Factors affecting postoperative survival of patients with insufficient union following osteoporotic vertebral fractures and impact of preoperative serum albumin on mortality

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Research article

Keywords: Osteoporotic vertebral fractures, Mortality, Serum albumin

Posted Date: December 3rd, 2019

DOI: https://doi.org/10.21203/rs.2.18119/v1

Version of Record: A version of this preprint was published on August 10th, 2020. See the published version at https://doi.org/10.1186/s12891-020-03564-z.

Abstract

Background: Numerous comparative studies of surgical procedures have focused on clinical and radiographical outcomes, as well as the effect of bone fragility on the outcome of spinal surgery; however, insights concerning a long-term risk of mortality or morbidity have been limited. Additionally, the effect of surgical therapy on survival after vertebral compression fractures remains controversial. To evaluate the preoperative factors that affected the long-term survival of patients who underwent spinal surgery for an insufficient union following osteoporotic vertebral fractures (OVF) and to determine long-term mortality.

Methods: We retrospectively reviewed the cases of 105 consecutive patients who underwent spinal surgery for OVF. Morbidity was estimated using the Kaplan-Meier method and a log-rank test. To determine which risk factors led to death among the OVF cases, the preoperative backgrounds of patients were analyzed. Kaplan-Meier curves were used to estimate survival based on the preoperative albumin levels of ≤3.5 g/dL (hypoalbuminemia) versus >3.5 mg/dL.

Results: The mean follow-up for survival was 4.1 ±0.8 years. Two years after surgery, 15% of patients with OVF had died. The ratio of male-to-female was significantly higher for patients with OVF who died than for those who were still alive. No significant difference in mortality was observed among surgical procedures for OVF. Multivariate analysis revealed that only serum albumin ≤3.5 g/dL was a significant risk factor for long-term postoperative mortality of people with OVF.

Conclusions: Preoperative hypoalbuminemia was associated with long-term postoperative mortality following surgery for OVF.

Introduction

Osteoporotic vertebral fractures (OVF) are the most common type of fragility fractures, and they have become more prevalent as the proportion of the population that is older continues to increase.[1] Reports indicate that OVF increase overall mortality.[2, 3] Conventionally, OVF are viewed as benign and treated with conservative methods such as rest, immobilization, drugs, and bracing.[4] However, vertebral fractures sometimes fail to unite, resulting in progressive kyphosis due to vertebral collapse and/or pseudarthrosis. Affected patients often endure persistent back pain and/or neurological deficits.[5] Despite conservative treatment, the prevalence of an insufficient bone union among elderly patients with OVF reportedly ranges from 10.0% to 13.5%. The quality of life and activities of daily living of these patients are reduced severely.[6, 7] Despite the various surgical procedures proposed for the management of an insufficient bone union following OVF, optimal surgical procedures have not yet been clearly established. This is because of the poor general condition and frequent instrumentation failure resulting from low bone quality in elderly patients. Numerous comparative studies of surgical procedures have focused on clinical and radiographical outcomes, as well as the effect of bone fragility on the outcome of spinal surgery.[8, 9] However, insights concerning the long-term risk of mortality or morbidity are limited.

Additionally, the effect of surgical therapy on survival after vertebral compression fractures remains controversial.[10, 11] To establish an effective treatment strategy for patients with OVF, the long-term postoperative mortality of patients who have undergone surgery for OVF, and the preoperative risk factors predictive of mortality after surgery, should be elucidated.

In the present study, we sought to evaluate the preoperative factors affecting the long-term survival of patients who underwent spinal surgery for an insufficient bone union following OVF and determine long-term mortality.

Methods

Patient Cohort and Surgery

A total of 105 consecutive patients, with delayed osteoporotic thoracolumbar vertebral fractures, who underwent spinal surgery, were followed-up for a minimum of 6 months (Table 1). Surgeries were conducted by three board certified spinal surgeons at a single institution between 2010 and 2018. Initially, all patients with OVF were treated conservatively, and none of them had neurological deficits immediately after injury. Treatment options, including the use of a brace or drug therapy, or both, were selected by individual physicians based on their experience. Surgical treatment was indicated for all 105 patients because they had progressive neurological deficits or continuous severe lower back pain caused by vertebral collapse.

Three surgical procedures were applied in the treatment of the patients in this study (Table 1). Forty-nine patients underwent posterior decompression and short-segment fixation by vertebroplasty. This was accomplished with implanted hydroxyapatite blocks via the pedicle of the fractured vertebra and was combined with fixation of the two vertebrae above and one below with a pedicle screw. Another 18 patients received balloon kyphoplasty, and 38 patients underwent anterior spinal decompression and fusion, performed using a titanium cage and supplemented with posterior percutaneous pedicle screw fixation.

Postoperative Mortality

Mean follow-up for survival was 4.1 ± 0.8 years. The primary endpoint was death by the close of the study period, which ended in March 2019. Data were censored if the patient survived until the end of the study period. If a recent follow-up was not available from clinical records, patients were contacted by telephone to confirm their survival.

Data Collection

For each patient who underwent spinal surgery for OVF, we searched clinical records and a laboratory database. Only measurements recorded 1–14 days before the date of surgery were used for preoperative measurements of body mass index (BMI), left ventricular ejection fraction (LVEF) measured using an echocardiogram, serum albumin, B-type natriuretic peptide (BNP), creatinine clearance (CCr), and preoperative neurological impairment (according to a modified Frankel classification). Standardized bone mineral density (BMD, % young adult men [YAM]) measurements at the lumbar spine (L2–L4) and the femoral neck were performed using a Lunar Prodigy dual-energy X-ray absorptiometry system (General Electric) at baseline. The American Society of Anesthesiologists (ASA) classification is a readily available and widely-accepted method for stratification of surgical patients according to their perioperative risk.[12] The visual analog scale (VAS) score for the lumbar spine and leg were evaluated at the time of hospital admission and 1 year after surgery.

Statistical Analyses

Continuous variables were compared using unpaired *t* tests and categorical variables were assessed using Fisher's exact test for baseline characteristics between deceased patients versus those who had survived 2 years after surgery. Crude and adjusted hazard ratios (HRs) of mortality, using Cox proportional univariate and multivariate models, were calculated, respectively. We also illustrated Kaplan-Meier estimates of all-cause mortality according to serum albumin levels as a possible risk factor of death in the Cox multivariate model. A log-rank test was used to assess the significance of differences between Kaplan–Meier estimates. All statistical calculations were conducted using Prism software, version 8.0 (Graph Pad Software, La Jolla, CA) and SAS statistical software, version 9.4 (SAS Institute, Cary, NC, USA). R statistical software (version 3.6.1, R Project for Statistical Computing, Vienna, Austria) was used to generate Kaplan-Meier estimates. All reported p values were two-sided and $p<0.05$ indicated statistical significance.

Results

Patient characteristics between those who died versus those who survived 2 years after surgery.

Table 1 summarizes the characteristics of patients with OVF who underwent surgical procedures. Surgical invasion among procedures were compared in Figure2. Estimated blood loss in patients who treated with BKP was significantly lower than them in patient who treated VP (HA) + PF and ADF + PF. There was no significant difference of estimated blood loss between patients who treated with VP (HA) + PF and ADF + PF (Figure 2A). Operation time in patients who treated with BKP was significantly shorter than them in patient who treated VP (HA) + PF and ADF + PF. Operation time in patients who treated VP (HA) + PF was significantly shorter than them who treated with ADF + PF (Figure 2B). The VAS score for both the lumbar spine and leg were significantly improved 1 year after surgery compared to them at the time of hospital admission (Table2).

Two years after surgery, 19/75 patients (15%) with OVF had died. Table 3 summarizes the preoperative baseline characteristics of the patients with OVF who died compared with those who were still alive 2 years after surgery. There were no significant differences in the age, BMI, LVEF (%), BNP level, CCr, or BMD, follow-up period, estimated blood loss and operative time between groups. A significant difference in mortality among the three surgical procedures was not found (Table 3). In contrast, the ratio of male-to-females was significantly higher among the patients with OVF who died than for those who were still alive. Additionally, preoperative serum albumin levels and CCr were significantly lower in patients who died than in those who were still alive (Table 3).

Preoperative factors affecting the long-term survival of the patients who underwent spinal surgery for an insufficient bone union following OVF.

The presurgical hazard ratios (95% confidence interval) for mortality associated with patient characteristics are summarized in Table 4. According to a past report, hypoalbuminemia was defined as serum albumin 3.5 g/dL [13].The univariate analysis showed male gender, serum albumin <3.5g/dl, CCr <60mg/dl, and an ASA classification ≥3 were significant risk factors for postoperative mortality (Table 4). The multivariate analysis revealed hypoalbuminemia was the only significant risk factor for long-term postoperative mortality of OVF (adjusted hazard ratio was 3.37; p = 0.014; Table 4).

Effect of preoperative serum albumin level on postoperative mortality.

Based on the threshold values defined, there were two preoperative serum albumin levels, 3.5 g/dL and >3.5 g/dL.[14] Thirty-eight patients (36.2%) had hypoalbuminemia. The estimated risk of mortality at the final follow-up, using the Kaplan-Meier method, was significantly greater in patients with preoperative serum albumin 3.5 g/dL than in those with a serum albumin >3.5 g/dL (p<0.0001 for log-rank test; Fig. 2).

Discussion

Numerous studies have found an association between OVF and increased mortality, with pulmonary and cardiovascular-related deaths suggested as being explanatory factors for the excess mortality.[14–16] A past study showed a 2- to 8-times increased risk of age-matched mortality following OVF.[14] Surgical intervention is highly recommended for patients who have an insufficient bony union of OVF, persistent back pain, and/or neurological deficits.[15] Recently, interest has increased in the mortality and morbidity of patients who undergo spinal surgery.[16, 17] Additionally, numerous reports have surfaced for comparative studies of surgical procedures for OVF; these have focused on surgical invasiveness and complications[18] By contrast, the long-term survival of patients with an insufficient bony union of OVF after surgery remains largely unknown. A recent study indicated that instrumented fusion surgery for lumbar trauma in the elderly is associated not only with increased morbidity, but also with reduced mortality.[19] Therefore, we sought to elucidate the preoperative risk factors which may predict postoperative mortality. Interestingly, our study indicated no significant differences in postoperative mortality among the 3 different surgical procedures assessed for OVF. In contrast, preoperative serum albumin levels were significantly lower in the patients with OVF who died, than in those who remained alive. The present study shows a significant association between a low preoperative serum albumin level of 3.5 g/dL, and a reduction in overall survival for patients undergoing surgery for an insufficient union of OVF.

The association between lower malnutrition and mortality risk has been known in patients with hip fractures [20, 21]. Serum albumin is well known as an important marker of preoperative nutritional status. Low levels of serum albumin can be prognostic by way of influencing organ vascularization. Moreover, low levels of serum albumin may hinder antibiotic therapy, prolong inflammation, and prompt intravascular coagulation.

This study has some limitations. Firstly, this study had the small sample size and the duration of follow-up; a longer follow-up would have been preferable. Secondly, the cause of death in many cases could not be determined accurately, because if a recent follow-up was not available from clinical records, patients were contacted by telephone to confirm their survival. Third, we cannot mention whether surgical therapy and difference in surgical techniques had an impact on the patient's prognosis in present study. Further study is needed to clarify the strategy for selecting surgical procedures and to include OVF patients treated with conservative therapy. However, to our knowledge, this is the first report to indicate that preoperative hypoalbuminemia can predict poor postoperative survival in patients with an insufficient bony union following OVF. This result suggests that designing a treatment strategy that takes into consideration indications and optimal timing for OVF surgery may have clinical significance. Further studies are needed to investigate the effects on postoperative mortality of improving nutritional status before surgery.

Conclusion

Hypoalbuminemia was associated with increased postoperative mortality over the long-term following OVF surgery.

List Of Abbreviations

Osteoporotic vertebral fractures (OVF), Lumbar spinal canal stenosis (LSS), Body mass index (BMI), Left ventricular ejection fraction (LVEF), B-type natriuretic peptide (BNP) level, Creatinine clearance (CCr), Bone mass density (BMD), The American Society of Anesthesiologists (ASA)

Declarations

•Ethics approval and consent to participate

This study was approved by the ethical committee of Yamanashi University.

•Consent for publication

Not applicable

•Availability of data and material

Not applicable

•Competing interests

The authors declare that they have no competing interests

•Funding

There is no funding should be declared

•Authors' contributions

"TO analyzed and interpreted the patient data was a major contributor in writing the manuscript. HY concerted study design. KK demonstrated statistical exam. TN and OK collected patient data. HH was editorial supervisor of this study. All authors read and approved the final manuscript."

•Acknowledgements

None

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Tables

TABLE 1. **Preoperative characteristics and demographics of patients with OVF***

Patients with OVF	(N = 105)
Age at the time of admission, y	76.3 ± 7.5
Gender, female/male, n	65/40
BMI (kg/m^2)	22.4 ± 3.3
BMD (%YAM)	69.7 ± 13.5
Follow-up duration, months	28.3 ± 31.8
Intraoperative technique, n	
VP (HA) + PF	49
BKP	18
ADF + PF	38

*Mean ± standard deviation, unless otherwise indicated.
ADF, anterior spinal decompression and fusion; BKP, balloon kyphoplasty;
BMI, body mass index; BMD, bone mineral density; HA, hydroxyapatite; OVF, osteoporotic vertebral fractures; PF, posterior fixation; VP, vertebroplasty.

TABLE 2. Pre and postoperative patients VAS scores (lumbar and leg).

	Preoperative	1year after surgery	p value
VAS score (lumbar)	7.4 ± 3.4	5.8 ± 3.8	<0.05*
VAS score (leg)	6.7 ± 2.8	3.4 ± 2.1	<0.05*

*Mean ± standard deviation, unless otherwise indicated.
*P < 0.05 in the comparison between groups.
VSA = visual analog scale

TABLE 3. Patient characteristics between those who died versus those who survived 2 years after surgery

Characteristic	Died (n = 19)	Survived (n = 56)	p value†
Male gender, n (%)	11 (57.9)	16 (28.6)	0.029*
Age, years	79.1 (7.6)	75.6 (8.0)	0.10
BMI, kg/m^2	21.3 (3.1)	22.5 (3.0)	0.15
LVEF, %	70.3 (9.6)	71.9 (14.1)	0.65
Serum albumin, g/dL	3.4 (0.5)	3.9 (0.5)	0.0016*
BNP, pg/mL	45.3 (36.4)	44.9 (47.2)	0.98
CCr, mL/min	49.9 (20.1)	63.1 (21.6)	0.021*
BMD, %YAM	63.4 (14.0)	66.8 (13.4)	0.47
Follow-up, months	57.1 (21.2)	66.4 (25.3)	0.13
Duration of conservative treatment, months	4.4 (2.1)	4.6 (0.49)	0.21
Surgical procedures			0.087
VP (HA) + PF	8 (42.1)	23 (41.1)	
BKP	1 (5.3)	13 (23.2)	
ADF + PF	4 (21.1)	12 (21.4)	
ASA classification ≥3	7 (36.8)	6 (10.7)	0.016*
Modified Frankel classification			
C versus D or E	8 (47.1)	21 (38.2)	0.58
Estimated blood loss, ml	168 (155)	335 (499)	0.11
Operative time, min	162 (98.9)	201 (114.3)	0.13

†p value for Fisher's exact test or Student's t test.

*P < 0.05 in the comparison between groups.

Variables are presented as mean (standard deviation) unless noted otherwise.

ADF, anterior spinal decompression and fusion; ASA, American Society of Anesthesiologists; BMD, bone mass density; BKP, balloon kyphoplasty; n, number in group; BMI, body mass index; BNP, B-type natriuretic peptide; CCr, creatinine clearance; HA, hydroxyapatite; LVEF, left ventricular ejection fraction; PF, posterior fixation; VP, vertebroplasty; YAM, young adult male.

TABLE 4. Presurgery hazard ratios (95% CI) of mortality based on patient characteristics (N = 105)

Explanatory variable	Crude	p value	Adjusted HR†	p value
Male vs female gender	2.74 (1.17, 6.41)	0.021	1.82 (0.76, 4.40)	0.18
BMI ≥25 vs 18.5–24.9 kg/m^2 BMI ≥25 vs. 18.5–24.9 kg/m^2	1.45 (0.41, 5.09)	0.56	1.67 (0.44, 6.32)	0.45
BMI <18.5 vs 18.5–24.9 kg/m^2 BMI <18.5 vs. 18.5–24.9 kg/m^2	2.78 (0.99, 7.81)	0.052	2.81 (0.96, 8.25)	0.061
Serum albumin <3.5 g/dL	4.99 (2.00, 12.43)	0.0006	3.37 (1.28, 8.89)	0.014
CCr <60 mg/dL	3.40 (1.15, 10.06)	0.027	1.96 (0.63, 6.05)	0.25
ASA physical status classification ≥3	3.93 (1.68, 9.21)	0.0017	2.36 (0.93, 6.01)	0.072

†Explanatory variables were selected using $p<0.2$ in the univariate analysis for crude hazard ratios. All of the variance inflation factors in the multivariate model for the calculation of adjusted hazard ratios were <1.22, indicating there was no multicollinearity.

ASA, American Society of Anesthesiologists; BMI, body mass index; CCr, creatinine clearance; CI, confidence interval; HR, hazard ratio.

Figures

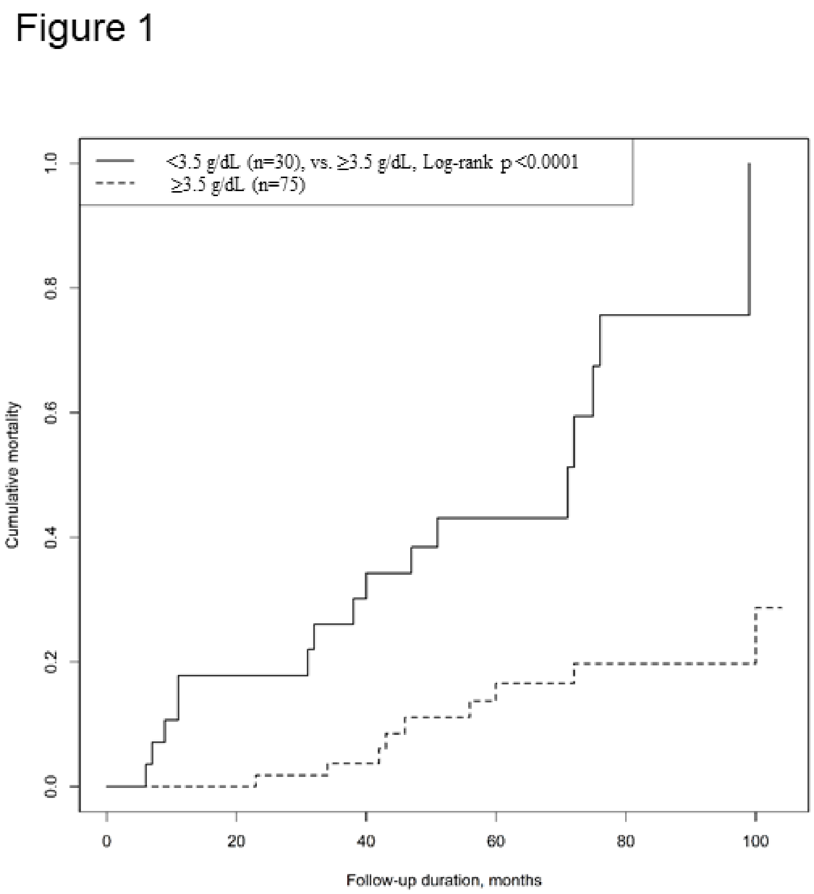

Figure 1

Overall survival comparison based on preoperative serum albumin levels (dashed line, ≤3.5 g/dL; solid line, >3.5 g/dL) using the Kaplan-Meier method.

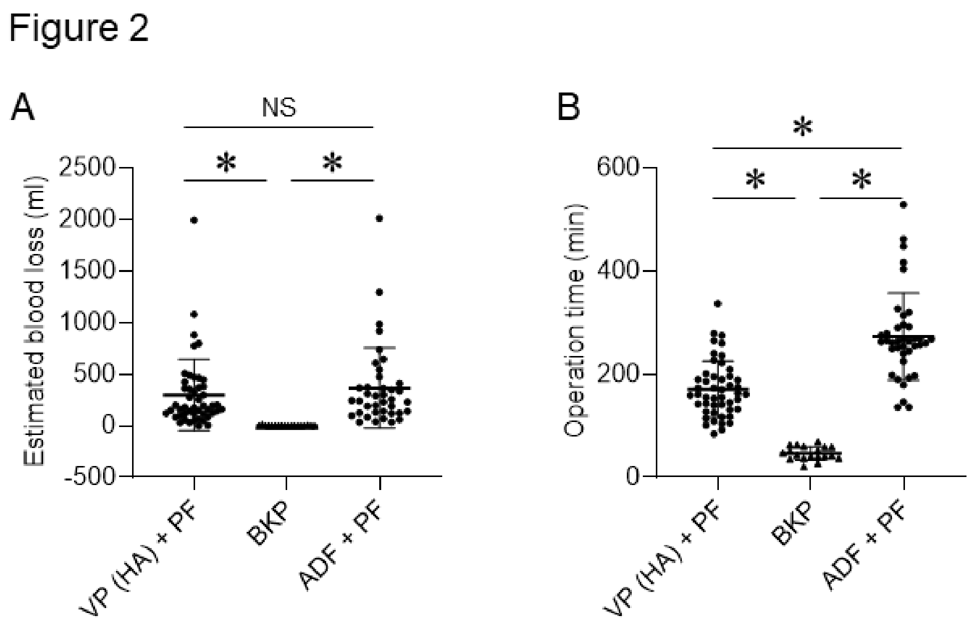

Figure 2

Comparisons of blood loss (A) and surgical time (B) among surgical procedures. ADF, anterior spinal decompression and fusion; BKP, balloon kyphoplasty; HA, hydroxyapatite; PF, posterior fixation; VP, vertebroplasty. *P < 0.05 NS = not significant. Data were analyzed using the unpaired T test.