JOURNAL OF COMPLEMENTARY MEDICINE RESEARCH, 2020
VOL 11, NO. 3
10.5455/jcmr.2020.11.03.03

RESEARCH ARTICLE

Open Access

Pain Reduction by Percutaneous Vertebroplasty for Vertebral Compression Fractures with and without Intravertebral Clefts

Hesam Abdolhoseinpour[1], Veit Rohde[2], Reza Akhavan-Sigari[2]*

[1]Department of Neurosurgery, Islamic Azad University, Tehran Medical Branch, Boali Hospital, Tehran, Iran

[2]Department of Neurosurgery, University Medical Center Göttingen, Georg-August-University Göttingen, Germany.

ABSTRACT

Background: Vertebroplasty has become a common treatment for relieving pain in osteoporotic vertebral fractures. However, there is contradictory evidence regarding its efficacy. The aim of this study was to determine the degree of pain relief offered by percutaneous vertebroplasty in the treatment of osteoporotic vertebral compression fractures (OVCFs) in patients with or without an intravertebral cleft.

Material and Methods: In this multicenter, randomized, placebo-controlled trial all patients who had one or multiple painful, unhealed compression fractures were randomly assigned to undergo vertebroplasty or a sham procedure. The patients in the vertebroplasty group were divided into two subgroups: A - with intravertebral cleft, and B - without intravertebral cleft. They were followed up for the mean pain reduction assessed by visual analogue scale (VAS), and changes in the quality of life using the osteoporosis and Roland-Morris disability questionnaire scores (RDQ) at 1, 6, and 12 months, and two years after the procedure.

Results: A total of 1,311 patients were studied (vertebroplasty 661, sham 650). The data showed that those with intravertebral clefts had significantly less severe back pain ($p = 0.01$) and functional disability ($p=0.03$) at month 12 compared to those without intravertebral cleft. However, the study groups did not differ significantly with respect to the pain score or the RDQ score at other measurement points ($p>0.05$). There was a trend in the RDQ score toward less pain in patients with filled clefts compared with patients without clefts after one and two years after surgery, this difference did not approach statistical significance.

Conclusion: We found no significant benefit of percutaneous vertebroplasty (PVP) over a sham procedure in patients with vertebral compression fractures with or without vertebral clefts 6 months after surgery. One and two years after surgery, there was a trend toward less pain.

ARTICLE HISTORY

Received April 11 2020,

Accepted May 8, 2020

Published September 6, 2020

KEYWORDS

Percutaneous vertebroplasty, Osteoporotic vertebral compression fractures, Pain, intravertebral cleft.

INTRODUCTION

The aging of the world's population has concentrated more on osteoporosis (OP). Osteoporosis is a chronic condition of reduced bone density, damage to the bone and increased bone fragility. An osteoporotic compression fracture (OVCF) is one of the most serious effects of OP, which may raise the impairment and mortality rates [1-3]. Inevertebral cleft is a structural alteration in ischemic vertebral osteonecrosis complicated in the late stage of OVCF

* **Contact** Reza Akhavan-Sigari, Georg-August-University Göttingen, Germany. reza.akhavan-sigari@med.uni-tuebingen.de
Tel.: +49-551-3966033

fracture and pseudoarthrosis [4] Figure 1. Further OCVFs correlated with intravertebral separation are observed with development of preoperative radiographic vertebral status assessments. In principle, nonunion and pseudoarthrosis can cause fracture instability, resulting in more extreme pain than in the absence of the intravertebral split [4]. In addition, the main risk factor for bone cement leakage is OVCF with intravertebral dividers [5]. The traditional treatment of OVCFs is bed rest, analgesics, physical therapy and antiresorption medicines. While the kyphotic deformities are not reversible by such conservative steps, they cause themselves comorbidities such as deep venous trombosis, osteopenia acceleration, respiratory problems and emotional problems [6,7].

Percutaneous vertebroplasty (PVP) is a minimally invasive procedure that has become more common as a potential treatment for OVCFs. This treatment consists of inserting the spinal needles under radiological supervision into the broken spine and injecting polymethyl-methacrylate (PMMA) or other bone cements in order to alleviate pain and improve the bone strength [8]. PVP was carried out in various forms, including those with intravertebral fractures, of vertebral compression fractures and drastic results resulted in its more widespread use [9]. The pain receptors in the underlying tissue tend to be modified in response to different stimuli after the cement is injected. As the mechanisms of pain relief, mechanical stabilization of the broken bone and thermal and chemical nerve endings damage caused by cement is suggested [10]. In contrast with conservative therapies, PVP is identified as immediate pain relief [11], and guidance recommends vertebroplasty for fractures not in response to traditional treatment [12]. Several limited unblinded randomized trials have demonstrated the efficacy of vertebroplasty in osteoporotic pain relief [13-15]. Nevertheless, conflicting evidence challenges its usefulness. There is also a lack of evidence from high-quality, randomized, controlled trials. For each analysis, methodological limitations revealed the benefit of vertebroplasty. The lack of blinding and the lack of real sham control has raised the concerns that the benefits observed represent a placebo response, which can be magnified by the invasion of the procedure [16]. Recent meta-analysis 21 clinical trials of high-to-moderate quality have also not demonstrated a beneficial impact of vertebroplasty in the treatment of acute or subacute osteoporotic vertebral fractures. In combination with vertebroplasty there have been several adverse effects including osteomyelitis, cord compression, sac damage and respiratory failure [17].

Taken together, the potential therapeutic effects of PVP versus nonspecific effects are uncertain in the absence of high quality data. We were therefore concerned to determine if percutaneous vertebroplasty was more effective in patients with intravertebral fracture clefts than in patients with no clefs compared with the placebo-controlled community. For this sense, we know this is the biggest, randomized, placebo-controlled, double-blind, multi-center analysis.

MATERIAL AND METHODS

Study design and participants

We performed a randomized, concurrent, placebo-controlled trial to assess the long-term efficacy and protection of vertebroplasty for alleviating pain and enhancing physical function in people with and without intravertebral clefts with painful vertebral compression. The protocol was previously documented [18].

The clinical review board accepted the study protocol and all participants agreed to participate in the trial in writing.

One or two recent vertebral compression fractures, recent vertebral compression fractures with the existence and described as a Grade 1 or higher collapse by Grade 1 grading method, were included,[19] chronic back pain at the fracture level that was not responsive to conservative therapy after a minimum waiting period of six weeks to see whether the fracture is present T5 to L5 vertebrae OVCFs have been included.

Potential participants who have undergone pre-spinal surgery, serious scoliosis, untreatable coagulopathy, neurologic illness, significant heart disease, chronic or sporadic spinal infection or suspected malignancy have been disqualified from participation.

The registration began in March 2006 and ended in December 2015. In February 2017, the follow-up phase began. A total of 2,453 patients have been reviewed and 1,311 have actually been included. Those have been assigned randomly to vertebroplasty (n=661) or a placebo operation that simulates vertebroplasty (n=650).

The vertebroplasty population involved is divided into two subsets: A-intravertebral cleft patients (n = 266), and B-intravertebral cleft patients (n = 395). Participants were followed up at 1, 6, 12 months and two years after the treatment for VAS ratings and quality of life and physical function. During the time of consent, patients were told that they would be permitted to move over over to the other treatment

one month or later after the operation if appropriate pain relief had not been obtained.

Randomisation and blinding

Computer participants were randomized in six groups with a randomization ratio of 1:1. Over 24 months of follow-up, participants, witnesses (other than neurosurgeons who conduct procedures) and outcome assessors were blinded to group assignments. The interventional and diagnostic radiologists should not be covered.

Surgical procedures

Percutaneous vertebroplasty with the patient in a prone, lordotic position was performed in local anesthesia and a body under the stenum and pelvis was positioned to help minimize the broken vertebral body by means of a transpedicular method. The entry point with a C-arm x-ray machine has been verified and labelled. The skin was then disinfected with clean towels. Lidocaine 1 percent was used for sub-cutaneous local anesthesia after located the skin incision 1-1.5 cm laterally at the pedicle lateral edge. A trocar is mounted in a fluoroscopic AP image on the lateral edge of the pedicle. Ideally, the position would be in the middle or slightly superior to the middle of the pedicle. The trocar must be relocated to the back margin of the vertebral body through the pedicle while retaining convergence and fluoroscopic control (Figure 2). The trocar tip should not overflow the pedicle 's media margin on an AP picture. Then you can test the location of the trocar tip and proceed to anterior 1/5th-1/4th of the vertebral body. Polymethylmethacrylate (PMMA) inserted progressively into the x-ray body and the bone concrete spread steadily. A placebo technique was used in the control group, simulating vertebroplasty. No anesthetic agent was used in the periosteum for immediate alleviation of pain. The vertebroplasty was gently tapped and PMMA cement was prepared for simulation.

All the treating physicians were highly experienced, carried out an average of around 200 procedures, undertook formal training in vertebroplasty, had the proper certification and carried out the procedure actively. All of the physicians strictly adhered to a detailed, standardized protocol. The analgesics were given in accordance with the standard procedure.

Assessment indices and outcomes

Baseline data obtained by a blinded assessor covered sex, age, height, weight, osteoporosis risk factors, alcohol use, history of fractures, bone mineral density measurements, and form of vertebral fractures [20]. In the study of Ostoporotic Fractures of Daily Living Activities (SOF – ADL)[21], the updated questionnaire Roland-Morris Disability (DRQ)[22], and a Timed Up and Go (TUG) test, we measured physical activity, calculating time required for raising from standard armchairs, walking for 3 metres, turning around, returning to the chair, then sitting down again[23]. RDQ has 24 products that measure the functional state of patients with back pain over the past 24 hours. This questionnaire has no answer scales but only the command: mark the box next to it when you read a sentence that describes you today. The RDQ ranges from zero (no back pain disability) to twenty-four (maximum back pain disability), with higher scores suggesting greater back pain disability [23].

We have assessed quality of life with the European Foundation for Osteoporosis (QUALEFFO) Quality of life questionnaire and with the scale of European Quality of Life–5 Dimensions (EQ–5D). The QUALEFFO is a 41-point questionnaire related to vertebral fracture and ostoporosis, with ratings between 0 and 100, with lower scores indicating a better quality of life [24]. The EQ-5D is a standardized indicator of medical status representing autonomy, self-care, restrictions on movement, pain and mental distress (scores of 0 to 1 with 1 suggesting perfect health and 0,074 showing a marginal clinic difference [25]). Other baseline variables included pain at rest, bed pain at night, pain frequency and pain bothersomes indi.

Following the surgery, the patients were tested for improvements in pain and function as well as any adverse effects using the mailed questionnaires at 1, 6 and 12 months and two years after the operation. The primary outcome was average discomfort over the previous week quantified using the analog visual standard for discomfort (VAS), where 0= no pain, 10 = worst pain imaginable and 1,5 min. The secondary findings were physical improvements over 12 months of the RDQ follow-up. Through the use of unanswered queries, adverse injuries, including accident fractures, were analyzed at each time.

STATISTICAL ANALYSIS

The mean ± standard deviation (SD) of all data is expressed. After the distribution of quantitative parameters was evaluated, it was analyzed the parametric data with application of t-test, ANOVA and other parametric tests, and, if necessary, comparison of non-parametric data with Kruskal – Wallis, Mann – Whitney U and other non-parametric steps. Measurement results, including VAS score, the front and back heights of the broken vertebral body, and a Mann-Whitney U test before and after VP, were compared. Student's t-test allowed distinctions between the two classes. Pearson correlation

coefficients were determined to determine the relationship between the lower pain value (VAS) and anterior vertebral height change and LKA. Statistically relevant showed $p<0.05$.

The primary outcome of our analysis was the average pain level for three months. The study was able to identify substantial differences in both primary and secondary results in more than 85 percent of 1.311 patients with a two-sided alpha of 0.05, based on a 2.0-point RDQ difference and a 1.5-point difference in the rating scale. In our figures, for the study, a sample of 496 participants per group would have 85% of the power to display, with standard variations of 30.0, a 2.5-unit benefit of pain-induced vertebroplasty over placebo induced on a double-sided Type 1 error rate of 5%.

All analyzes were carried out in compliance with the theory of intent to care. Baseline differences between groups were measured, as needed, with t-tests from students or non-parametric tests. Changes in pain and score levels for QUALEFFO, RDQ and EQ–5D were measured from baseline to 1 month, 6 months, 12 months, and 24 months with multiple linear regression tests. All findings are viewed as baseline changes. Therapy impacts and confidentiality intervals were determined using covariance analysis (ANCOVA) models optimized for simple outcomes calculation values, recruitment location and study-group variable as the interest predictor. In our post-hoc analyzes, we used functional regression models with an adjustment site and comparison of the outcome measures to assess the proportion of patients in each group who have increased their RDQ score by at least 30 per cent, and their pain rating by comparing their outcomes. All the P values mentioned are two-sided and have not been modified for multiple tests. Using R statistical tools, all statistical analyses were completed.

RESULTS

Patient characteristic

Overall, 661 patients (284 males and 377 females, aged 64-85 years, with a mean age of 73.2 years) with a total of 1,441 OVCFs were analysed and subjected to VP. Of these, 266 (658 OVCFs, 104 males, 162 females, 51-91 years, mean age 70.2 years) had an intravertebral cleft and 395 (783 OVCFs, 183 males, 212 females, 56-89 years, mean age 71.6 years) had no intervertebral cleft. The other 650 participants underwent sham surgery. The average number of vertebral bodies involved in Group A and B was 2.4 (658/266, range, 2 to 3) and 1.9 (783/395, range, 1 to 2), respectively. The mean age was significantly higher in the vertebroplasty group ($p<0.0001$), and the mean age in group A was higher than in group B ($p<0.0001$). Our data show that 53.1% of the participants were married or living with a partner. This is a significantly greater percentage than in the patients undergoing vertebroplasty (45.8%, $p=0.009$). The participants of the control group were more highly educated ($p<0.0001$), were less unemployed (higher score means unemployment in this variable) ($p=0.004$).

The percentages of patients taking opioids (86% vs 81.4%, $p=0.014$), Vit D supplementation (48% vs 40.2%, $p=0.005$), or with a history of previous fractures (54.9% vs 48.1%, $p=0.015$) were higher in the controls. While supplemental calcium consumption was more common among the patients received vertebroplasty (62.3% vs 75.8%, $p<0.0001$). In addition, the duration of corticosteroid use was greater in the vertebroplasty group ($p<0.0001$).

The control patients had more back-related disability as measured using the SOF-ADL and RDQ scales. The SOF–ADL score was statistically similar between group A and the control group, while it was significantly lower in group B compared to controls ($p=0.003$). The RDQ score was also significantly lower in both A and B groups than in the control group. Moreover, patients in group A had significantly lower RDQ scores than those in group B ($p<0.0001$). Group A had a significantly higher rank compared to the control group in the TUG test-sec, while group B was similar to controls in this regard ($p<0.0001$).

The QUALEFFO scores were significantly lower in the controls than in any other group. This represents a worsening of their quality of life ($p<0.0001$). The EQ-5D scores did not differ significantly between the study groups ($p>0.05$).

The data show that pain was more severe in the control patients. The vertebroplasty groups had a significantly lower pain and a lower average pain intensity after two years after surgery compared to the controls ($p<0.0001$) (Figure 3/4). Other baseline characteristics of the groups were similar (Table 1).

Table 1: Baseline characteristics of the groups

Characteristic	Vertebroplasty Group (N = 661) Subgroup A (with intravertebral cleft, (*n* = 266)	Subgroup B (without intravertebral cleft, (*n* = 395)	Control Group (N = 650)
Study center — no. (%)			
Azad Islamic University of Medical Sciences and Health Services, Boali Hospital, Tehran	113 (43)	162 (41)	294 (45)
University Medical Center Göttingen, Germany	69 (26)	118 (30)	177 (27)
Affiliated centers in Iran	84 (31)	115 (29)	179 (27)
Age — yr	74.2±14.0	73.4±9.4	69.8±9.2
Female sex — no. (%)	219 (82)	158 (40)	359 (55)
Duration of back pain — wk Median	9.5	9	10.5
Education — no. (%)			
Less than high school	147 (56)	202 (51)	273 (42)
High school	78 (29)	131 (33)	249 (38)
College graduate	41 (15)	62 (16)	128 (20)
living with partner — no. (%)	109 (41)	194 (49)	345 (53)
Employment status — no. (%)			
Employed full- or part-time	181 (68)	293 (74)	408 (63)
Retired	39 (15)	28 (7)	117 (18)
Disabled	31 (12)	33 (8)	69 (10)
Other	15 (5)	41 (11)	56 (9)
Vertebral bodies treated - no. (%)			
1	194 (73)	269 (68)	423 (65)
2	51 (19)	67 (17)	136 (21)
3	21 (8)	59 (15)	91 (14)
Use of opioid analgesic -no. (%)	210 (79)	328 (83)	559 (86)
Pain Frequency Index score*	3.5±0.6	3.2±0.6	3.3±0.7
Pain Bothersomeness Index score*	3.3±0.7	3.3±0.6	3.7±0.8
Duration of symptoms <6 wk - no. (%)	91 (34)	139 (35)	221 (34)
Body-mass index◊	26.7±5.8	25.2±5.5	25.3±5.5

Duration of corticosteroid use-yr‡ Median	3.0	2.7	2.2
Charlson Comorbidity index ♣	3.4±1.5	3.1±2.1	3.2±1.1
QUALEFFO total score ♫	55.7±11.2	58.2±14.8	62,8±12.2
Pain score ¥			
Overall	8.1±2.2	7.7±4.1	7.9±2.8
At rest	4.6±2.8	4.9±.2.6	4.9±3.5
In bed at night	4.8±3.6	3.5±3.8	4.1±3.2
Average pain intensity during past 48 hr ϴ	6.9±2.4	7.2±2.7	7.6±1.6
EQ–5D score ††	0.57±0.22	0.48±0.26	0.54±0.33
SOF–ADL score ʅ	11.2±3.4	10.9±2.8	11.5±2.7
RDQ score╪	14.6±3.2	16.2±4.2	18.2±3.8
Timed Up and Go test — sec ☯	22.3±5.7	20.5±8.8	24.9±13.8
Medication for osteoporosis - no. (%)			
Any	245 (92)	346 (87)	597 (92)
Calcium supplements	197 (74)	304 (77)	405 (62)
Vitamin D	112 (42)	154 (39)	312 (48)
Bisphosphonates	218 (82)	336 (85)	527 (81)
One or more previous vertebral fractures — no. (%)	117 (44)	201 (51)	357 (55)
Severity of fracture -no./total no. of fractures (%)⇮			
Mild	105/338 (31)	177/521 (34)	245/877 (28)
Moderate	166/338 (49)	209/521 (40)	412/877 (47)
Severe	67/338 (20)	135/521 (26)	220/877 (25)

* Scores on the Pain Frequency Index and Pain Bothersomeness Index range from 0 to 4, with higher scores indicating more severe pain.

◊ The body-mass index is the weight in kilograms divided by the square of the height in meters.

♣ Scores on the comorbidity index range from 0 to 28, with higher scores indicating greater severity.

♫ Scores on the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) range from 0 to 100, with higher scores indicating worse quality of life.

‡ The data are based on a total of 252 participants in the vertebroplasty group (subgroup A: 143 participants; subgroup B: 109 participants) and 275 in the placebo group who reported using corticosteroids.

¥ Pain was assessed on a scale of 0 to 10, with higher numbers indicating more pain and with 1 as the minimal clinically important difference.

ϴ The pain-intensity rating ranges from 0 (no pain) to 10 (worst pain).

†† Standardized instrument for measuring generic health status. Scores on the European Quality of Life–5 Dimensions (EQ–5D) questionnaire range from 0 to 1, with 1 indicating perfect health and 0.07 representing the minimal clinically important difference. Scores were available for 496 participants in the vertebroplasty (subgroup A: 271 participants; subgroup B: 225 participants) group and 474 in the placebo group.

ʅ Scores on the Study of Osteoporotic Fractures–Activities of Daily Living (SOF–ADL) scale range from 0 to 18, with higher scores indicating more back-related disability.

⇮ The severity of the fracture was assessed according to the semiquantitative grading system of Genant et al.[17], on a scale of 0 to 3, with higher numbers indicating greater vertebral collapse.

☯ The Up and Go test measures the time required to rise from a standard arm chair, walk 3 m, turn around, return to the chair, and sit down again.22 Results were available for 36 participants in the vertebroplasty group and 37 in the placebo group.

╪ Scores on the Roland–Morris Disability Questionnaire (RDQ). Range from 0 to 23 (higher scores indicating more severe disability).

Table 2. Primary and Secondary Outcomes (Intention-to-Treat Analyses)[1]

Measure	Vertebroplasty Group (N = 661)		Control Group (N = 650)	Treatment Effect of group A[2] (95% CI)	Treatment Effect of group B[3] (95% CI)	P Value Subgroup A[2]	P Value Subgroup B[3]
RDQ[4]	Subgroup A (with intravertebral cleft, (*n* = 266)	Subgroup B (without intravertebral cleft, (*n* = 395)					
At baseline	18.6±2.8	16.5±3.6	19.5±4.1				
At 1 month	16.0±5.2	15.7±2.2	14.5±5.1	−0.6 (−2.7 to 0.9)	−0.9 (−2.1 to 1.9)	0.32	0.56
At 6 months	12.4±5.0	14.8±4.7	14.3±5.5	−0.5 (−2.4 to 1.3)	−0.6 (−2.2 to 1.5)	0.28	0.51
At 12 months	12.0±6.3	13.2±4.8	14.7±6.1	3.7 (−1.3 to 2.8)	1.5 (−0.3 to 1.8)	**0.03**	0.36
At 2 years	12.0±2.3	13.1±2.1	14.8±3.7	2.6 (-1.1 to 2.2)	1.6 (-1.6 to 2.3)	0.11	0.22
Pain intensity[5]							
At baseline	9.9±2.0	8.7±2.2	7.9±1.8				
At 1 month	5.2±2.1	7.7±4.2	6.4±2.9	−0.2 (−1.5 to 0.8)	−0.6 (−1.7 to 2.8)	0.43	0.33
At 6 months	4.3±2.5	6.9±3.9	5.5±2.3	0.1 (−0.8 to 1.6)	0.1 (−0.8 to 2.6)	0.28	0.56
At 12 months	3.1±2.1	3.6±2.1	5.9±3.0	4.7 (−0.3 to 1.9)	4.1 (−0.2 to 1.2)	**0.01**	0.41
At 2 years	2.2±1.1	2.7±3.2	6.9±1.1	3.6 (-1.3 to 2.2)	2.9 (-1.8 to 2.7)	0.17	0.39

Primary outcome

Comparing between groups, the VAS score was significantly different between groups A and B at 12 months. The mean VAS score at month 12 in group A was 3.1±2.1 and 3.6±2.1 in group B (treatment effect (95% confidence interval [CI]), 4.7 (−0.3 to 1.9) vs 4.1 (−0.2 to 1.2); p = 0.01).

However, the study groups did not differ significantly with respect to the VAS pain score at other measurement points (p>0.05). The mean pain-intensity ratings at month 24 were 2.2±1.1, 2.7±3.2, and 6.9±1.1 in the groups A, B, and controls, respectively (Table 2).

Secondary outcomes

The study groups did not differ significantly on the RDQ score at any of the measurement points except at month 12, where the RDQ score differed significantly between groups A and B (treatment effect (95% confidence interval [CI]), 3.7 (−1.3 to 2.8) vs 1.5 (−0.3 to 1.8); p=0.03) (Figure 5). The mean RDQ scores at month 24 were 12.0±2.3, 13.1±2.1, and 14.8±3.7 in the groups A, B, and controls, respectively (Table 2).

[1] Plus–minus values are means ±SD

[2/3] Between-group A and B comparisons, confidence intervals, and P values were calculated with the use of analysis-of-covariance models with adjustment for study group assignment.

Negative treatment effects favor the control procedure, and positive treatment effects favor vertebroplasty.

[4] Scores on the Roland–Morris Disability Questionnaire (RDQ) range from 0 to 23, with higher scores indicating more severe disability.

[5]Scores on the pain-intensity scale range from 0 (no pain) to 10 (worst pain).

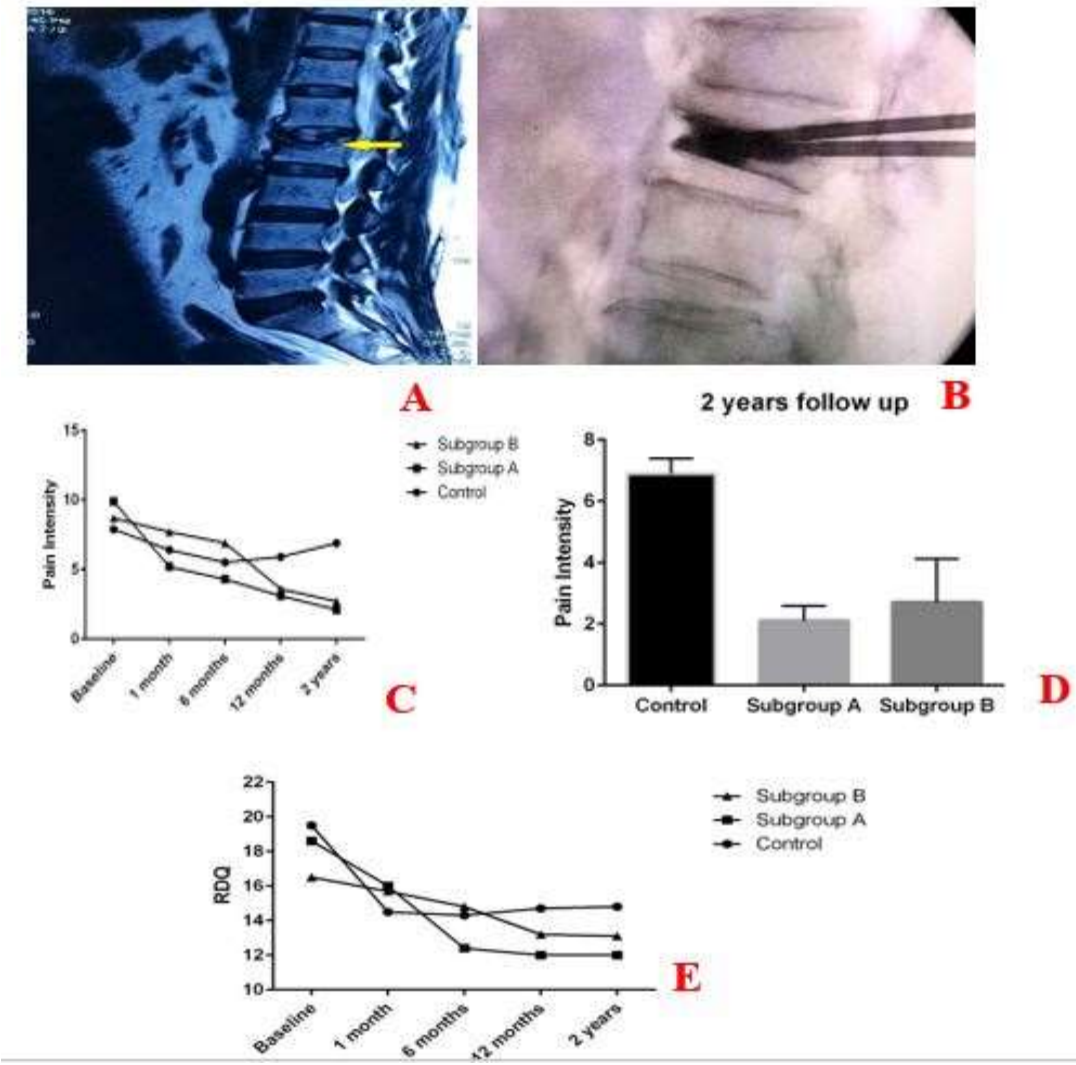

Figure 1: A: 74-year-old woman with osteoporotic vertebral compression fracture. Sagittal T2-weighted MR image shows well-demarcated focus of T2 hyperintensity and characteristic of intravertebral fracture cleft (yellow arrow). B: Radiograph after injection of cement shows immediate characteristic opacification of cleft with dense filling of geographic, well-demarcated intravertebral cavity.C: Overall pain intensity after 1,6,12 and 24 months. D: Figure 4: Pain intensity after 24 months. E: Overall Roland-Morris disability questionnaire scores after 1,6,12 and 24 months.

Discussion

We found no greater benefit from vertebroplasty than a placebo procedure in patients with severe stress fractures at one month , six months, 12 months and 24 months after surgery. Among care groups pain and physical function were modestly improved over the two-year follow-up period, but there were no major intergroup variations at any point except at month 12. We observed that patients with intravertebral splints had substantially decreased back pain and less functional problems at month 12 than people without intravertebral splints following vertebroplasty.

Nonetheless, at the end of the second year after surgery this beneficial effect reduced and there was no substantial difference in the measurement of pain and physical function between patients undergoing a placebo operation or patients with or without intravertebral splints with vertebroplasty.

Over the past 20 years, the use of vertebroplasty has significantly increased and has been generally accepted over clinical practice, although there has been no credible evidence that it is effective [27,28]. To our knowledge, this research is currently the most significant blinding clinical trial in this area, and the large sample size helps us to compare vertebroplasty 's efficacy with the sham procedure accurately. This trial confirms the findings of earlier high-quality clinical trials and Cochrane reviews, which have demonstrated no vertebroplasty benefits over 24 months of follow-up. Proof has previously been shown that the outcomes are not different due to pain duration [19].

While VERTOS II [11], VAPOUR [29] and Chen's [30] have been studied, the findings of Kallmes et al. (19), Australian Buchbinder and colleagues [31] and VERTOS IV (INVEST) [32] show pain relief and pain-related impairment in patients diagnosed with w-treating compression fractures are similar After vertebroplasty, Clark et al . found no benefit from pain relief in acute osteoprotic fractures[29]. Nonetheless, the possibility of reporting errors is high and some reports have been pre-specified. The primary result was stated inconsistently. The placebo method definition also varies from the published protocol to the results papers [17].

Chen et al. observed a beneficial effect of vertebroplasty on the pain relief and improved functional outcomes of patients with recurrent extreme pain and chronic stress fractures [30]. The risk for the success, identification, and attrition of this study is high as they conducted a full review, excluding seven of their 50 conservative care participants. Uncontrolled or improperly regulated trials seem to have overestimated any vertebroplasty benefit [17].

Our results show that pain relief and physical function in key patients were much higher than in non-key patients for the 12-month follow-up, although this beneficial impact decreased two years after service. The development of focal necrosis and fibrocartilaginous tissues is related to vertebral fracture keys [5]. Only one study has compared the pain relief between patients with and without vertebral clefts after vertebroplasty. According to our results, the pain rates of filled key patients were close to the pain rates after two years without keys [5].

There were some drawbacks to our analysis. Next, there was more back-related weakness and more severe pain in the vertebroplasty community before the operation. The potential impact of the placebo effect on outcomes in this trial therefore remains uncertain. Furthermore, although the treatment groups' age ranges are comparable to previous research (mean age ranged from 63.3 to 80 years)[16], the mean age in the vertebroplasty community was substantially higher than in the sham-operated group. The period of the use of corticosteroids in the vertebroplasty community was also longer. The intravertebral cleft in pre-operational imaging has been shown to be the independent indicator of a favorable outcome following vertebroplasty [33]. A older age suggests that an intravertebral break occurs [33] but there are no data to demonstrate the only effect of age on the outcome of vertebroplasty. Certain risk factors for osteoporotic fracture death are age and corticosteroind therapy, but no data have confirmed their adverse effects on vertebroplasty [34]. Second, MRI and X-rays are not sensitive enough to identify the keys seen during fluoroscopy prior to cement injections [5]. Therefore, the number of unfilled fracture keys in our population could not be determined.

CONCLUSION

In conclusion, our data do not support the argument that vertebroplasty is advantageous compared to a placebo operation after 6 months of surgery of vertebral compression fractures with or with our vertebral keys. There was a trend towards less suffering one and two years after surgery. So far as we are aware, this study is the biggest clinical blind study to date. The broad sample capacity gave it the power to test the vertebroplasty effect on this outcome. We have compared the sample groups for all medical procedures and factors that may have influenced their outcomes. The data indicate a trend for less pain in filled split patients relative to patients without splitting. The preferential filling of the intravertebral splints during percutaneous vertebroplasty can explain these findings.

ACKNOWLEDGEMENTS

No applicable

FUNDING

No

ETHICAL STATEMENT

All the procedures in human participant studies were performed in compliance with the institutional or national study committee's ethical guidelines and with its 1964 Helsinki declaration and subsequent revisions or equivalent ethical standards. And the institutional board of review approved by the Göttingen Medical Center University, Georg August-Göttingen University, Germany

CONFLICTS OF INTEREST

None

REFERENCES

1. Ha K-Y, Lee J-S, Kim K-W, Chon J-S. Percutaneous vertebroplasty for vertebral compression fractures with and without intravertebral clefts. J Bone Joint Surg Br. 2006;88(5):629-33.
2. Marcucci G, Brandi ML. Kyphoplasty and vertebroplasty in the management of osteoporosis with subsequent vertebral compression fractures. Clin Cases Miner Bone Metab. 2010;7(1):51.
3. Doody O, Czarnecki C, Given M, Lyon SM. Vertebroplasty in the management of traumatic burst fractures: a case series. J Med Imaging Radiat 2009; 53(5):489-92.
4. Libicher M, Appelt A, Berger I, Baier M, Meeder P-J, Grafe I, et al. The intravertebral vacuum phenomen as specific sign of osteonecrosis in vertebral compression fractures: results from a radiological and histological study. Eur Radiol 200717(9):2248-52.
5. Wiggins MC, Sehizadeh M, Pilgram TK, Gilula LA. Importance of intravertebral fracture clefts in vertebroplasty outcome. AJR Am J Roentgenol 2007;188(3):634-40.
6. Kim K-W, Cho K-J, Kim S-W, Lee S-H, An M-H, Im J-H. A nation-wide, outpatient-based survey on the pain, disability, and satisfaction of patients with osteoporotic vertebral compression fractures. Asian Spine J 2013;7(4):301-7.
7. Ma X-L, Xing D, Ma J-X, Xu W-G, Wang J, Chen Y. Balloon kyphoplasty versus percutaneous vertebroplasty in treating osteoporotic vertebral compression fracture: grading the evidence through a systematic review and meta-analysis. Eur Spine J 2012;21(9):1844-59.
8. Barr JD, Barr MS, Lemley TJ, McCann RM. Percutaneous vertebroplasty for pain relief and spinal stabilization. Spine 2000;25(8):923-8.
9. Calmels V, Vallée J-N, Rose M, Chiras J. Osteoblastic and mixed spinal metastases: evaluation of the analgesic efficacy of percutaneous vertebroplasty. Am J Neuroradiol 2007;28(3):570-4.
10. Cotten A, Dewatre F, Cortet B, Assaker R, Leblond D, Duquesnoy B, et al. vertebroplasty for osteolytic metastases and myeloma: effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up. Radiology 1996;200(2):525-30.
11. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. The Lancet 2010;376(9746):1085-92.
12. McGraw JK, Cardella J, Barr JD, Mathis JM, Sanchez O, Schwartzberg MS, et al. Society of Interventional Radiology quality improvement guidelines for percutaneous vertebroplasty. J Vasc Interv Radiol 2003;14(9):S311-S5.
13. Thillainadesan J, Schlaphoff G, Gibson K, Hassett G, McNeil H. Long-term outcomes of vertebroplasty for osteoporotic compression fractures. J Med Imaging Radiat Oncol. 2010;54(4):307-14.
14. Álvarez L, Alcaraz M, Pérez-Higueras A, Granizo JJ, de Miguel I, Rossi RE, et al.Percutaneous vertebroplasty: functional improvement in patients with osteoporotic compression fractures. Spine 2006;31(10):1113-8.
15. Layton KF, Thielen K, Koch C, Luetmer P, Lane J, Wald J, et al. Vertebroplasty, first 1000 levels of a single center: evaluation of the outcomes and complications. Am J Neuroradiol 2007;28(4):683-9.
16. Moerman DE, Jonas WB. Deconstructing the placebo effect and finding the meaning response. Ann Intern Med 2002;136(6):471-6.
17. Buchbinder R, Johnston RV, Rischin KJ, Homik J, Jones CA, Golmohammadi K, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev 2018;4:CD006349-CD.
18. Gray LA, Jarvik JG, Heagerty PJ, Hollingworth W, Stout L, Comstock BA, et al. INvestigational Vertebroplasty Efficacy and Safety Trial (INVEST): a randomized controlled trial of percutaneous vertebroplasty. BMC Musculoskelet Disord 2007;8(1):126.
19. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. The Cochrane Database of Systematic Reviews. 2018 Apr;4:CD006349. DOI: 10.1002/14651858.CD006349.pub3.
20. Genant HK, Wu CY, Van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res. 1993 8(9):1137-48.

21. Ettinger B, Black DM, Nevitt MC, Rundle AC, Cauley JA, Cummings SR, et al. Contribution of vertebral deformities to chronic back pain and disability. J Bone Miner Res 1992;7(4):449-56.
22. Patrick DL, Deyo RA, Atlas SJ, Singer DE, Chapin A, Keller RB. Assessing health-related quality of life in patients with sciatica. Spine 1995;20(17):1899-908; discussion 909.
23. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142-8.
24. Lips P, Cooper C, Agnusdei D, Caulin F, Egger P, Johnell O, et al. Quality of life in patients with vertebral fractures: validation of the quality of life questionnaire of the European Foundation for Osteoporosis (QUALEFFO). Osteoporos Int. 1999;10(2):150-60.
25. Brooks R, Group E. EuroQol: the current state of play. Health policy. 1996;37(1):53-72
26. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? Medical care. 1996:73-84.
27. Lad SP, Patil CG, Lad EM, Hayden MG, Boakye M. National trends in vertebral augmentation procedures for the treatment of vertebral compression fractures. Surg Neurol. 2009;71(5):580-4.
28. Leake C, Brinjikji W, Cloft H, Kallmes DF. Trends of inpatient spine augmentation: 2001–2008. AJNR Am J Neuroradiol 2011; 32: (8)1464-8.
29. Clark W, Bird P, Gonski P, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial. The Lancet. 2016;388(10052):1408-16.
30. Chen D, An Z-Q, Song S, Tang J-F, Qin H. Percutaneous vertebroplasty compared with conservative treatment in patients with chronic painful osteoporotic spinal fractures. J Clin Neurosci. 2014;21(3):473-7.
31. Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. N Engl J Med. 2009;361(6):557-68.
32. Firanescu CE, de Vries J, Lodder P, et al. Vertebroplasty versus sham procedure for painful acute osteoporotic vertebral compression fractures (VERTOS IV): randomised sham controlled clinical trial. bmj. 2018 361:k1551.
33. Denoix E, Viry F, Ostertag A, et al. What are the predictors of clinical success after percutaneous vertebroplasty for osteoporotic vertebral fractures? Eur Radiol. 2018;28(7):2735-42.
34. Diamond TH, Bryant C, Browne L, Clark WA. Clinical outcomes after acute osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous vertebroplasty with conservative therapy. Med J Aust. 2006;184(3):113-7.