Retrospective Study

Correlation Analysis Between Basic Diseases and Subsequent Vertebral Fractures After Percutaneous Kyphoplasty (PKP) for Osteoporotic Vertebral Compression Fractures

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Background: Percutaneous kyphoplasty (PKP) is a widely accepted surgical treatment modality for painful osteoporotic vertebral compression fractures. The risk factors cause of subsequent vertebral fractures after PKP are debated.

Objectives: To evaluate risk factors for the occurrence of new vertebral compression fractures after PKP.

Study Design: A retrospective study.

Setting: A single-center inpatient population.

Methods: A total of 921 patients (1,152 vertebrae) with PKP were investigated. Among those patients, 111 patients (155 levels) incurred refractures after PKP.

Results: The average bone mineral density was -3.27 in the "refracture"group and -3.00 in the "no fracture" group (P = 0.031). Morbidities of women were significantly higher in the "refracture" group (90.99%) compared with the "no fracture" group (81.73%) (P = 0.015). Among the basic diseases, several diseases (history of previously fracture, previously osteoporosis, gallstone disease, stomach disease, and ovariectomy) are associated with refractures after PKP (P < 0.05). And antiosteoporotic treatment (calcium + vitamin D or zoledronate) after PKP can also significantly reduce the occurrence of refracture (P < 0.000). In addition, logistic regression analysis also showed that most of the above contents had significant correlation with the refracture after PKP (P < 0.05), except for gallstone disease (P = 0.362).

Limitations: Retrospective study, single center.

Conclusion: Osteoporosis is the main cause of refracture after PKP. Elderly women were found to be more susceptible than elderly men to refracture. Patients with a history of previously fracture, previously osteoporosis, stomach ulcer, and ovariectomy are more likely to be refracture. Antiosteoporosis treatment (calcium + vitamin D or zoledronate) after PKP can reduce the risk of refracture.

Key words: Osteoporosis, percutaneous kyphoplasty, vertebral compression fractures, bone mineral density

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Osteoporosis is the most common disease of the elderly, and often leads to fragility vertebral compression fractures (VCFs). The annual incidence of VCFs is 10.7/1000 in women and 5.7/1000 in men (1). It is the major cause of pain and disability in the elderly population (2). Conservative management, including taking painkillers, bed rest, physical therapy, and preventing future fractures, may fail to relieve pain and frequently lead to a substantial negative impact on quality of life (3,4).

Percutaneous kyphoplasty (PKP) or percutaneous vertebroplasty (PVP) is a minimally invasive and a widely accepted surgical treatment for symptomatic osteoporotic vertebral compression fractures (OVCFs) (5,6). With the extensive use of PKP, the occurrence of subsequent vertebral fractures after kyphoplasty has attracted more and more attention. Known risk factors for OVCFs include the degree of osteoporosis, women, history of fractures, older age, dementia, smoking, alcoholism, inactivity, corticosteroids, estrogen deficiency, and so on (7). However, the cause of refracture (the new vertebral body or the PKP vertebral body) after kyphoplasty is not clear. Many scholars believe that osteoporosis itself is the main factor leading to refracture after PKP.

Therefore, the purpose of this study was to investigate the relationship between the refracture after PKP and the risk factors [age, gender, height, weight, body mass index (BMI), bone mineral density (BMD) score of the lumbar vertebra, surgical segment of vertebral body, smoking/alcoholism situation, other diseases, the treatment of osteoporosis after PKP, and so on.]. This could help identify patients at higher probability of recurrent fractures, for whom the proper approach could be taken from the beginning.

Methods

Patients

Between January 2008 to May 2017, 1,042 cases of vertebral fracture with pain and other symptoms received PKP treatment. All the patients had severe back pain which was refractory to conservative therapy, such as bed rest and treatment with analgesics and antiosteoporotic medication. The pain region was consistent with the presence of oedema in the fractured vertebra found on magnetic resonance imaging. Final, 96 patients with diseases such as hemangioma, multiple myeloma, or spine metastatic pathologic fractures and 25 patients lost to follow-up were rejected.

In total, 921 cases (763 women, 158 men) with 1,152 segments were included in this research. The average follow-up time was 42.63 ± 22.18 months (6-102 months). The mean age of the patients was 72.06 ± 8.95 years (50-93 years) at the time of operation. The mean BMI of the patients was 22.74 ± 3.50, and the mean BMD was -3.03 ± 1.21 standard deviation (SD). Among those patients, 111 patients incurred new vertebral fractures after kyphoplasty. All patients were assigned into "refracture" (111 patients) or "no fracture" (810 patients) groups. In the "refracture" group, 9 patients had 2 times that of refractures after PKP, and 2 patients had 3 times that of refracture after PKP. Final, 51 cases were adjacent vertebral fractures, 67 cases were non-adjacent vertebral fractures, and 6 cases were refracture of the surgical vertebral body.

Surgical Technique

All PKP was performed according to standardized procedures, and procedures were performed under general anesthesia using fluoroscopic guidance. Initially, patients were placed in the prone position with a bolster placed under the sternum and pelvis. Under the guidance of fluoroscopy, the trocar and cannula systems were inserted into the fractured vertebral body through the transpedicular approach. Then, the trocar was removed and the sacculus was placed through the cannula and into the anterior three-fourths of the vertebral body in the lateral view. The sacculus was filled with contrast medium slowly and removed. Finally, the bone cement (polymethyl methacrylate) was gradually inserted to fill the space when it became doughy and could stand at the tip of the bone cement inserter. If the bone cement reached the posterior one-fourth of the vertebral body or there was obvious leakage, the operation was stopped immediately.

Data Collection

Information are analyzed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA), and are presented as the mean ± SD for continuous variables or as percentages (%) for categorical variables. The t test for continuous variables and the Chi square test for categorical variables were used to evaluate the difference between patients with or without new VCFs. The multifactor analysis was carried out by logistic retrospective analysis.

Results

Among the 921 patients with PKP, 111 (12.05%,

101 women, 10 men) experienced refracture after PKP. The initial fracture occurred between T4 and L5, but it was most common at the thoracolumbar junction. L1 and T12 were the most easily fracture sites (Fig. 1). Out of 111 patients with 124 new post-PKP VCFs, 54.03% (67) were nonadjacent vertebra fractures, 41.13% (51) were adjacent vertebra fractures, and 4.84% (6) were refracture of the surgical vertebral body. As with the initial vertebral fracture, the segment of recurrent fracture was mainly concentrated in the thoracolumbar junction (Fig. 2).

A detailed history of medical treatment was reviewed in all patients. Among them, the most underlying disease was hypertension (373 patients, 40.5%) and diabetes (118 patients, 12.8%). In addition, there were many common diseases, such as heart disease (83 patients, 9%), stomach ulcer (35 patients, 3.8%), tumor history (58 patients, 6.3%), lung disease (73 patients,7.9%), gallstone disease (74 patients, 8.0%), ovariectomy (16 patients, 1.7%), and so on. In all patients, there were 29 cases (3.1%) of smoking, 43 cases (4.7%) of alcoholism, and 27 cases (2.9%) of long-term use of glucocorticoid. We also traced the treatment of antiosteoporosis in all patients after PKP. Among them, 768 patients (83.4%) were able to receive long-term oral calcium and vitamin D, 444 patients (48.2%) received intravenous zoledronic acid, and 51 (5.54%) patients were treated with alendronate (Table 1). Of all the patients, 131 (14.22%) did not use antiosteoporotic drugs, 295 (32.03%) received calcium and vitamin D alone, 17 (1.85%) received zoledronic acid alone, and 5 (0.54%) received alendronate alone. Only 473 patients (51.36%, 427 zoledronic acid, 46 alendronate) were treated with zoledronic acid/alendronate + calcium + vitamin D.

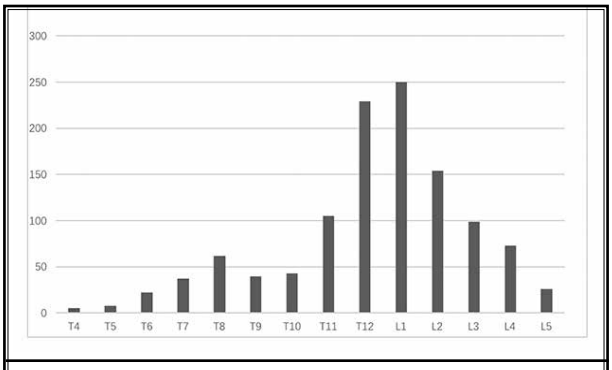

Fig. 1. *Number of treatments per vertebral level.*

Table 1. *A list of basic medical conditions for patients.*

Variable	Cases (Percentage)	Variable	Cases (Percentage)
Hypertension	373 (40.50%)	Abnormal liver function	23 (2.50%)
Diabetes	118 (12.81%)	Arthritis	19 (2.06%)
Heart disease	83 (9.01%)	Adenomam-mectomy	19 (2.06%)
Gallstone disease	74 (8.03%)	Abnormal renal function	18 (1.95%)
Lung disease	73 (7.93%)	Ovariectomy	16 (1.73%)
History of previously fracture	67 (7.27%)	Parkinson	12 (1.30%)
Tumor history	58 (6.30%)	Mental illness	6 (0.65%)
Appendectomy	36 (3.91%)	Splenectomy	3 (0.33%)
Stomach diseases	35 (3.80%)	Smoking	29 (3.15%)
Cerebral infarction	32 (3.47%)	Alcoholism	43 (4.70%)
History of osteoporosis	29 (3.10%)	Use of glucocorticoid	27 (2.93%)
Thyroidectomy	24 (2.61%)	Alendronate	51 (5.54%)
Calcium + vitamin D	768 (83.39%)	Zoledronic acid	444 (48.21%)

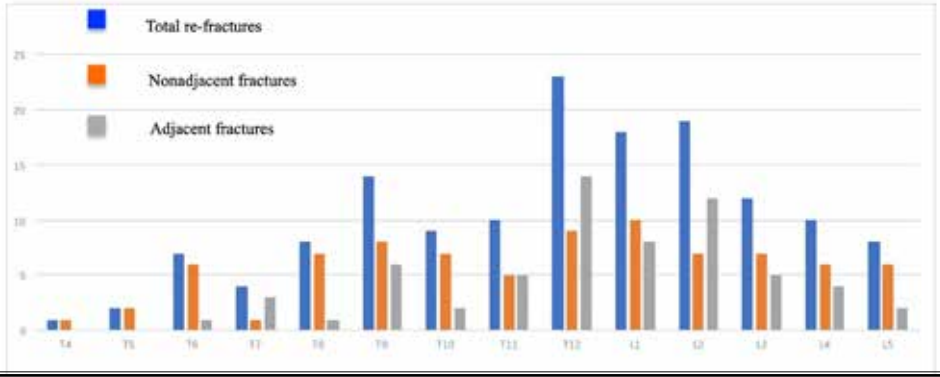

Fig. 2. *Segmental distribution of recurrent vertebral fractures.*

Table 2 shows the comparison between the "refracture" group and the "no fracture" group. The age, height, weight, and BMI exhibited no significant differences between the "refracture" group and the "no fracture" group. The T-score of the spinal BMD in the "refracture" group was -3.27 ± 1.14, while the BMD was -3.00 ± 1.22 in the "no fracture" group (P = 0.031). The prevalence rate of women in the "refracture" group (90.99%) was significantly higher than that in the "no fracture" group (81.73%) (P = 0.015). Among the numerous basic diseases, several diseases are associated with refractures after PKP. Before the occurrence of OVCFs, patients with a history of previously fracture or history of osteoporosis are more prone to refracture after PKP (P < 0.000). In addition, patients with gallstone disease, stomach ulcer, or ovariectomy are more likely to have refractures (P < 0.05). And oral calcium + vitamin D or zoledronic acid intravenously can significantly reduce the risk of refracture (P < 0.000). But patients with alendronate were significantly higher in the "refracture" group (12.61%, 14/111) compared with the "no fracture" group (4.57%, 37/810) (P = 0.001).

Table 2. *The comparison between the "refracture" group and the "no fracture" group by constitutional factors.*

Variable	No fracture group (810)	Refracture group (111)	*P* value
Age (year)	72.04 ± 9.18	72.19 ± 7.11	0.839
No of female (%)	662 (81.73%)	101 (90.99%)	0.015*
Mean body height (cm)	157.59 ± 6.62	157.82 ± 5.39	0.683
Mean body weight (kg)	56.62 ± 10.25	56.77 ± 9.53	0.888
Mean BMI (kg/m^2)	22.73 ± 3.48	22.80 ± 3.68	0.851
Mean spinal BMD (T-score)	-3.00 ± 1.22	-3.27 ± 1.14	0.031*
Smoking	23 (2.84%)	6 (5.41%)	0.147
Alcoholism	39 (4.81%)	4 (3.60%)	0.571
Use of glucocorticoid	22 (2.72%)	5 (4.50%)	0.295
Calcium + vitamin D	701 (86.54%)	67 (60.36%)	0.000*
Zoledronic acid	430 (53.09%)	14 (12.61%)	0.000*
Alendronate	37 (4.57%)	14 (12.61%)	0.001*
Hypertension	321 (39.63%)	52 (46.85%)	0.146
Diabetes	108 (13.33%)	10 (9.01%)	0.201
Heart disease	72 (8.89%)	11 (9.91%)	0.725
Gallstone disease	56 (6.91%)	18 (16.22%)	0.001*
Lung disease	60 (7.41%)	13 (11.71%)	0.115
History of previously fracture	47 (5.80%)	20 (18.02%)	0.000*
Tumor history	50 (6.17%)	8 (7.21%)	0.674
Appendectomy	33 (4.07%)	3 (2.70%)	0.661
Stomach diseases	20 (2.47%)	15 (13.51%)	0.000*
Cerebral infarction	25 (3.09%)	7 (6.31%)	0.082
History of osteoporosis	15 (1.85%)	14 (12.61%)	0.000*
Thyroidectomy	20 (2.47%)	4 (3.60%)	0.700
Abnormal liver function	19 (2.34%)	4 (3.60%)	0.637
Arthritis	15 (1.85%)	4 (3.60%)	0.389
Adenomammectomy	14 (1.73%)	5 (4.50%)	0.054
Abnormal renal function	16 (1.96%)	2 (1.80%)	1.000
Ovariectomy	11 (1.36%)	5 (4.50%)	0.017*
Parkinson	10 (1.23%)	2 (1.80%)	0.962
Mental illness	6 (0.74%)	0 (0.00%)	1.000
Splenectomy	2 (0.25%)	1 (0.90%)	0.806

*Statistically significant.
Abbreviations: BMI, body mass index; BMD, bone mineral density.

Multivariate logistic regression analysis was performed for gender, BMD, ovariectomy, gallstone disease, stomach ulcer, history of previously fracture, history of osteoporosis, oral calcium + vitamin D, and zoledronic acid intravenously (Table 3). The results showed that most of the above contents were risk factors for the refracture after PKP, except for gallstone disease [P = 0.362, odds ratio (OR) 1.419,95% confidence interval (CI) (0.669, 3.012)]. The risk of refracture after PKP is 2.672 times higher in women than in men. [P = 0.012, 95% CI (1.246, 5.729)]. The lower the T-value of BMD, the higher the risk of refracture after PKP. [P = 0.021, OR 0.787, 95% CI (0.643, 0.964)]. Ovariectomy can increase the risk by 3.808 times [P = 0.041, 95% CI (1.054, 13.758)], and stomach ulcer can increase the risk by 7.923 times [P = 0.000, 95% CI (3.278, 19.149)]. The

Table 3. *Multivariate logistic regression analysis between "refracture" group and "no fracture" group.*

Variable	*P* value	OR	95% CI
Gender	.012*	2.672	1.246, 5.729
BMD	.021*	.787	0.643, 0.964
Calcium + vitamin D	.000*	.313	0.187, 0.525
Gallstone disease	.362	1.419	0.669, 3.012
Stomach diseases	.000*	7.923	3.278, 19.149
History of previously fracture	.000*	4.827	2.433, 9.578
History of osteoporosis	.000*	11.454	4.469, 29.361
Ovariectomy	.041*	3.808	1.054, 13.758
Zoledronic acid	.000*	.131	0.069, 0.248

*Statistically significant.
Abbreviation: BMD, bone mineral density.

history of previously fracture can increase the risk by 4.827 times [*P* = 0.000, 95% CI (2.433, 9.578)], and the history of osteoporosis can increase the risk by 11.454 times [*P* = 0.000, 95% CI (4.469, 29.361)]. Zoledronic acid can reduce the risk to 0.131 [*P* = 0.000, 95% CI (0.069, 0.248)], and oral calcium + vitamin D can reduce the risk to 0.313 [*P* = 0.000, 95% CI (0.187, 0.525)].

Discussion

PKP is a widely used surgical method for symptomatic OVCFs. With the extensive use of PKP, the occurrence of refracture after kyphoplasty has attracted more and more attention. The reported incidence of refracture after PKP ranges from 8% to 52% (8,9). Most of the new VCFs after PKP were previously reported to occur in the adjacent vertebrae (10,11). However, many articles reported that the nonadjacent vertebra fracture is more likely to happen after PKP (12). Similarly, we also find that refracture after PKP occurred most often in nonadjacent vertebrae. In this study, out of 111 patients with 124 new post-PKP VCFs, 67 (54.03%) were nonadjacent vertebra fractures, compared with 51 (41.13%) adjacent vertebra fractures. And 6 (4.84%) were refractures of the surgical vertebral body. Indeed, more fractures were not adjacent, but only 2 vertebral bodies are adjacent and the nonadjacent could be any of over 14 other vertebral bodies (only the number of thoracic and lumbar vertebrae was included). Excluding all other factors (such as mechanics, and so on) and assuming the probability of adjacent and nonadjacent vertebral fractures is the same, the number of nonadjacent vertebral fractures should be 7 times that of adjacent vertebral fractures. From this study, we can conclude that the probability of adjacent vertebral fractures is 5.328 times that of nonadjacent vertebral fractures. So, from the perspective of probability, the risk of refracture in an adjacent vertebral body is higher than that in a nonadjacent vertebral body. However, in the real sense, the incidence probability can't be calculated by the number of adjacent or nonadjacent vertebrae. Because we found from Fig. 1 that the incidence rate of each vertebral body is different, and the highest L1 (250 patients) is 50 times of the lowest T4 (5 patients), while the incidence of T1-T3 itself is 0. In addition, we did not find obvious difference in the distribution of adjacent vertebral fractures and nonadjacent vertebral fractures from Fig. 2. Therefore, we believe that nonadjacent vertebral fractures are more common in clinical practice.

Osteoporosis is a major risk factor for vertebral compression fractures (13). The level of BMD reflects the degree of osteoporosis (14,15). In 2 recent meta-analyses (16,17), low BMD is a high-risk factor for refracture after PVP. Our results also confirm that low BMD is an important risk factor for refracture after PKP. In this research, the average T-value of lumbar BMD was (-3.27 ± 1.14) SD in the "refracture group" and (-3.00 ± 1.22) SD in the "no fracture" group, the difference was statistically significant (*P* = 0.031). Multivariate logistic regression analysis also suggested that low BMD is a high-risk factor for refracture after PKP [*P* = 0.021, OR 0.787, 95% CI (0.643, 0.964)].

Osteoporosis, which is slow but sure to nibble away at the bone, may have been ignored for many years until it is finally exposed to fractures of almost all vertebrae without any cause. Until recently, osteoporosis has been diagnosed only after the patient presented with painful fractures. In this study, most of the patients were diagnosed with osteoporosis for the first time because of these vertebral fractures. When patients are diagnosed with osteoporosis before these fractures, they are more likely to have refractures. In this study, 29 (3.15%, 29/921) patients had a history of osteoporosis before VCF occured. And 14 (12.61%, 14/111) patients had history of osteoporosis in the "refracture" group, while only 15 (1.85%, 15/810) patients in the "no fracture" group (P = 0.000). Logistic regression analysis also suggested that a history of osteoporosis was a high-risk factor for refractures after PKP. The history of osteoporosis can increase the risk of refracture after PKP by 11.454 times [*P* = 0.000, 95% CI (4.469, 29.361)]. This result indicates that history of osteoporosis is a hazard factor.

Patients who have had fractures in the past will have a significantly increased risk of another fracture in the future (18). Patients who have a history of fracture in other parts (previously fracture before the occurrence of OVCF are more likely to have vertebral fractures again. In this research, 67 (7.27%, 67/921) patients had a history of previously fracture. And 20 (18.02%, 20/111) patients had a history of previously fracture in the "refracture" group, while only 47 (5.80%, 47/810) patients in the "no fracture" group (*P* = 0.000). Logistic regression analysis also suggested that history of previously fracture was a high-risk factor for refractures after PKP. The history of previously fracture can increase the risk of refracture after PKP by 4.827 times [*P* = 0.000, 95% CI (2.433, 9.578)]. This result indicates that history of previously fracture is a risk factor.

Gender is another important risk factor for refracture after PKP. Most studies believe that women are more prone to VCFs (19,20). In this study, 763 (82.84%, 763/921) patients were women, and 101 (13.24%, 101/763) of them suffered refracture. However, the proportion was only 6.33% (10/158) male (P = 0.015). Logistic regression analysis also suggested that gender was a high-risk factor for refractures after PKP. The risk of refractures in women was 2.672 times as high as men [P = 0.012,95% CI (1.246, 5.729)]. Our results show that women are more likely to refracture than men.

Gallstone disease may be another cause of refracture after PKP. Gallstone disease is frequent in the general population with a prevalence of 10% (21). And more than 500,000 of cholecystectomies are performed annually in the United States (22). Through numerous literature analysis, it is found that gallstone diseases are correlated with lower 25-hydroxyvitamin D [25 (OH) D] levels. And many literatures were reported that 25 (OH) D levels in cholecystectomy were lower than in noncholecystectomy patients (23). In this research, the incidence of gallbladder disease is 8% (74/921). By comparing the 2 groups, we found that patients with gallstone disease were more likely to have refracture after PKP. Eighteen (16.22%, 18/111) patients had gallstone disease in the "refracture" group, while only 56 (6.91%, 56/810) patients in the "no fracture" group (P = 0.001). Although logistic regression analysis did not indicate a significant correlation between gallstone disease and refracture [P = 0.362, OR 1.419,95% CI (0.669, 3.012)]. Gallstone disease can reduce the level of 25 (OH) D, so we think gallstone disease is associated with osteoporosis.

Stomach ulcer is another risk factor for refracture after PKP. The human stomach has many important physiological functions that are lost when a gastrectomy procedure is performed or a stomach is damaged. Through literature analysis, it is found that patients with gastritis or gastrectomy are more likely to develop osteoporosis (24-26). In this study, the incidence of stomach ulcer is 3.8% (35/921). However, in the "refracture" group, the incidence of stomach ulcer was as high as 13.51% (15/111) (P < 0.000). Logistic regression analysis also indicated that patients with gastric diseases were more likely to have refractures after PKP. Refracture risk was 7.923-fold higher in the stomach ulcer compared to the no stomach ulcer [P = 0.000, 95% CI (3.278, 19.149)]. Therefore, we believe that patients with gastric diseases are more likely to have recurrent fractures after PKP.

The ovaries are the reproductive organs of women. Their function is to produce eggs and steroid hormones. The removal of an ovary will directly lead to the imbalance of hormones in the body, and even lead to the termination of the source of estrogen. Many osteoporosis models are officially made by removing animal ovaries to make animal models (27,28). In this study, 16 (1.73%) cases of female patients had ovariectomy history, of which 5 (4.5%) patients had refractures (P = 0.017). Logistic regression analysis also indicated that patients with ovariectomy history were more likely to have refractures after PKP. Ovariectomy can increase the risk of refractures by 3.808 times [P = 0.041, 95% CI (1.054, 13.758)].

Alendronate is currently widely used as an antiosteoporosis drug. This oral bisphosphonate has been prescribed for millions of patients in 80 different countries worldwide (14). It has been reported that the vertebral fracture rate was reduced by 59% after one year of alendronate therapy (29). In this research, only 51 (5.45%) patients received alendronate treatment after PKP. However, there were 14 cases of refracture after PKP, and the incidence of refracture was as high as 12.61% (14/111) (P = 0.001). We believe that this result may be caused by the following reasons: adverse gastrointestinal event, low alendronate use rate, poor patient compliance, and so on.

Zoledronate is another widely used antiosteoporosis drug. As shown in the HORIZON study, zoledronate significantly reduced bone turnover and increased BMD at one year in postmenopausal women with osteoporosis (30). Over a 3-year period, the risk of vertebral morphometric fractures was reduced by 70%. Zoledronate was compared with alendronate (31), it has the advantages of convenient use and good clustering. It is reported that the curative effect of osteoporosis treatment is higher than that of alendronate (32). In this study, 444 cases were treated with zoledronate, and then only 14 (3.15%) patients had refractures (P = 0.000). Through logistic regression analysis, we can find that the risk of recurrent fractures after PKP is reduced by 0.131 [P = 0.000, 95% CI (0.069, 0.248)].

Calcium is the most abundant mineral in the human body, and most of it (about 99%) is deposited in bones. There is no doubt that calcium is the basic factor in the prevention and treatment of osteoporosis (33). Vitamin D, as the most important regulator of calcium metabolism, has the following effects on bone: promoting calcium absorption, promoting calcium into bone, reducing calcium excretion in kidney, and so on. Many guidelines for the

treatment of osteoporosis have clearly pointed out that calcium and vitamin D are the most basic treatment for osteoporosis (34,35). We can see its position in the treatment of osteoporosis. In this study, 768 patients used oral calcium and vitamin D, and then only 67 (8.72%, 67/768) patients had refractures (P = 0.000). Logistic regression analysis found that the risk of refracture decreased by 0.313 [P = 0.000, 95% CI (0.187, 0.525)].

In addition, we analyzed the situation of osteoporosis drugs independently. We found distinct differences in understanding osteoporosis among different doctors: 131 (14.22%) patients were completely untreated with antiosteoporotic drugs, 295 (32.03%) patients received calcium and vitamin D alone, 17 (1.85%) patients received zoledronic acid alone, and 5 (0.54%) patients received alendronate alone. Only 473 cases (51.36%, zoledronic acid 427 cases, and 46 cases of alendronate) were treated with zoledronic acid/alendronate + calcium + vitamin D, however, it is precisely the world's most classic antiosteoporosis treatment plan. As a top university affiliated hospital in China, the prevention and treatment of osteoporosis has not met the requirement. The proportion of anti-osteoporosis was only 85.78%, while the proportion of standardized drugs was only 51.36%. It is inferred that Chinese orthopedic doctors have a lower understanding of osteoporosis and need to further improve the understanding of osteoporosis in the countrywide department of orthopedic doctors and standardize the treatment of osteoporosis.

Limitations

There are some viewpoints and limitations to our research to be considered. First, as a retrospective study, some inherent limitations are unavoidable. Future prospective studies will better verify these findings. Second, our data were obtained from only one institution. Multicenter research may be more representative. Lastly, some mechanical problems (data about cement leakage, vertebral height recovery, postoperative Cobb angle improvement, and so on) are not included in this study. In many literatures, the above data may be related to the occurrence of refracture.

Conclusion

We analyzed the types and hazard factors of refracture after PKP. We found that the incidence of nonadjacent vertebral fractures was higher than that of adjacent vertebral fractures after PKP. Osteoporosis is the main cause of refracture after PKP. Low BMD is an important risk factor for the occurrence of new VCFs after PKP. Elderly women are more likely to have refractures after PKP than elderly men. Patients with a history of previously fracture, previously osteoporosis, stomach ulcer, and ovariectomy are more likely to be refractured after PKP. Antiosteoporosis treatment (oral calcium + vitamin D or zoledronic acid intravenously) after PKP can reduce the risk of refracture after PKP.

Author Contributions: Drs Ning Lei, Zhu Jungao, and Tian Shen contributed equally to this study. Drs Ning Lei, Zhu Jungao, and Tian Shen had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Hu Ziang, Liu Chao, Zhao Xiangde, and Li Xiang designed the study protocol. Dr Ning Lei managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Drs Wan Shuanglin and Fan Shunwu provided revisions for intellectual content and final approval of the manuscript.

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