INTERVENTIONAL

Chronic obstructive pulmonary disease (COPD) patients with osteoporotic vertebral compression fractures (OVCFs): improvement of pulmonary function after percutaneous vertebroplasty (VTP)

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Abstract

Objectives To investigate the changes of respiratory function in patients affected by chronic obstructive pulmonary disease (COPD) with single dorsal osteoporotic vertebral compression fractures (OVCFs) treated with vertebroplasty (VTP).

Methods Forty-five patients affected by COPD and single dorsal OVCF underwent VTP (29 men, 16 women; mean age 71.4 years, range 65–77 years). Inclusion criteria were magnetic resonance findings of bone marrow oedema, without intracanal bone fragments and refractory pain to medical treatment for at least 3 months. Osteoporosis was assessed by bone densitometry. Spirometry was performed before and after treatment.

Results A significant VAS-score decrease was observed 1 week after VTP, with a subsequent decrease over time; vital capacity (VC) and forced vital capacity (FVC) improved over time, reaching a plateau at 3 months. Forced expiratory volume at 1 s (FEV_1) did not significantly differ between the pre-VTP values and follow-up values. A significant correlation was observed between VAS-score values and VC, and VAS-score values and FVC. No significant correlation was observed between VAS-score values and FEV_1 values.

Conclusions VTP improves restrictive ventilatory impairment in patients with moderate and severe COPD affected by single thoracic OVCFs. We recommend this treatment in the management of these patients.

Key Points
• *Osteoporosis is a major comorbidity in chronic obstructive pulmonary disease (COPD) patients.*
• *Pain due to osteoporotic vertebral compression fractures worsens respiratory failure in COPD.*
• *Vertebroplasty improves ventilatory impairment in COPD patients with osteoporotic vertebral compression fractures.*

Abbreviations
COPD   Chronic obstructive pulmonary disease
OVCFs   Osteoporotic vertebral compression fractures
VTP   Vertebroplasty
PMMA   Polymethylmethacrylate

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Introduction

Osteoporosis represents a significant cause of morbidity and mortality, which is becoming increasingly prevalent with the ageing of the population [1, 2]. Vertebral compression fractures (VCFs) are the most common fractures associated to osteoporosis, although they often remain unidentified in about half of patients that do not experience pain symptoms. Due to the peculiar kinetic of the spine, 80 % of pathological vertebral

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fractures are located at the dorsal-lumbar passage; the most frequent sites of osteoporotic vertebral fractures are, in decreasing order, L1, D12 and L2 [3]. VCFs usually cause back pain, more or less intense depending on the site and number of the fractures and their severity, which may affect the patients' quality of life. Other consequences of VCFs are represented by spinal misalignment and kyphosis. They may therefore reduce the activities of everyday life, cause respiration dysfunction and increase the prevalence of lung disease [4, 5].

Osteoporosis has been widely recognised as a major co-morbidity in chronic obstructive pulmonary disease (COPD) patients, being present in 36–60 % of patients with COPD, a rate that is two to five fold higher than that detectable in age-matched healthy subjects [5, 6]. The underlying causes of osteoporosis in COPD remain unclear, but several factors are significantly related to reduced bone density in COPD, including older age, female sex, and body mass index (BMI). The relationship with other proposed factors, such as tobacco smoking, physical inactivity and corticosteroid therapy, is still controversial [6–8].

Percutaneous vertebroplasty (VTP) is a minimally invasive technique employing the injection of liquid polymethylmethacrylate (PMMA) cement into a fractured vertebral body [9, 10].

VTP was first reported in the literature in 1987 by Galibert and Deramond [11], for the treatment of a cervical vertebral haemangioma. In the following years, evolution of cement and expansions of indications have resulted in several useful vertebral augmentation procedures [12]. VTP is now considered a safe and effective procedure for the treatment of Osteoporotic VCFs (OVCFs) [13–17]. Pain relief and improvement of mobility and function after VTP is immediate, long lasting and is considered significantly better than conservative medical treatment [18–20].

The aim of our study was to investigate the effects of VTP and the changes of respiratory function in COPD patients with single dorsal VCFs due to osteoporosis.

Materials and methods

Patient population and preoperative management

From September 2011 to August 2013, we observed in our department 123 patients with COPD affected by OVCFs. All patients reported that severe back pain, resistant to conservative treatment, occurred no later than 3 months before. Those reporting radicular pain and symptoms suggestive for neurological involvement were excluded.

The diagnosis and selection of patients was made by a pulmonologist and interventional radiologist in consensus, on the basis of clinical history and physical examination;

treatment indications were made by an interventional radiologist based on imaging findings.

All patients presented a VCF at spine radiography. Diagnosis was confirmed by spine magnetic resonance (MR) examination. In some cases, computed tomography was also performed in order to exclude the interruption of vertebral posterior wall with the potential for intracanal bone fragment (Fig. 1).

Inclusion criteria were a single dorsal vertebral involvement, with MR findings of bone marrow oedema, without intracanal bone fragments and refractory pain to conventional medical treatment from at least 3 months. The osteoporotic condition was assessed by bone densitometry, and spirometry was performed before and after treatment.

A total of 45 patients were enrolled (29 men, 16 women; mean age 71.4 years, range 65–77 years) and underwent VTP treatment. All patients continued their drug therapy for osteoporosis and COPD and were encouraged to terminate their analgesic or anti-inflammatory therapy the days after VTP procedure.

Our inner Ethical Committee approved the study protocol and written informed consent was obtained from all patients before VTP procedure.

Percutaneous procedure—operative technique and devices

All procedures were performed under fluoroscopic guidance in an angiographic suite (Allura Xper FD 20; Philips Healthcare, Best, The Netherlands) with patients in the prone position with the spine slightly hyperextended. All procedures were performed under local anaesthesia with close monitoring of the anaesthetist (buffered lidocaine/bupivacaine 1 %/0.25 % for skin incision; ropivacaine 10 mg/ml for periosteal anaesthesia). The access was through the left pedicle in all cases using a 13-G× 150 mm straight injection cannula (OptiMed, Ettlingen, Germany), according to the habit of the first operator. Our technique did not differ from the standard well-established technique widely used, described elsewhere [21]. The cement, polymethylmethacrylate (PMMA; OptiMed, Ettlingen, Germany), was injected inside the vertebral body as uniformly as possible under fluoroscopic control (Figs. 2 and 3).

The duration of the whole procedure was approximately 25–30 min. After the procedure, the patient was placed in a supine position and asked to lie in bed motionless for at least 4 hours to allow complete consolidation of the PMMA prior to axial loading. In the absence of complications, patients were discharged 4–6 h after the procedure. Antibiotics (cefazolin) were administered the day of procedure. In eight patients with diabetes, antibiotic coverage was extended up to 3 days after the procedure.

Fig. 1 A 72-year-old woman with osteoporosis and COPD. MR imaging shows an acute T8 compression fractures with deformity of the vertebral body. **a** Sagittal T1-weighted: low signal intensity in the collapsed T8 vertebral body compared with the normal bone marrow in other adjacent vertebral bodies. **b** Sagittal T2-STIR: bone marrow high signal intensity secondary to oedema

Clinical assessment and follow-up

All patients underwent physical and neurological examination prior to and after the VTP procedure.

During the screening period, the use of analgesic and anti-inflammatory drugs, as well as osteoporosis and COPD therapy, was recorded. No deaths were observed in the 12-month follow-up period.

Pain intensity was evaluated by an 11-point visual analogue scale (VAS) score (0 = absence of pain, 10 = unbearable pain) administered before, 1 week, 3 months and 12 months after the procedure.

Spirometric examination was performed before (baseline) and 1 week, 3 months and 12 months after treatment. In accordance with the literature we considered as benchmarks percentage vital capacity (VC %), percentage forced vital capacity (FVC %), and percentage forced expiratory volume in 1 s (FEV_1 %).

Statistical analysis

The correlations between VAS score and VC, VAS score and FVC, VAS score and FEV_1 were evaluated by non-parametric Spearman test. The difference between the baseline, 1-week, 3-month and 12-month values in VAS score, VC, FVC and FEV_1 were evaluated using the Wilcoxon matched-pairs signed rank test. A p value lower than 0.05 was considered significant. Data were expressed as mean value ± standard deviation (SD). Statistical analyses were performed using commercial software (Graph-pad Prism 5, San Diego, CA).

Fig. 2 A 79-year-old man with osteoporosis and COPD. Fluoroscopic biplanar post-procedure control in the lateral (**a**) and antero-posterior (**b**) view. Optimal and uniform distribution of PMMA within T6 vertebral body
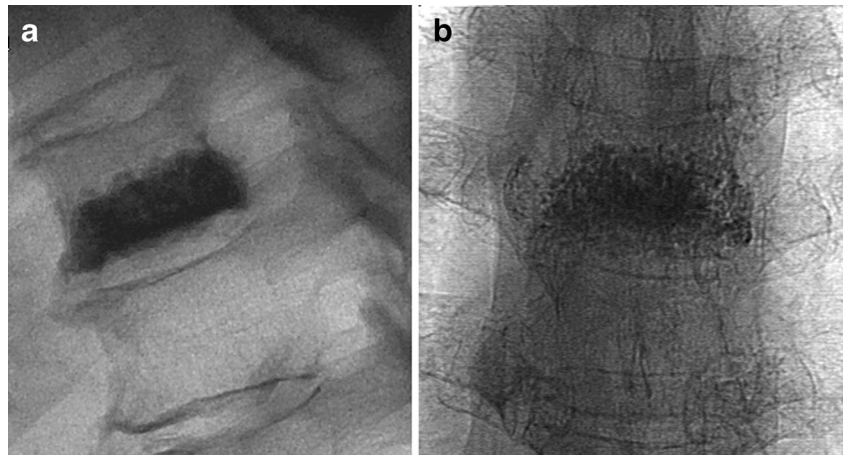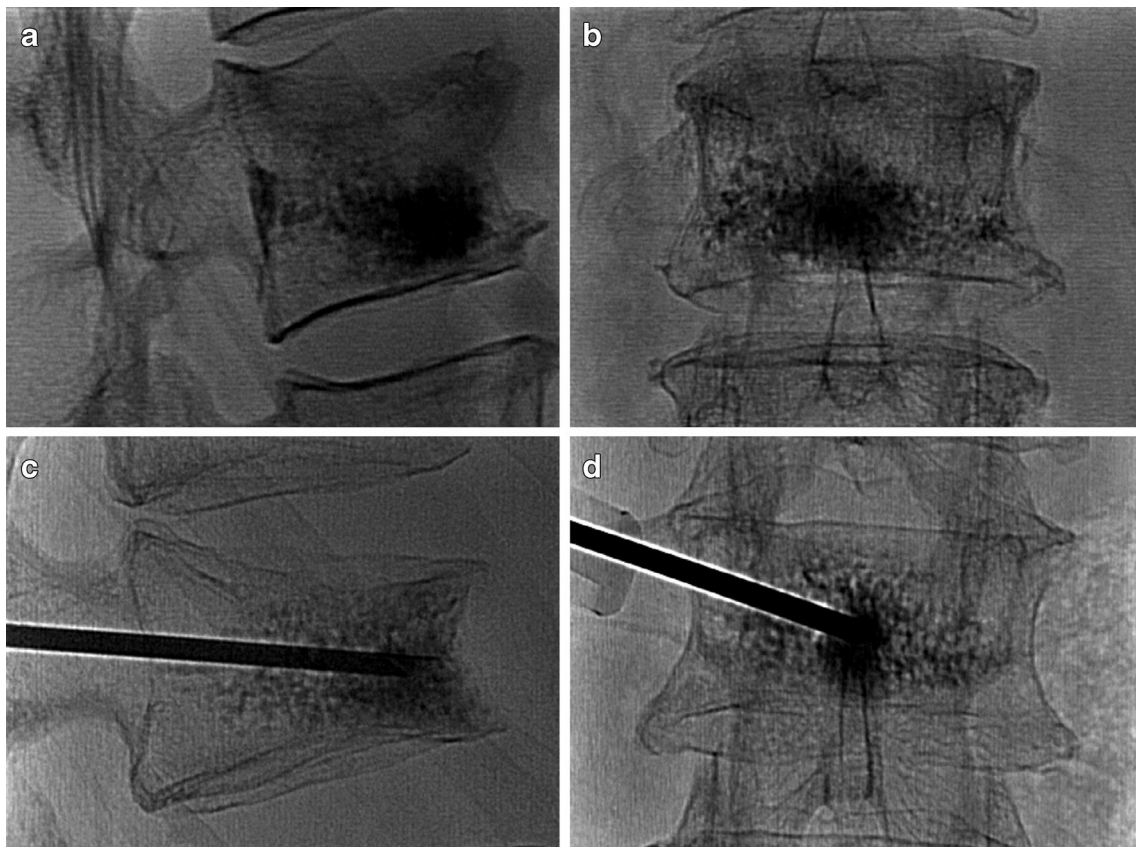
Fig. 3 Fluoroscopic end-procedure control lateral (**a**) and antero-posterior (**b**) view; notice cement filling of the basivertebral vein near posterior vertebral wall. Intraprocedure fluoroscopic lateral (**c**) and antero-posterior (**d**) view of another patient showing injection cannula still in place inside the vertebral body with the tip close to the anterior vertebral wall during the last phases of cement injection; notice cement spread throughout the middle third of vertebral body although the tip is so far anteriorly located

Results

Twelve months of follow-up were completed for all 45 patients. A significant variation ($p<0.001$) between the VAS-score values, VC and FVC values obtained before the procedure and those obtained at 1 week, 3 months and 12 months after treatment was recorded without significant changes in FEV throughout the follow-up period (Fig. 4). A marked decrease in pain was observed 1 week after the procedure, with a subsequent slight but continuous decrease over time (Table 1); VC % and FVC % values slightly and continuously improved over time, reaching a plateau at 3 months (Tables 2 and 3). FEV_1 values did not significantly differ between the pre-VTP ones and the ones obtained 1 week after the procedure ($p=0.6840$), at 3 months' ($p=0.5140$) and at 12 months' follow-up ($p=0.9496$) (Table 4). A significant correlation was observed between VAS-score values and VC % ($p=0.0167$), and VAS-score values and FVC % ($p=0.0028$); the correlation between the VAS-score values and FEV_1 values was not significant ($p=0.6583$) (Fig. 5).

Discussion

OVCFs are known to result in impaired respiratory function through reduction of thoracic mobility and postural deformity, especially in patients with co-existent pulmonary disease, such as COPD patients [22]. Back pain due to acute and sub-acute thoracic OVCFs limits movements of the thorax and can represent a factor contributing to ventilatory disturbance in COPD patients, influencing the involvement of accessory muscles to improve the change of air volume and increasing muscular effort [23, 24].

In this study VTP was performed in patients with symptomatic thoracic OVCFs affected by moderate/severe COPD (according to the GOLD severity scale) with the aim of relieving thoracic back pain. The pain improvement was evaluated through an 11-point VAS score and the related pulmonary functional outcome was assessed through spirometric parameters: VC, FVC and FEV_1.

Consistent with previous results reported in the literature, VAS score assessment demonstrates a significantly higher improvement of symptoms with significant pain reduction
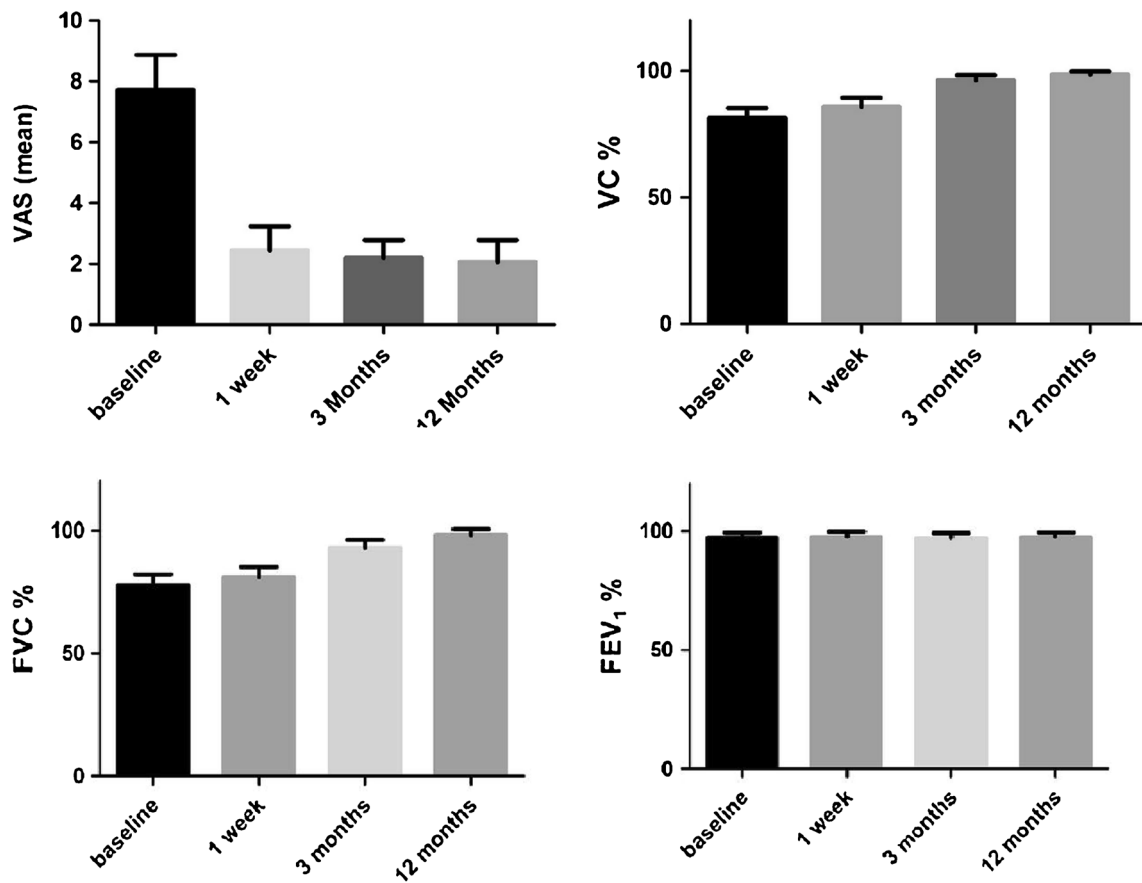
Fig. 4 Graphical representation of the mean VAS score (**a**), VC % (**b**), FVC % (**c**) and FEV$_1$ (**d**) values before VTP (baseline) and at 1 week, 3 months and 12 months of follow-up evaluation. The improvement was significant for VAS, VC and FVC. FEV$_1$ values did not change significantly over the whole 1 year follow-up period

already 1 week after VTP, maintained during long-term follow-up without further significant modification [18, 25–27]. In accordance with these studies, we observed a progressive improvement of spirometric parameters such as VC and FVC 1 week after VTP, with further gradual improvement over the entire follow-up period. In another trial, Dong et al. [5] also reported an improvement of pulmonary function after both VTP and kyphoplasty (KPT). In this study, VC and

FVC were already significantly increased 3 days after procedures, whereas maximum voluntary ventilation (MVV) started to improve 3 months later.

The improvement in pulmonary function was paralleled by decreased VAS values showing significant correlation between them [5]. MVV values reflect the respiratory muscle endurance and are reduced in osteoporotic patients due to their inactivity. Women with osteoporosis typically have impaired

Table 1 Descriptive statistical analysis of VAS-score values before VTP (baseline) and at 1 week, 3 months and 12 months of follow-up evaluation

VAS	Baseline	1 week	3 months	12 months	*p* value
Minimum	5.000	1.000	1.000	1.000	<0.05
25th percentile	7.000	2.000	2.000	2.000	<0.05
Median	8.000	2.000	2.000	2.000	<0.05
75th percentile	9.000	3.000	2.000	2.000	<0.05
Maximum	10.00	5.000	4.000	4.000	<0.05
Mean	7.733	2.444	2.200	2.067	<0.05
SD	1.136	0.7850	0.5878	0.7198	-
SEM	0.1694	0.1170	0.08762	0.1073	-
Lower 95 % CI of mean	7.392	2.209	2.023	1.850	-
Upper 95 % CI of mean	8.075	2.680	2.377	2.283	-

Pain reduction is significant and almost immediate since the first week, with a smaller but steady further improvement over the following follow-up checks

SD standard deviation, *SEM* standard error of the mean

Table 2 Descriptive statistical analysis of VC values before VTP (baseline) and at 1 week, 3 months and 12 months of follow-up evaluation

VC%	Baseline	1 week	3 months	12 months	p value
Minimum	75.00	80.00	93.00	97.00	<0.05
25th percentile	78.00	83.00	94.00	97.00	<0.05
Median	82.00	86.00	96.00	98.00	<0.05
75th percentile	85.00	89.00	98.00	100.0	<0.05
Maximum	87.00	92.00	100.0	100.0	<0.05
Mean	81.53	85.91	96.31	98.60	<0.05
SD	3.900	3.636	2.065	1.286	-
SE M	0.5814	0.5420	0.3078	0.1917	-
Lower 95 % CI of mean	80.36	84.82	95.69	98.21	-
Upper 95 % CI of mean	82.70	87.00	96.93	98.99	-

There is a gradual and significant improvement of VC over each step of the 1-year follow-up period

SD standard deviation, *SEM* standard error of the mean

lung volumes, restricted rib mobility, reduced respiratory muscle endurance and reduced isometric muscle strength [28]. Since both VC and FVC directly correlate with restrictive respiratory impairment, which is in turn correlated with thoracic pain, we can assume that the analgesic effect of VTP can reduce restriction of thoracic movements, thus improving ventilation in COPD patients. However, if we consider the different timing of evolution between the VAS score and spirometric parameters, it is unlikely that pain reduction by itself is the only factor involved in such improvement. In this context, it is more likely that pain reduction may allow wider thoracic/costal movements over time, thus improving the strength of respiratory muscles and eventually leading to improvement of the restrictive syndrome.

Tanigawa et al. [23] evaluated the effects of VTP on respiratory function in patients with acute/subacute OVCFs occurring at single or multiple levels in the thoracic, thoracic-lumbar and lumbar segments. They reported significant pain reduction in all patients, independent of the number of levels involved and on their segmentary localisation. However, significant improvement of FVC was reported exclusively in the group with thoracic involvement, independent of single- or multiple-level involvement. They concluded that pain is the main determinant of such restrictive syndromes, owing to

decreased thoracic motion. Alleviation of local kyphosis was also considered a contributing factor, but mainly in the cases of multiple level OVCFs.

Several previous studies underlined the role of reduction of kyphosis and restored vertebral height in the improvement of pulmonary function in OVCF patients [5, 29, 30]; in these studies the authors underline the dual role of KPT for both back pain relief and restoration of vertebral body height and kyphotic wedge angle. Dong et al. [5] stated that patients with thoracic OVCFs might obtain more benefit from KPT than VTP because of reduction of local kyphotic angle (LKA) and its related back pain relief. Other studies in contrast suggested that improvement of sagittal alignment and restoration of vertebral body height did not significantly influence respiratory air exchange and LKA did not show correlation with any parameter of pulmonary function. Yang et al. [24] reported that, despite the reduction of LKA in their patients being clinically significant, correlation with lung functional parameters was not significant: as for VTP, balloon KPT contribution acted only on pain relief, which was demonstrated to be the major cause of impairment of lung volumes and reduction of respiratory muscle endurance. A systematic review of osteoporosis-related kyphosis and respiratory function impairment demonstrates that declines in VC secondary to kyphosis

Table 3 Descriptive statistical analysis of FVC values before VTP (baseline) and at 1 week, 3 months and 12 months of follow-up evaluation

FVC%	Baseline	1 week	3 months	12 months	p value
Minimum	70.00	75.00	88.00	94.00	<0.05
25th percentile	74.00	78.00	90.00	96.00	<0.05
Median	78.00	81.00	93.00	100.0	<0.05
75th percentile	82.00	84.50	95.00	100.0	<0.05
Maximum	85.00	88.00	100.0	100.0	<0.05
Mean	77.80	81.18	92.96	98.22	<0.05
SD	4.495	4.013	3.309	2.383	-
SEM	0.6701	0.5982	0.4933	0.3552	-
Lower 95 % CI of mean	76.45	79.97	91.96	97.51	-
Upper 95 % CI of mean	79.15	82.38	93.95	98.94	-

There is a gradual and significant improvement of FVC over each step of the 1-year follow-up period

SD standard deviation, *SEM* standard error of the mean

Table 4 Descriptive statistical analysis of FEV$_1$ values before VTP (baseline) and at 1 week, 3 months and 12 months of follow-up evaluation

| FEV$_1$%	Baseline	1 week	3 months	12 months
Minimum	94.00	94.00	94.00	94.00
25th percentile	95.50	95.00	95.00	95.50
Median	98.00	98.00	97.00	97.00
75th percentile	99.00	100.0	98.50	99.00
Maximum	100.0	100.0	100.0	100.0
Mean	97.36	97.53	97.07	97.44
SD	1.956	2.282	2.082	2.018
SEM	0.2916	0.3402	0.3104	0.3008
Lower 95 % CI of mean	96.77	96.85	96.44	96.84
Upper 95 % CI of mean	97.94	98.22	97.69	98.05
p value	-	0.6840	0.5140	0.9496

There is no significant correlation among the values of the FEV$_1$ at each follow-up check

SD standard deviation, *SEM* standard error of the mean

seem modest and directly related to the number of vertebral fractures and degree of kyphosis [31]. Moreover, according to Chen et al. [32], VTP does not seem to significantly affect vertebral body height. Accordingly, many cases in which increased vertebral height was reported seem to be mostly secondary to dynamic mobility of the vertebral body itself.

In a recent study, Kelekis et al. [33] reported another interesting effect of VTP. They performed a prospective comparative electronic baropodometer registration analysis of weight projection areas in feet of patients with OVCFs treated with VTP and treated conservatively. Pain related to compression fractures not only affect respiratory dynamic but also produce wide and deep effects on overall body posture that ultimately influence load distribution between left and right feet and among different regions of the same sole. They reported a statistical variation and normalisation of load weight distribution before and after VTP that was not found in the group of patients treated conservatively. These results suggest that baropodemeter analysis could be potentially used as another objective index to evaluate the outcome.

According to these considerations and grounding on our experience we do not believe that vertebral body height restoration after VTP, when its happening is significant, could exercise significant influence on the outcome of these patients. Moreover, because we restricted the study to single-level OVCF, the local kyphotic angle improvement would be minimal, or at least not significant for the purpose of pulmonary function improvement. However, the position of the patients on the operating table is prone with the spine slightly hyperextended, which should widen the fracture lines, allowing more cement to diffuse easily into the vertebral body and thus improving stabilisation.
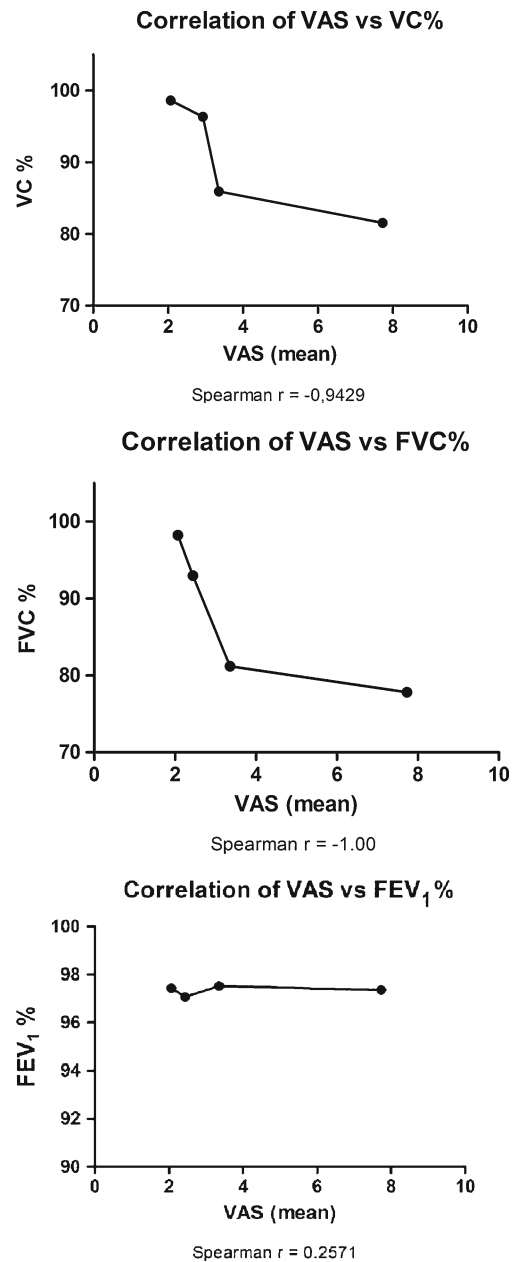
Fig. 5 Graphical representation of the crossed-correlation results between the VAS score, VC%, FVC%, and FEV$_1$ values using the Spearman test. A significant ($p<0.001$) correlation between VAS score and VC% ($r=-0.9429$), as well as VAS score and FVC% ($r=-1.0000$) resulted (**a**, **b**). The correlation between VAS score and FEV$_1$ was not significant ($r=-0.2571$) (**c**)

During the follow-up period we did not find new vertebral collapses, neither adjacent nor distant.

VAS values showed a steep decrease during the first week, whereas these remained almost stable during the following follow-up checks, showing only minimal further improvement, which in some cases was not statistically significant. These results are congruous with the generally and widely recognised effect of VTP. The further minimal VAS improvement after 1 month can be considered a result of the overall

better physical condition of the patients rather than an intrinsic effect of the procedure itself, whose effects are usually almost immediately evident.

There were no other complications related to the procedure, such as significant cement leakages or infections in the treated region. Thoracic pain beyond the involved level showed a steep decrease since the first days after procedure, keeping quite stable and significantly reduced after 1 month and over the following follow-up period. Some patients who complained about lower back pain unrelated to the vertebral collapse before the procedure, continued to complain steadily after the procedure. We have not been able to detect any influence of such lower back pain on the outcome of these patients. Indeed, the improvement of VC and FVC of patients complaining of lower back pain did not show a significant difference, compared with the other patients.

As mentioned above, the choice to restrict the study to patients with only single vertebral collapse, with the purpose to ease the evaluation of the results and scavenge further bias, represents an evident limitation. Another limitation, apart from the small population of patients, is the absence of a control group. An optimal evaluation of the effect of VTP on respiratory function in COPD patients would require a randomised controlled study comparing VTP with a control group, such as a conservative treatment group, a sham-treated group or a group receiving respiratory rehabilitation. In addition, the choice to observe our patients over a 12-month period may have some disadvantages. Indeed, in such a short period of observation, the incidence of respiratory complications—such as acute COPD exacerbations—is lower and this could have influenced the results. Regarding the use of VTP compared with KPT, in addition to the considerations listed above, some advantages of VTP over KPT that should be considered are shorter operation time, smaller amount of PMMA required, reducing the incidence of complications, as well as the lower overall cost of VTP [11, 12, 34–38].

However VTP is a treatment of proven effectiveness in reducing pain secondary to acute OVCFs. Notwithstanding the above mentioned limitations, it also appears to be effective in improving VC and FVC of patients with COPD.

Conclusions

VTP treatment has led to improvement of both respiratory impairment and overall quality of life for patients affected by single thoracic OVCFs with moderate or severe COPD. We therefore recommend this treatment in the management of such patients.

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