ORIGINAL RESEARCH

Superoxide Dismutase and Glutathione Reductase as Indicators of Oxidative Stress Levels May Relate to Geriatric Hip Fractures' Survival and Walking Ability: A Propensity Score Matching Study

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Background: Oxidative stress status may affect bone metabolism and regeneration. However, few studies reported whether oxidative stress could impact the outcomes of hip fractures. This study aimed to explore if superoxide dismutase and glutathione reductase, the critical antioxidant enzymes, correlated with the prognosis of hip fractures.

Methods: Patients with hip fractures were extracted from our database, and those who met the inclusion criteria were analyzed. Propensity score matching was used to reduce the influence of confounding factors, and ROC curves based on matched populations were created to determine the optimal cutoff points of SOD and GR. Then, outcomes between SOD or GR and outcomes of hip fractures were compared.

Results: Out of 301 patients enrolled in this study, 50 patients died within one year. After a 1:1 PSM, the patients with less than 1-year survival had significantly lower SOD ($p = 0.026$) and GR ($p = 0.021$) than those who were still alive at one year. Logistics analysis showed that low SOD and low GR may be independent risk factors for 6-month survival, 1-year survival, 6-month free walking ability, and 1-year free walking ability.

Conclusion: SOD and GR may be the independent risk factors for survival and walking abilities of hip fractures.

Keywords: hip fractures, oxidative stress, superoxide dismutase, glutathione reductases, prognosis

Introduction

With the aggravation of the aging society, more and more elderly people suffer from fractures.[1] Hip fractures have become one of the most common and severe fractures in the old, and the incidence is increasing.[2] With the deterioration of the organs and lack of regeneration ability, the elderly with hip fractures, especially those accompanied by a variety of basic diseases, may have a poor prognosis even after surgery.[3] Poor bone regeneration is associated with nonunion of hip fractures, and the hip is the location that bears huge force, which results in a long stay in bed.[4] Unable to get up and walk may cause severe complications, such as pneumonia, decubitus, and thrombosis, which are the main cause of death for patients with hip fractures after surgeries.[5] Therefore, the potent ability of bone regeneration may accelerate the rehabilitation of hip fractures, then reduce the stay in bed and improve the survival rate and life quality.

Bone regeneration is a tightly regulated procedure that involves two types of cells: the osteoblasts and the osteoclasts. Osteoclasts play pivotal roles in bone resorption while osteoblasts involve in bone-forming. Both of them are critical in bone metabolism.[6] After the fracture, the broken end of the bone may stimulate inflammation by releasing inflammatory factors and promoting the chemotactic movement of immunocytes.[7] The inflammation causes cellular damage, and then

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free radicals, such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), were accumulated, resulting in oxidative stress.[8] Oxidative stress may interrupt the balance of bone metabolism and lead to abnormal bone generation, which makes patients who are suffering fractures have long bed-stay, fracture nonunion, and poor outcomes.[9] Many intrinsic enzymes may neutralize oxidative stress, such as superoxide dismutase (SOD), glutathione reductases (GR), and others. These enzymes can protect DNA, enzymes, and other cell structures from the damage of oxidative stress.[10]

SOD are the metalloproteins, and they have a remarkable efficiency in catalyzing the dismutation of superoxide and regulating oxidative stress.[11] Similarly, GR regulates oxidative stress by catalyzing the reduction of oxidized glutathione (GSSG) to GSH.[12] As the two widely used intrinsic antioxidant enzymes in clinical application, SOD and GR had been proven to be biomarkers of oxidative status in many pathological and physiological processes including bone regeneration.[13–16] However, how the SOD or GR correlate with outcomes of hip fracture has rarely been reported. In our study, we aimed to explore the relationships between oxidative stress and outcomes of hip fractures and identify if the levels of SOD and GR, the critical antioxidant enzymes, were associated with the survival and free walking ability of patients who underwent surgeries due to hip fracture.

Materials and Methods
Study Design and Data Collection
This study was a retrospective study using the data of patients admitted to the Department of Traumatology, Shanghai East Hospital, Tongji University, School of Medicine, Shanghai, China. The study was performed according to the Declaration of Helsinki and was approved by the Institutional Ethics Committee of East Hospital. Written informed consent was obtained from all participants enrolled in this study. All patient-related data were anonymized to ensure confidentiality.

The data of patients enrolled in this study were extracted from our database which was based on the data of all patients admitted to our department with hip fractures in recent five years. In our study, the data of patients who fulfilled the inclusion criteria and not met the exclusion criteria in the database were extracted. The inclusion criteria were set as below: (1) aged ≥50 years; (2) treated with surgeries; (3) underwent surgeries between January 2019 and February 2021. The exclusion criteria were as follows: (1) with high-energy mechanism fractures; (2) with pathological fractures; (3) with acute or severe liver diseases.

Baseline characteristics were collected and reviewed, including age, sex, height and weight, residence, the position of fracture, type of fracture, fractures history, smoking and alcoholism history, hip fracture type, polytrauma, surgical procedures, anesthesia, time from injury to surgery, electrocardiogram and chest radiograph, hemoglobin (Hb), international normalized ratio (INR), blood glucose (GLU), albumin (ALB), superoxide dismutase (SOD) and glutathione reductase (GR). Major comorbidities were reviewed and the Charlson comorbidity index (CCI) was calculated.[17] The diagnosis of electrocardiogram and chest radiograph were reviewed and evaluated by the corresponding author (Dr. Sun), and those may impact the prognosis of hip fractures were considered abnormal. All the laboratory test data analyzed in our study including SOD and GR were the data of the first routine test when patients were admitted to our hospital, and all laboratory tests were conducted immediately.

Follow Up and Outcomes
All patients in our database had been or were being followed up for one year. The status of patients who visited our outpatient clinic regularly was recorded by our colleagues while others were followed up via telephone. Survival time in our study was identified as the time from surgery to death caused by any disease. The patients with more than one-year survival were defined as censored data. Patients who were able to handle the daily activities without assistance were considered to have free walking abilities. Outcomes in this study were the statues of survival and free walking at 3 months, 6 months, and 1 year after surgery.

Statistical Analyses
Continuous variables were presented as mean ± standard deviation and evaluated by independent Student's *t*-test for normally distributed variables, and by Wilcoxon rank-sum test for non-normally distributed data. Categorical variables

were expressed as count (percent) and compared by chi-square test or Fisher's exact test. Baseline characteristics of the patients grouped by survival status at one year were summarized and compared. Then, a 1:1 PSM (propensity score matching) with a caliper of 0.2 in R software was used to reduce the influence of confounding factors and the baseline features were also examined for populations after matching. ROC curves were established to determine the optimal cutoff points of SOD and GR according to Youden Index.

Stepwise regression was used to identify if multiple co-linear relationships existed between SOD and GR. Similarly, Spearman's rank correlation coefficient was calculated to explore the correlation between SOD and GR. Cox analysis was used to identify the risk factors of 1-year survival, and SOD and GR in different types of variables were included. Moreover, outcomes were compared in patients divided by the levels of SOD and GR. Kaplan-Meier and Log rank tests were used for the analysis of 1-year survival. Then, Logistics regression was performed to identify the predicted value of SOD and GR for survival and free walking abilities at 6 months and 1 year after surgery. All $p < 0.05$ were considered statistically significant and statistical analyses were performed using SPSS version 26.0 (IBM, Armonk, NY, USA), GraphPad Prism version 8.0.1 (GraphPad Software San Diego, USA), and R software version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results
Study Population
Out of 604 patients who underwent hip surgeries for hip fractures between January 2019 and February 2021 in our hospital, 303 patients were excluded because of the unavailable data of SOD and GR, loss of following up, and miss of the inclusion. Finally, 301 patients were analyzed (Figure 1). All the surgical procedures for the patients were carried out by the senior author (Guixin, Sun) or in the presence and supervision of him, which may reduce the impact of the operator factor. Almost all the patients with intertrochanteric fractures were treated by internal fixation (only two cases underwent arthroplasty), while patients with femoral neck fractures were treated by internal fixation or arthroplasty (Figure 1). Patients were not allowed to bear any weight for 1 week after surgery, followed by partial weight bearing, then full weight bearing at 4 weeks. All the patients were able to walk independently before surgery.

Then the baseline characteristics were compared between the patients who survived more than one year and less than one year as shown in Table 1. Baseline features of patients grouped by type of surgery were also summarized in Supplementary Table 1. Many factors that may affect the outcomes of the patients were significantly different in the groups divided by 1-year survival (Table 1), so PSM was used to reduce the bias of the covariables.

PSM and Identification of Optimal Cutoff Points of SOD and GR
After PSM, there was no significant difference in covariables between the two groups (Table 1). As shown in the Figure 2A and B, in the PSM population, the levels of SOD of patients with more than 1-year survival were significantly higher than those with less than 1-year survival ($p = 0.026$, Figure 2A), as well as GR ($p = 0.021$, Figure 2B). To determine the most suitable cutoff points SOD and GR, ROC curves in the matched patients were established for SOD (area under the ROC curve, 0.635; $p = 0.026$; Figure 2C) and GR (area under the ROC curve, 0.640; $p = 0.021$; Figure 2D). According to Youden Index, the cutoff points of SOD and GR were 112.5 U/mL and 52.5 U/L, respectively. The patients with more than SOD levels of 112.5 U/mL were identified as high SOD while others as low SOD. Similarly, patients were also labeled as high GR and low GR according to GR of 52.5 U/L.

SOD and GR Were Risk Factors for Survival
Stepwise Regression showed that the tolerance between SOD and GR was 0.998 and the VIF (variance inflation factor) was 1.002, which suggested that there might be no multiple co-linear relationships between SOD and GR. Spearman correlation coefficient between SOD and GR was 0.045, which meant there was no significant correlation between SOD and GR. Four models were established based on Cox regression: Model 1 and Model 3 were adjusted for age, type of fracture, hypertension, Hb, CCI score, sex, time from injury to surgery, and ALB, while Model 2 and Model 4 were fully adjusted. Continuous SOD and GR were analyzed in Model 1 and Model 2 and grouped SOD and GR were included in Model 3 and Model 4. Model 1 and Model 3 were direct entry models while Model 2 and Model 4 were conditional
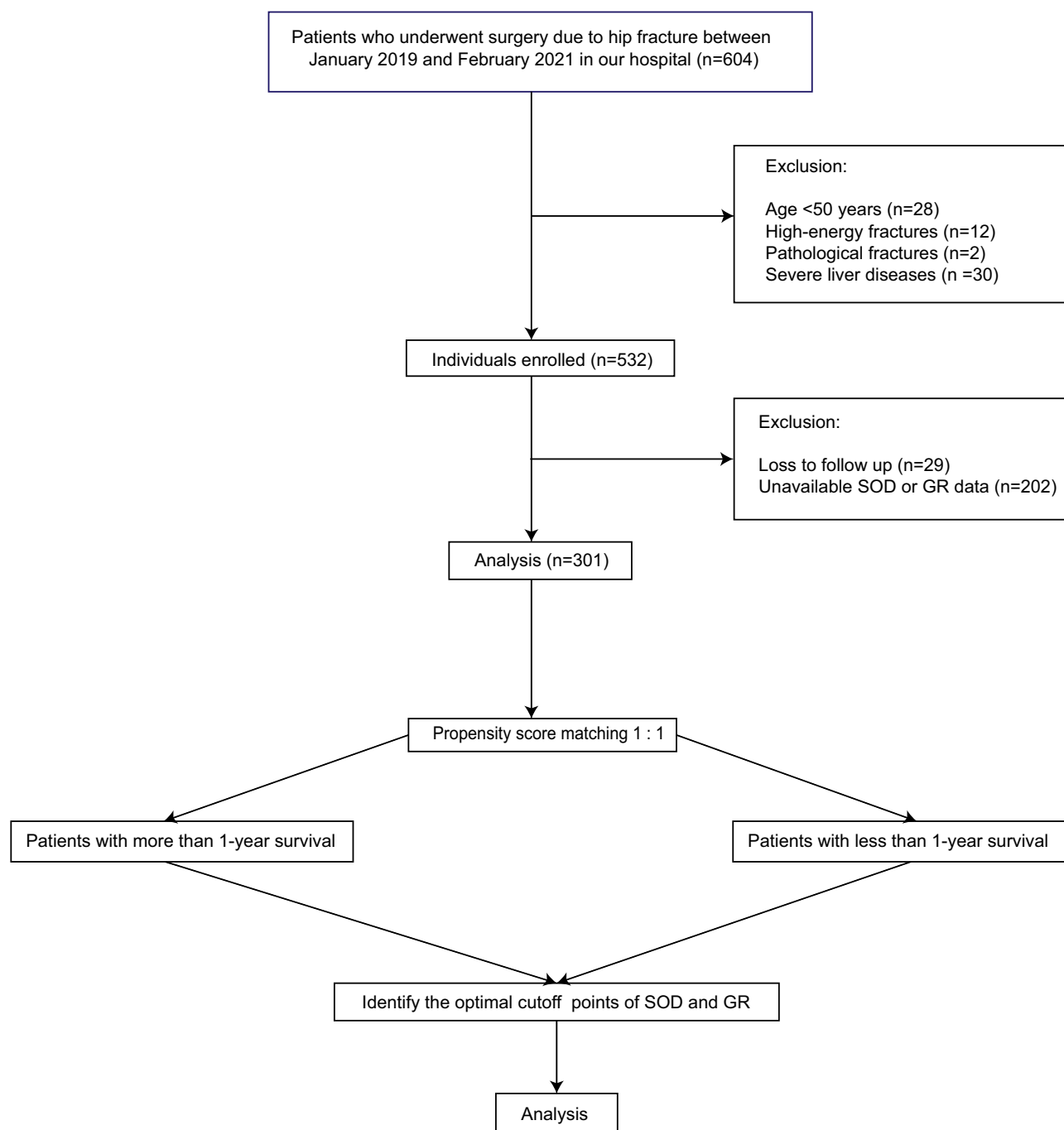
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┌─────────────────────────────────────────────────┐
│ Patients who underwent surgery due to hip fracture between │
│         January 2019 and February 2021 in our hospital (n=604)  │
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Exclusion:

Age <50 years (n=28)
High-energy fractures (n=12)
Pathological fractures (n=2)
Severe liver diseases (n =30)

Individuals enrolled (n=532)

Exclusion:

Loss to follow up (n=29)
Unavailable SOD or GR data (n=202)

Analysis (n=301)

Propensity score matching 1 : 1

Patients with more than 1-year survival

Patients with less than 1-year survival

Identify the optimal cutoff points of SOD and GR

Analysis

Figure 1 Flowcharts of our study.

stepwise forward models. As shown in Table 2, patients with higher SOD and GR may have decreased death risk. Patients with low SOD (≤112.5 U/mL) showed a 196.5% increase in death risk (HR = 2.965, CI: 1.605–5.476) in Model 3 and 169.0% (HR = 2.690, CI: 1.480–4.890) in Model 4. Similarly, death risk rose by 199.1% for patients with low GR in Model 3 (HR = 2.991, CI: 1.671–5.355) and 173.6% in Model 4 (HR = 2.736, CI: 1.563–4.792). The predictive value of all four models was measured and represented by C indices, and all models showed great prediction power (C indices: 0.832 for model 1; 0.822 for model 2; 0.831 for model 3; 0.821 for model 4; Supplementary Table 2). Survival probability between groups divided by different levels of SOD and GR was proved to be significantly different (For SOD groups: $p < 0.001$; For GR groups: $p = 0.006$). The patients with high SOD had significantly high survival probabilities than those with low SOD, as well as GR (Figure 3).

Table 1 Baseline Characteristics of Patients Grouped by the Status of 1-Year Survival for Unmatched and PSM Population

Variables	Unmatched Population			Matched Population		
	Survival ≤ 1 Year (n=50)	Survival > 1 Year (n=251)	P-value	Survival ≤ 1 Year (n=46)	Survival > 1 Year (n=46)	P-value
Demographic characteristics						
Sex (female)	40 (80.0%)	173 (68.9%)	0.116	37 (80.4%)	37 (80.4%)	>0.999
Age (years)	83.48 ± 7.58	74.08 ± 9.84	<0.001	83.37 ± 7.67	83.35 ± 7.30	0.760
BMI (kg/m2)	23.09 ± 3.35	23.10 ± 4.16	0.967	22.93 ± 3.22	23.42 ± 3.63	0.475
Residence (rural)	3 (6.0%)	9 (3.6%)	0.688	3 (6.5%)	1 (2.2%)	0.617
Fractures history (yes)	7 (14.0%)	39 (15.5%)	0.783	7 (15.2%)	7 (15.2%)	>0.999
Smoking history (yes)	2 (4.0%)	18 (7.2%)	0.609	2 (4.3%)	2 (4.3%)	>0.999
Alcoholism history (yes)	1 (2.0%)	7 (2.8%)	0.751	1 (2.2%)	1 (2.2%)	>0.999
Position of fracture (right)	23 (46.0%)	109 (43.4%)	0.738	20 (43.5%)	18 (39.1%)	0.672
Surgery-related variables						
Location of fracture (transcervical)	23 (46.0%)	143 (57.0%)	0.154	21 (45.7%)	17 (37.0%)	0.397
Surgical procedures (arthroplasty)	24 (48.0%)	117 (46.6%)	0.858	21 (45.7%)	18 (39.1%)	0.527
Anesthesia (spinal)	1 (2.0%)	2 (0.8%)	0.421	0 (0.0%)	0 (0.0%)	>0.999
Time from injury to surgery (Days)	6.16 ± 4.71	5.63 ± 6.62	0.084	6.00 ± 4.77	4.93 ± 2.82	0.150
CCI score (>4)	15 (30.0%)	48 (19.1%)	0.084	13 (28.3%)	14 (30.4%)	0.819
Electrocardiogram (abnormal)	30 (60.0%)	143 (57.0%)	0.692	28 (60.9%)	26 (56.5%)	0.672
Chest radiograph (abnormal)	30 (60.0%)	114 (45.4%)	0.059	28 (60.9%)	27 (58.7%)	0.832
Hypertension (yes)	35 (67.0%)	124 (49.4%)	0.008	31 (67.4%)	31 (67.4%)	>0.999
Polytrauma (yes)	5 (10.0%)	29 (11.6%)	0.752	4 (8.7%)	4 (8.7%)	>0.999
Laboratory findings						
Hb (g/L)	108.40 ± 21.37	116.24 ± 19.95	0.003	106.67 ± 19.79	103.39 ± 18.79	0.848
INR	1.04 ± 0.07	1.05 ± 0.14	0.538	1.04 ± 0.07	1.03 ± 0.09	0.576
GLU (mmol/L)	6.99 ± 2.96	6.71 ± 3.03	0.542	6.99 ± 3.03	6.96 ± 2.76	0.519
ALB (g/L)	36.88 ± 4.78	38.30 ± 4.32	0.066	36.76 ± 4.78	36.45 ± 3.86	0.584
SOD (U/mL)	116.66 ± 26.93	139.67 ± 27.89	>0.001	116.13 ± 27.48	133.00 ± 29.40	0.026
Glutathione reductase (U/L)	53.04 ± 13.23	59.27 ± 12.28	0.003	54.04 ± 12.64	59.70 ± 10.39	0.021

Notes: Continuous variables were expressed as mean ± standard deviation and categorical variables were presented as count (percent).
Abbreviations: BMI, body mass index; Hb, Hemoglobin; INR, international normalized ratio; GLU, blood glucose; ALB, albumin; SOD, superoxide dismutase; GR, glutathione reductases.

Outcomes

Then, outcomes were compared between high SOD groups and low SOD groups, as well as between high GR groups and low GR groups, respectively. Patients in the high SOD group have significantly more favorable survival and walking abilities at 3 months, 6 months, and one year than patients in the low SOD group. Likewise, patients with high levels of GR showed a significantly higher survival rate and free walking ability rate at 3 months, 6 months, and 1 year compared with those with low levels of GR (Table 3). Outcomes of patients with intertrochanteric fractures and femoral neck fractures were also summarized in Supplementary Table 1. To further prove the prognosis value of SOD and GR, logistics models fully adjusted for survival and free walking ability at 6 months and 1 year were established by conditional stepwise forward methods and the results are shown in Table 4. As shown in Table 4, low SOD and low GR may be independent risk factors for 6-month survival, 1-year survival, 1-year free walking ability, and 1-year free walking ability (Table 4).
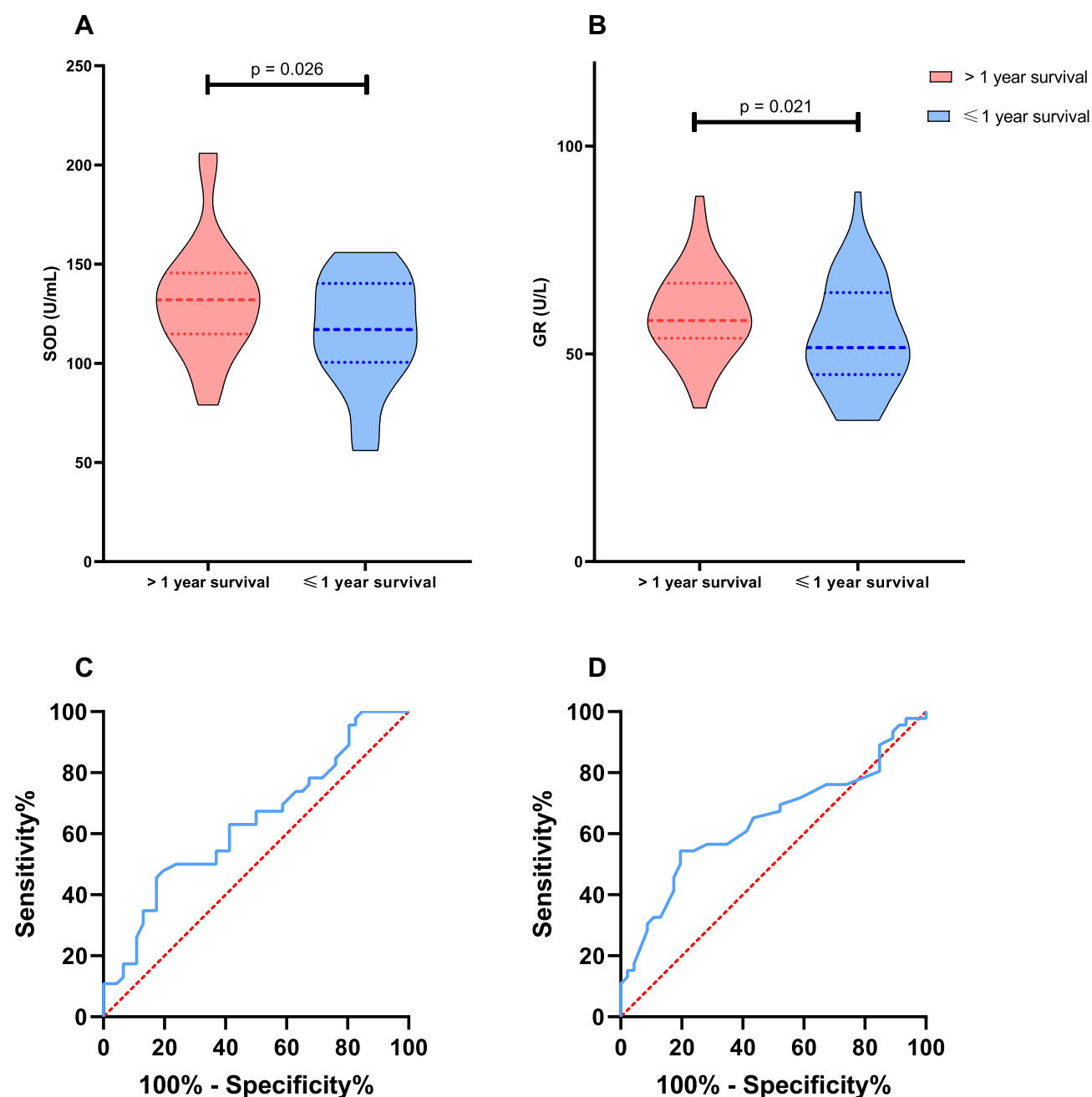
Figure 2 Serum levels of SOD and GR in the patients with Hip fracture after surgery grouped by one-year survival (**A** and **B**), and ROC curves of SOD and GR for one-year survival (**C** and **D**). (**A** and **B**) The patients who survived more than one year had significantly higher SOD levels (p = 0.026) than those who survived less than one year in the PSM population, as well as GR (p = 0.021); (**C** and **D**) Both SOD (AUROC: 0.635) and GR (AUROC: 0.640) were able to predict the 1-year survival according to the ROC curves.

Discussion

In this study, we found that the patients with high SOD or GR may have a more favorable prognosis than those with low SOD or GR. In clinical practice, the predictive value of SOD and GR could be used for elderly patients. As we all know, many factors may impact the outcomes of patients with hip fractures, so PSM was performed to reduce the bias caused by co-factors, such as age, sex, fracture types, and as shown in Table 1, all basic features between groups did not differ significantly. The cutoff points according to the ROC curve in the population after PSM may have a better predictive value. GR may rise in the patients with severe liver disease, so the patients with severe liver disease were excluded to remove the impact of liver disease.[18] Cox analyses also showed that SOD and GR, whether in continuous form or

Table 2 Cox Regression Analyses of 1-Year Survival Adjusted for Different Factors

Variables	Model 1		Model 2	
	HR (95% CI)	p	HR (95% CI)	p
Age	1.077 (1.038, 1.117)	<0.001	1.077 (1.042, 1.113)	<0.001
SOD (continuous)	0.976 (0.965, 0.988)	<0.001	0.977 (0.966, 0.989)	<0.001
GR (continuous)	0.969 (0.944, 0.994)	0.016	0.969 (0.945, 0.994)	0.014
	Model 3		Model 4	
	HR (95% CI)	p	HR (95% CI)	p
Age	1.078 (1.039, 1.118)	<0.001	1.077 (1.042, 1.112)	<0.001
SOD (≤ 112.5 U/mL)	2.965 (1.605, 5.476)	0.001	2.690 (1.480, 4.890)	0.001
GR (≤ 52.5 U/L)	2.991 (1.671, 5.355)	<0.001	2.736 (1.563, 4.792)	<0.001

Notes: Model 1 and Model 3 were adjusted for age, type of fracture, hypertension, Hb, CCI score, sex, time from injury to surgery, and ALB. Model 2 and Model 4 were fully adjusted. Continuous SOD and GR were analyzed in Model 1 and Model 2. Grouped SOD and GR were included in Model 3 and Model 4. Model 1 and Model 3 were direct entry models while Model 2 and Model 4 were conditional stepwise forward models.

grouped form, were all associated with survival. The patients with higher SOD or GR seem to have less death risk. This result was also proved in logistics analysis.

SOD and GR are pivotal antioxidant enzymes that could defend our cells from the damage of oxidative stress. Many factors, including fractures, may result in increased oxidative damage via inflammatory pathways and so on, which may consume the efficiency of the antioxidant defense system.[7,10] Therefore, we believe that the patients with high SOD or GR may have strong abilities to defend their bones from oxidative stress, and then are more likely to have a more satisfactory rehabilitation. Many studies had shown how the status of oxidative stress impacts bone remolding and bone healing. As we mentioned above, there are two types of cells involve the bone remolding: osteoblasts and osteoclasts. The oxidative stress affects bone metabolism by regulating the balance between osteoblasts and osteoclasts: oxidative stress could increase osteoclastogenesis and apoptosis of osteoblast and osteocyte, and decrease the activity of osteoblast and differentiation to the osteoblast cell lineage.[19] It is proved that antioxidants can reduce the expression of the receptor activator of NF-kB ligand (RANKL) and increase the expression of osteoprotegerin,[20] and osteoclastogenesis can be upregulated by increased RANKL and decreased osteoprotegerin.[21] Animal studies have shown that oxidative stress induced by H_2O_2 can reduce osteoblast differentiation and decrease differentiation markers.[22]
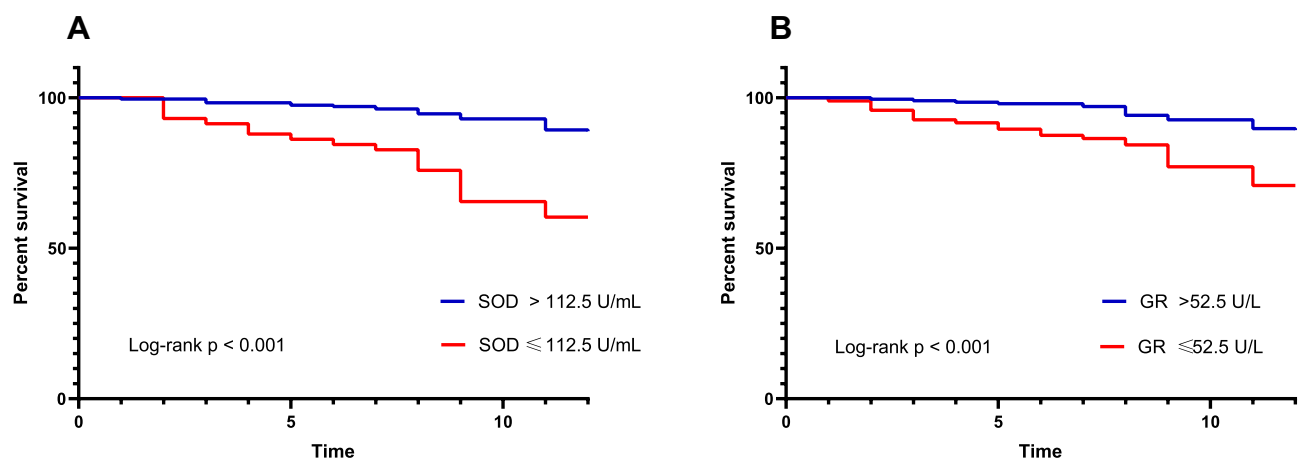

Figure 3 Kaplan–Meier analyses of one-year survival based on optimal serum levels of SOD (112.5 U/mL) and GR (52.5 U/L). (**A**) Kaplan–Meier analysis showed that SOD values of 112.5 U/mL significantly differentiated patients who died within one year and survived more than one year (p < 0.001), (**B**) SOD values of 52.5 U/L significantly differentiated patients who died within one year and survived more than one year (p < 0.001).

Table 3 Comparison of Outcomes of All Patients in Our Study

Outcomes	Total (N=458)	SOD			GR		
		SOD ≤ 112.5 U/mL	SOD > 112.5 U/mL	P-value	GR ≤ 52.5 U/L	GR > 52.5 U/L	P-value
3-month mortality	9 (3.0%)	5 (8.6%)	4 (1.6%)	0.018	7 (7.3%)	2 (1.0%)	0.008
6-month mortality	16 (5.3%)	9 (15.5%)	7 (2.9%)	<0.001	12 (12.5%)	4 (2.0%)	<0.001
1-year mortality	50 (16.6%)	23 (39.7%)	27 (11.1%)	<0.001	28 (29.2%)	22 (10.7%)	<0.001
3-month independent walking rate	58 (19.3%)	6 (10.3%)	52 (21.4%)	0.055	10 (10.4%)	48 (23.4%)	0.008
6-month independent walking rate	164 (54.5%)	17 (29.3%)	147 (60.5%)	<0.001	36 (37.5%)	128 (62.4%)	<0.001
1-year independent walking rate	202 (67.1%)	22 (37.9%)	243 (74.1%)	<0.001	49 (51.0%)	153 (74.6%)	<0.001

Table 4 Logistics Regression for Mortalities at 6 Months and 1 Year and Free Walking Abilities at 6 Months and 1 Year

	6-Month Mortality		1-Year Mortality		6-Month Free Walking Ability		1-Year Free Walking Ability	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
SOD (continuous)	0.975 (0.953, 0.997)	0.025	0.975 (0.961, 0.989)	<0.001	1.016 (1.005, 1.026)	0.003	1.017 (1.006, 1.028)	0.003
GR (continuous)	0.929 (0.880, 0.979)	0.006	0.964 (0.936, 0.992)	0.012	1.037 (1.014, 1.061)	0.002	1.043 (1.006, 1.028)	0.001
SOD (≤ 112.5 U/mL)	4.071 (1.300, 12.751)	0.016	3.613 (1.715, 7.609)	0.001	0.416 (0.204, 0.847)	0.016	0.331 (0.163, 0.673)	0.002
GR (≤ 52.5 U/L)	7.193 (2.114, 24.475)	0.002	3.613 (1.715, 7.609)	<0.001	0.354 (0.199, 0.631)	<0.001	0.316 (0.171, 0.583)	<0.001

Note: All models were conditional stepwise forward models and fully adjusted.

Many population studies had suggested that populations with potent antioxidant status may have a better bone mass density (BMD) than those with oxidative stress status.[23] In a recent study, the serum levels of RANKL, OPG, and 8-hydroxy-2-deoxyguanosine as the marker of oxidative stress were measured to explore the implication of oxidative stress in bone metabolism based on the populations of healthy people and patients with osteoporosis, and the positive and independent correlation between increased oxidative stress markers and the subgroup of osteoporosis was found.[24] A study conducted in Japan showed that the markers of oxidative stress may predict hip fractures.[25] However, if the oxidative markers can predict the outcomes of hip fractures has not been reported. Therefore, in our study, SOD and GR, as critical antioxidant enzymes, were used to explore whether patients with potent antioxidant status can have a favorable survival and walking ability.

There are some limitations to our study. First, as a retrospective single-center study, this study contended with the missing follow-up and unavailable data of SOD and GR. Next, the values of SOD and GR were extracted from the first laboratory test when patients were admitted to our department. The serum levels of SOD and GR may fluctuate, which may cause bias in our results. However, we believe the data of patients at the first time may better show the daily situation. Moreover, the types of fracture were divided into intertrochanteric fractures and femoral neck fractures instead of more strict classification such as OTA/AO classification. Lastly, there may be some potential co-factors that we did not include in our analysis. We believe our study may also indicate the relationship between SOD or GR and outcomes of hip fractures despite the limitations we mentioned above.

Low levels of SOD or GR may indicate poor antioxidant status and predict poor outcomes, so we may hypothesize that neutralizing oxidative stress may provide a better prognosis for our patients with hip fractures. Decreasing oxidative stress and increasing antioxidant ability may face the potent prospect of clinical application for improving the outcomes of hip

fractures. Many studies based on animal models had reported the potential novel treatment of fractures by regulating the oxidative status. Ilyas et al developed a new biomaterial based on amorphous silicon oxynitride. This fracture healing material may release Si^{+4}, which may enhance SOD and then stimulate osteogenesis.[26] Many studies also reported the potential efficiency of SOD mimic in antioxidation.[27,28] Many population studies showed that the patients with a higher intake of antioxidant nutrients may face a lower risk of hip fractures.[29,30] Consistently, it was also reported that antioxidant vitamin E or C supplements may be associated with decreased bone resorption in nonsmoking postmenopausal women.[31] However, few had demonstrated an effect of supplemental antioxidants on the prognosis of hip fractures. We look forward to proving the hypothesis through experimental population studies with a high level of evidence.

Conclusion

SOD and GR may be the independent risk factors for survival and walking abilities of hip fractures.

Data Sharing Statement

The data is unavailable because of the concern for patient privacy.

Ethics Approval and Informed Consent

This study was an observational study using the data of patients admitted to the Department of Traumatology, Shanghai East Hospital, Tongji University, School of Medicine, Shanghai, China. The study was performed according to the Declaration of Helsinki and was approved by the Institutional Ethics Committee of East Hospital. Written informed consent was obtained from all participants enrolled in this study.

Consent for Publication

We declare that all authors have seen and approved the final version of the manuscript being submitted and that all authors have confirmed that the details of any images, videos, recordings, etc can be published.

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Disclosure

The authors declare that no conflicts of interest exist in this work.

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