support the findings of this study are available from Dr. Jun-Sing Wang but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Dr. Jun-Sing Wang.

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## References

1. Delmas, P. D. *et al.* Underdiagnosis of vertebral fractures is a worldwide problem: The Impact study. *J. Bone Miner. Res.* **20**, 557–563 (2005).
2. Majumdar, S. R. *et al.* Incidental vertebral fractures discovered with chest radiography in the emergency department: Prevalence, recognition, and osteoporosis management in a cohort of elderly patients. *Arch. Intern. Med.* **165**, 905–909 (2005).
3. Cosman, F. *et al.* Spine fracture prevalence in a nationally representative sample of US women and men aged ≥40 years: Results from the National Health and Nutrition Examination Survey (NHANES) 2013–2014. *Osteoporos. Int.* **28**, 1857–1866 (2017).
4. Ensrud, K. E. *et al.* Prevalent vertebral deformities predict mortality and hospitalization in older women with low bone mass. Fracture intervention trial research group. *J. Am. Geriatr. Soc.* **48**, 241–249 (2000).
5. Wardlaw, D. *et al.* Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (Free): A randomised controlled trial. *Lancet* **373**, 1016–1024 (2009).
6. Klazen, C. A. *et al.* Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): An open-label randomised trial. *Lancet* **376**, 1085–1092 (2010).
7. Clark, W. *et al.* Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): A multicentre, randomised, double-blind, placebo-controlled trial. *Lancet* **388**, 1408–1416 (2016).
8. Gerling, M. C. *et al.* Cement augmentation of refractory osteoporotic vertebral compression fractures: Survivorship analysis. *Spine (Phila Pa 1976)* **36**, E1266–E1269 (2011).
9. Olsen, M. A. *et al.* Risk factors for surgical site infection following orthopaedic spinal operations. *J. Bone Jt. Surg. Am.* **90**, 62–69 (2008).
10. Pull ter gunne, A. F. *et al.* A methodological systematic review on surgical site infections following spinal surgery: Part 1: Risk factors. *Spine (Phila Pa 1976)* **37**, 2017–2033 (2012).
11. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* **26**, S5–S20 (2003).
12. Lau, E., Ong, K., Kurtz, S., Schmier, J. & Edidin, A. Mortality following the diagnosis of a vertebral compression fracture in the medicare population. *J. Bone Jt. Surg. Am.* **90**, 1479–1486 (2008).
13. Cauley, J. A., Thompson, D. E., Ensrud, K. C., Scott, J. C. & Black, D. Risk of mortality following clinical fractures. *Osteoporos. Int.* **11**, 556–561 (2000).
14. Jalava, T. *et al.* Association between vertebral fracture and increased mortality in osteoporotic patients. *J. Bone Miner. Res.* **18**, 1254–1260 (2003).
15. Levy, H., Seydafkan, S., Rice, J. D., Easley, K. A. & Tangpricha, V. Comparative efficacy of vertebroplasty, kyphoplasty, and medical therapy for vertebral fractures on survival and prevention of recurrent fractures. *Endocr. Pract.* **18**, 499–507 (2012).
16. McCullough, B. J., Comstock, B. A., Deyo, R. A., Kreuter, W. & Jarvik, J. G. Major medical outcomes with spinal augmentation vs conservative therapy. *JAMA Intern. Med.* **173**, 1514–1521 (2013).
17. Kurra, S., Metkar, U., Lieberman, I. H. & Lavelle, W. F. The effect of kyphoplasty on mortality in symptomatic vertebral compression fractures: A review. *Int. J. Spine Surg.* **12**, 543–548 (2018).
18. Ong, K. L., Beall, D. P., Frohbergh, M., Lau, E. & Hirsch, J. A. Were VCF patients at higher risk of mortality following the 2009 publication of the vertebroplasty "sham" trials?. *Osteoporos. Int.* **29**, 375–383 (2018).
19. Guzman, J. Z. *et al.* The impact of diabetes mellitus on patients undergoing degenerative cervical spine surgery. *Spine (Phila Pa 1976)* **39**, 1656–1665 (2014).
20. Liow, M. H. L. *et al.* Poorer fusion outcomes in diabetic cervical spondylotic myelopathy patients undergoing single-level anterior cervical discectomy and fusion does not compromise functional outcomes and quality of life. *Spine (Phila Pa 1976)* **43**, 477–483 (2018).
21. Phan, K., Kim, J. S., Lee, N., Kothari, P. & Cho, S. K. Impact of insulin dependence on perioperative outcomes following anterior cervical discectomy and fusion. *Spine (Phila Pa 1976)* **42**, 456–64 (2017).
22. Paschou, S. A. *et al.* Type 2 diabetes and osteoporosis: A guide to optimal management. *J. Clin. Endocrinol. Metab.* **102**, 3621–3634 (2017).
23. Lecka-Czernik, B. Diabetes, bone and glucose-lowering agents: Basic biology. *Diabetologia* **60**, 1163–1169 (2017).
24. Browne, J. A., Cook, C., Pietrobon, R., Bethel, M. A. & Richardson, W. J. Diabetes and early postoperative outcomes following lumbar fusion. *Spine (Phila Pa 1976)* **32**, 2214–2219 (2007).
25. Umpierrez, G. E. *et al.* Hyperglycemia: An independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J. Clin. Endocrinol. Metab.* **87**, 978–982 (2002).
26. O'Neill, P. A., Davies, I., Fullerton, K. J. & Bennett, D. Stress hormone and blood glucose response following acute stroke in the elderly. *Stroke* **22**, 842–847 (1991).
27. Gallagher, J. M., Erich, R. A., Gattermeyer, R. & Beam, K. K. Postoperative hyperglycemia can be safely and effectively controlled in both diabetic and nondiabetic patients with use of a subcutaneous insulin protocol. *JB JS Open Access* **2**, e0008 (2017).
28. Woo, E., Ma, J. T., Robinson, J. D. & Yu, Y. L. Hyperglycemia is a stress response in acute stroke. *Stroke* **19**, 1359–1364 (1988).
29. Wass, C. T. & Lanier, W. L. Glucose modulation of ischemic brain injury: Review and clinical recommendations. *Mayo Clin. Proc.* **71**, 801–812 (1996).
30. Mizock, B. A. Alterations in carbohydrate metabolism during stress: A review of the literature. *Am. J. Med.* **98**, 75–84 (1995).
31. Rodrigues, B. & McNeill, J. H. The diabetic heart: Metabolic causes for the development of a cardiomyopathy. *Cardiovasc. Res.* **26**, 913–922 (1992).
32. Rayyan-Assi, H., Feldman, B., Leventer-Roberts, M., Akriv, A. & Raz, I. The relationship between inpatient hyperglycaemia and mortality is modified by baseline glycaemic status. *Diabetes Metab. Res. Rev.* **37**, e3420 (2021).
33. Plummer, M. P. *et al.* Dysglycaemia in the critically ill and the interaction of chronic and acute glycaemia with mortality. *Intensive Care Med.* **40**, 973–980 (2014).

34. Maitra, S., Mikhail, C., Cho, S. K. & Daubs, M. D. Preoperative maximization to reduce complications in spinal surgery. *Glob. Spine J.* **10**, 45s–52s (2020).

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## Author contributions
Y-HL and J-SW designed and conducted the research. Y-HL, Y-TL, W-CW, Y-CW, K-HC, C-CP, C-HL and S-FY contributed acquisition of data, analysis, and interpretation of data. Y-HL and J-SW wrote the first draft of the manuscript. Y-HL, Y-TL, W-CW, Y-CW, K-HC, C-CP, C-HL and S-FY revised the manuscript critically for important intellectual content. All authors approved the final draft of the manuscript.

## Competing interests
The authors declare no competing interests.

## Additional information
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