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Kyphoplasty for Elderly Patients With Vertebral Compression Fractures—Do We Save Lives? Mortality Rates Analysis Comparison in a Long-Term Follow-Up Cohort

Raphael Lotan, MD, MHA[1], Yossi Smorgick, MD[2], Yoram Anekstein, MD[2], Oren Rudik, MD[1], Ilia Prosso, MD[1], and Oded Hershkovich, MD, MHA[1]

Abstract

Study Design: Retrospective cohort.

Objectives: We aimed to compare a large cohort of patients with vertebral compression fractures (VCF) treated in 2 centers using different protocols (conservative vs BKP) and compare mortality rates on a long-term follow-up.

Methods: Retrospective cohort held in 2 medical centers (W and AH). All patients admitted with VCF from November 2008 to January 2015 were enrolled in the study. Exclusion criteria were patients admitted with non-osteoporotic pathological fractures (such as metastatic or MM).

Results: Our study included 208 patients treated for VCF, 127 were treated with BKP (88 females, 69.3%) and 81 were treated conservatively (59 females, 72.8%). Patients from Centre W were older and frailer compared to the patients from AH center (Average age 75.12 $\pm$ 11.16 vs 69.13 $\pm$ 9.61 years and Frailty score of 0.16 $\pm$ 0.1 vs 0.12 $\pm$ 0.1 respectively, T-test, $p < 0.01$ for both). Hazard ratios (HR) for age, female gender and frailty were significant for increased mortality, frailty had the highest HR of 182.42 (CI 29.05-1145.33, $p < 0.01$). Multivariate Cox model was fitted and after accounting for Gender, Age and Frailty, no significant difference was found between the 2 medical centers mortality rates ($p = 0.59$), thus no difference in mortality rates between BKP and conservative treatment in our study.

Conclusion: long-term follow-up following BKP treatment for VCF did not show a reduced mortality rate compared to conservative treatment after accounting for frailty, age and gender. Frailty was the most important factor in predicting mortality. Further RCTs are needed to compare the quality of life differences between the 2 treatment strategies.

Keywords

osteoporotic fractures, vertebral compression fractures, mortality

Introduction

Osteoporotic vertebral compression fractures (VCF) are frequent diagnosis in the elderly, more common in women, with more than a million cases per year.[1] As the occurrence of osteoporosis worldwide is rising the National Osteoporosis Foundation have estimated the prevalence to be approximately 9 million adults in the United States and an additional 43 million with low bone mass, placing all at increased risk for VCF.[2] VCFs can cause considerable morbidity both acute and chronic, leading to functional limitations, constant pain, loss of autonomy, and respiratory difficulties.[3,4] VCF produce intractable pain, contributable to kyphosis and reduces patient's quality of life greatly.[5,6] The vicious cycle begins with a VCF kyphotic

[1] Department of Orthopedic Surgery, Wolfson Medical Center, Holon, Israel, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[2] Spine Unit, Assaf Harofeh Medical Center, Zerifin, Israel, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Corresponding Author:
Oded Hershkovich, Ha-Lokhamim St 62, Holon, 5822012, Israel.
Email: oded.hershkovich@gmail.com

deformity, leading to persistent back pain due to biomechanical load changes, leading to higher susceptibility to adjacent fractures due to increased kyphosis, further escalating the kyphotic deformity, causing more pain and disability and vice versa.[7] In most cases, the initial treatment of VCF would include pain control with resuming of activity as promptly as possible accompanied by physical therapy.[8] Before the application of percutaneous minimally invasive surgery, the traditional analgesics and bed rest were the main therapeutic measures. Even Though most patients with VCF gradually improve with conservative treatment, intractable pain, decreased self-esteem, senile kyphosis, mood disorders and increased mortality have been frequently reported.[9-11] The traditional approach was to offer percutaneous vertebroplasty (VP) or percutaneous balloon kyphoplasty (BKP) to patients who did not show any timely significant pain relief under conservative treatment or for patients who were unable to tolerate oral analgesics and were left restricted to bed rest. Controversy intensified following publications of 2 randomized controlled studies comparing outcomes of VP and sham procedure,[10,11] versus others who still backed the role of VP.[12,13] The debate intensified with more recent publications which put further question marks on the benefit of those procedures.[14,15] Others have pointed to significant flaws in those publications (Timing of surgery, the technique used etc.) still supporting the use of BKP and VP in the acute phase of VCF, leaving this clinical dilemma open for debate.[16]

BKP is a frequently applied method of minimally invasive surgical treatment for VCF, designed to treat the fracture-related pain and spinal deformity.[17] Good clinical results and some restoration of the vertebral body height have been reported with BKP.[18-22] The utilization of BKP for VCF patients is quite frequently reported for both multilevel as well as single-level VCFs.[23-26]

Mortality among patients suffering VCF is an issue being discussed extensively within the literature as surgeons measure the cons and pros of treating those patients either conservatively or operatively. The prevalence of VCF is approximately 5.4% in adults aged 40 years but raises to 18% in those 80 years and older, making it a very common elderly ailment.[27] At that age group, VCF can lead to a downward spiral of symptoms and morbidity, ranging from pain and disability to impaired pulmonary and respiratory function.[28] Mortality rates have been reported with up to 72% at 5 years and 90% at 7 years following VCF.[29-31] Conservative treatment is considered as the main first line of treatment, including narcotics, analgesics, braces and immobilization, although may be poorly tolerated in elderly patients. Side effects, such as constipation and increased risk of falls have been reported[32,33] as well as opioid dependency.[34] Minimal invasive surgical interventions such as VP and BKP can potentially improve pain, function, quality of life[19,33,35] and by some decrease mortality rates. Studies have shown that BKP compared to conservative treatment reduced mortality rates by 25%-55%.[36-39]

We aimed to compare a large cohort of patients with VCFs treated in 2 separate centers with different treatment protocols (conservative vs BKP) and compare mortality rates on a long-term follow-up.

Methods

A retrospective cohort held in 2 medical centers (W and AH). All patients admitted with a diagnosis of VCF from November 2008 to January 2015 were enrolled in the study. Exclusion criteria in both centers were non-osteoporotic pathological vertebral fractures, such as metastatic origin or due to multiple myeloma.

All patients admitted in AH medical center were treated conservatively according to the department's policy while in W medical center patients underwent BKP procedure for their VCF. In W medical center 4 patients were lost to follow-up. Those were patients with minimal VCF (AO type A1 fractures with minimal upper endplate collapse and mobile from day 1) treated conservatively by the emergency department team and not by the orthopedic team, lost to follow-up, thus removed from the study. Demographic data collected included: Age, gender, past medical history records and a calculated Frailty score before admission.

Frailty score was calculated based on the clinical records of each patient and were summed on a clinical scale scoring system including points for the medical history of cerebral pathology, cognition impermeant, falls, ambulation, paraplegia, DM, Syncope, psychotic background, thyroid pathology, seizures, chronic heart failure, depression, malignancy, ulcers, cardiac disease, incontinence, Parkinson disease, renal impairment, respiratory compromise and history of myocardial infarction. Parameters were summed and compared between the 2 cohorts.[40]

The medical center IRB committee has given this study its approval without the need for formal consent due to its retrospective anonymous character. The statistical analysis was generated using SAS Software, Version 9.4. Continuous variables were presented by Mean $\pm$ Std or Median and IQR, Categorical variables were presented by (N, %). Chi-square was used to compare categorical variables (Gender); T-Test for normal continuous variables (Age and Frailty). Two Survival endpoints were calculated: Survival at end of follow-up (EOF) and Survival up to 1 year.

The Kaplan-Meier model, with the Log-rank test, was used to generate survival curves for Survival. The Cox Proportional Hazards model was used to calculate Hazard Ratios (HR) for Survival.

Results

Our cohort included 208 patients treated for VCF from 2 independent medical centers. Each center admitted and treated patients with VCS according to its treatment protocol. In Center W patients were treated with BKP while in AH center patients were treated conservatively.

Of the 208 patients, 127 were treated with BKP (88 females, 69.3%) and 81 were treated conservatively (59 females,

Table 1. Age, Gender and Frailty by Centers.

		Hospital	
		AH center	W center
N		127	81
Age	**N**	127	81
	Mean	69.13	75.12
	Std	9.61	11.16
	Min	51.00	50.00
	Q1	61.00	67.00
	Median	70.00	78.00
	Q3	77.00	84.00
	Max	89.00	92.00
Frailty score	**N**	127	79
	Mean	0.12	0.16
	Std	0.10	0.10
	Min	0.00	0.00
	Q1	0.05	0.09
	Median	0.09	0.18
	Q3	0.18	0.23
	Max	0.45	0.41
Gender		88	59
Female	**N**		
	%	59.86	40.14
Male	**N**	39	22
	%	63.93	36.07

W center patients were older and frailer (T-test, $p < 0.01$ for both), no significant difference was found for Gender (Chi-Square, $p = 0.64$).

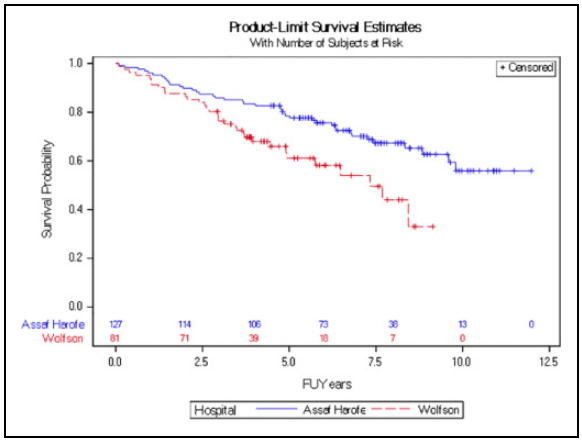

Figure 1. Kaplan-Meier plot, compares survival at EOF between the 2 centers.

72.8%). Patients from center W were older and frailer compared to the patients from AH center (Average age 75.12 ± 11.16 vs 69.13 ± 9.61 years and Frailty score of 0.16 ± 0.1 vs 0.12 ± 0.1 respectively, T-test, $p < 0.01$ for both). There was no significant difference found for Gender (Chi-Square, $p = 0.64$) as presented in Table 1.

Kaplan Meier plot comparing survival rates of BKP versus conservative treatment showed worse survival rate (Log-rank test, $p < 0.01$) for the BKP cohort (Figure 1).

Univariant analysis for both cohorts was done and hazard ratios (HR) were calculated for all parameters including age, frailty score, gender, and type of treatment, separately. All univariant analysis parameters were found to be statistically significant for increased mortality, with Frailty being the most significant. HR was 1.98 for the Medical center (W center Vs AH center; CI 1.22-3.19, $p < 0.01$), for Gender (Male Vs Female) HR was 1.93 (CI 1.22-3.08, $p < 0.01$), for Age HR was 1.11 (CI 1.08-1.14, $p < 0.01$) and for Frailty HR was 182.42 (CI 29.05-1145.33, $p < 0.01$).

As patients from W center were found to be older and frailer than AH patients, multivariate analysis was needed to examine the true effect of treatment selection after accounting for the group's inhomogeneity. Multivariate Cox model included Medical center, Gender, Age and Frailty and was fitted to see if the medical center effect (=equals the type of treatment given) persists after adjustment. In this model, the treatment method was not significant to the mortality rates ($p = 0.59$) as shown in Table 2.

After accounting for Gender, Age and Frailty, no significant difference was found in mortality rate between BKP and conservative treatment ($p = 0.59$).

Discussion

VCF are more common in the elderly population with a higher incidence in women. Mortality among patients who develop VCF is an issue being discussed extensively. Studies have reported that mortality rates are higher in patients with VCFs compared to those who did not develop VCFs.[30,41,42] Mortality in patients with VCF is multifactorial with associated comorbidities, number of vertebral fractures, age, sex, and socioeconomic status have been reported as risk factors affecting the survival rates. The causes of death in VCF patients are mostly

Table 2. Cox Multivariate Model Results.

Analysis of maximum likelihood estimates

Parameter		DF	Parameter estimate	Standard error	Chi-Square	Pr > ChiSq	Hazard ratio	95% hazard ratio confidence limits	
Medical center	**W** center	1	0.15046	0.27710	0.2948	0.5871	*1.162*	0.675	2.001
Gender	**Male**	1	0.97599	0.25394	14.7713	0.0001	*2.654*	1.613	4.365
Age		1	0.10153	0.01696	35.8521	<.0001	*1.107*	1.071	1.144
Frailty score		1	2.62182	1.13455	5.3402	0.0208	*13.761*	1.489	127.167

After accounting for Gender, Age and Frailty, no significant difference was found between the 2 medical centers.

from associated comorbidities and less from the fracture-related causes.[43,44]

As in our study, age is also associated with increased mortality rates in VCF patients. Mortality rates have been reported to be higher in older VCFs patients than in younger patients in some reports regardless of the treatment given and to increase with age.[45,46] In our study, the impact of age was quite modest (HR = 1.11, $p < 0.01$) out of all parameters studied (Age, sex, and frailty). The selection of treatment did not matter at all (HR = 1.162, $p = 0.59$). Females with VCF have been reported to have higher mortality rates compared to males[29,47] and our study supports this as well with HR of 2.654 ($p = 0.0001$). Frailer patients with lower socioeconomic status and more comorbidities such as malnutrition, obesity, and smoking have also been associated with higher mortality rates.[37,46] Frailty in our study was the most important parameter in predicting death with an HR of 13.761 ($p = 0.02$). This was the main difference between the 2 medical centers and the reason mortality rates were higher in absolute numbers at W center, where all patients were operated. Remarkably, despite their frailty scores, no patient was excluded from being able to undergo BKP.

The role of surgical intervention in symptomatic patients with VCFs is complex and controversial.[10-16] The impact of surgical interventions for patients with VCFs on mortality is inconclusive.[31,38,48,49] Yet, studies have reported that surgical procedures have decreased the fracture-related death in VCFs patients compared with conservative treatments.[50] Studies reported on BKP have shown improvements in postoperative pain, decreased the use of pain medications like opioids and NSAIDs, and also improved postoperative mobility potentially allowing better outcomes for those patients long-term wise by avoiding the harmful sequelae of immobility.[19,33,35]

In contrary to our assumption that BKP potentially can improve survival due to early mobilization and disruption of the vicious cycle discussed above, we could not find this advantage for BKP over conservative treatment in our long-term cohort.

Our study compared BKP with conservative treatment, we had no cases of VP therefor we cannot refer to the possible differences mentioned in the literature between VP and BKP. Although both equally reported to have diminished postoperative pain, improved disabilities, and postoperative complications, kyphoplasty has the advantage of better restoration of the kyphotic angle and potential improvement of pulmonary function.[21] In our study, despite preforming BKP we still could not find an advantage in survival rates over conservative treatment.

There are no good quality prospective randomized studies on the effect of BKP on mortality outcomes. There are only a few published studies, with most of these studies being retrospective cohorts. Our study could be compared to an RCT in some ways since patients treated in each medical center presented randomly and the researchers had no impact on treatment selection, other than the rigid local department protocol. Yet the retrospective data collection and the study protocol, however, makes this study less than an RCT would be.

The lack of equality between the intervention and the conservative groups is a major disadvantage of several studies done in this field, with patients being either relatively young[39] or older and frailer with multiple comorbidities.[45] These differences make it very hard to define the patient population that can potentially benefit most from BKP. Although our study faced the same issue, we believe that the extent of this study, its long-term follow-up and the multivariant analysis performed, overcomes this matter, and offers a solid comparison between the 2 treatment approaches.

Despite being extensive and comparable to an RCT this study has its limitations. The main limitation is being a retrospective study nonrandomized to the treatment offered. Another limitation is the inhomogeneity our the study groups regarding age and frailty score.

Further large scale multicenter prospective RCTs may reveal survival rate differences in favor of BKP that could not be proven by the cohort presented. The study presented did not examine the effect of BKP on quality of life and adjacent fractures, that have a profound effect on the patient's outcome.

According to our study, the most important parameter in predicting patient's mortality is the frailty score, summing the patient's overall medical status.

Conclusion

long-term follow-up following BKP treatment for VCF did not show a reduced mortality rate compared to conservative treatment after accounting for frailty, age and gender. Frailty was the most important factor in predicting mortality. Further RCTs are needed to compare the quality of life differences between the 2 treatment strategies.

Authors' Note

IRB approval was given by Edith Wolfson Medical Center, Holon, Israel, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel IRB committee

Declaration of Conflicting Interests

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ORCID iD

Oded Hershkovich, MD, MHA https://orcid.org/0000-0003-2975-9152

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