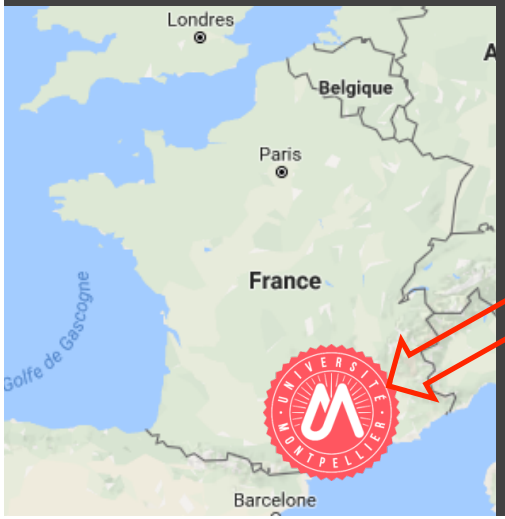
Journées Francophones d'Imagerie Médicale

Management of osteoporotic vertebral fracture : place of vertebroplasty

Pr Catherine Cyteval

Montpellier



Percutaneous vertebroplasty (VP)
Injection of cement (usually PMMA in the vertebral body)
Goals:
- Improve bone strength
- Reduce pain

- Efficiency?
  For which fractures: acute or chronic?

- Complication: leaks

- Evolution of the spine
  - Decrease in the height of the vertebra
  - Fracture of other vertebrae

Efficiency

Deramond H. , Gallibert P. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results Radiol Clin North Am 1998

Cotten et coll. Percutaneous vertebroplasty: state of the art Radiographics 1998

Cyteval et coll. acute osteoporotic vertebral collapse: open study on percutaneous injection of acrylic surgical cement AJR 1999

Barr et coll. Percutaneous Verteb for Pain Relief and Spinal Stabilization Spine 2000.

Huy et coll. Prospective Analysis of Clinical Outcomes after Percutaneous Vertebroplasty for Painful Osteoporotic Vertebral Body Fractures AJNR 2005

Effectiveness on acute pain episode

In 2009 more than 100 open study publications

Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial

Caroline A H Klazen, Paul N M Lohle, Jolanda de Vries, Frits H Jansen, Alexander V Tielbeek, Marion C Blonk, Alexander Venmans, Willem Jan J van Rooij, Marinus C Schoemaker, Job R Juttmann, Tjoen H Lo, Harald J J Verhaar, Yolanda van der Graaf, Kaspar J van Everdingen, Alex F Muller, Otto E H Elgersma, Dirk R Halkema, Hendrik Fransen, Xavier Janssens, Erik Buskens, Willem P Th M Mali

Klazen et al. Lancet 2010

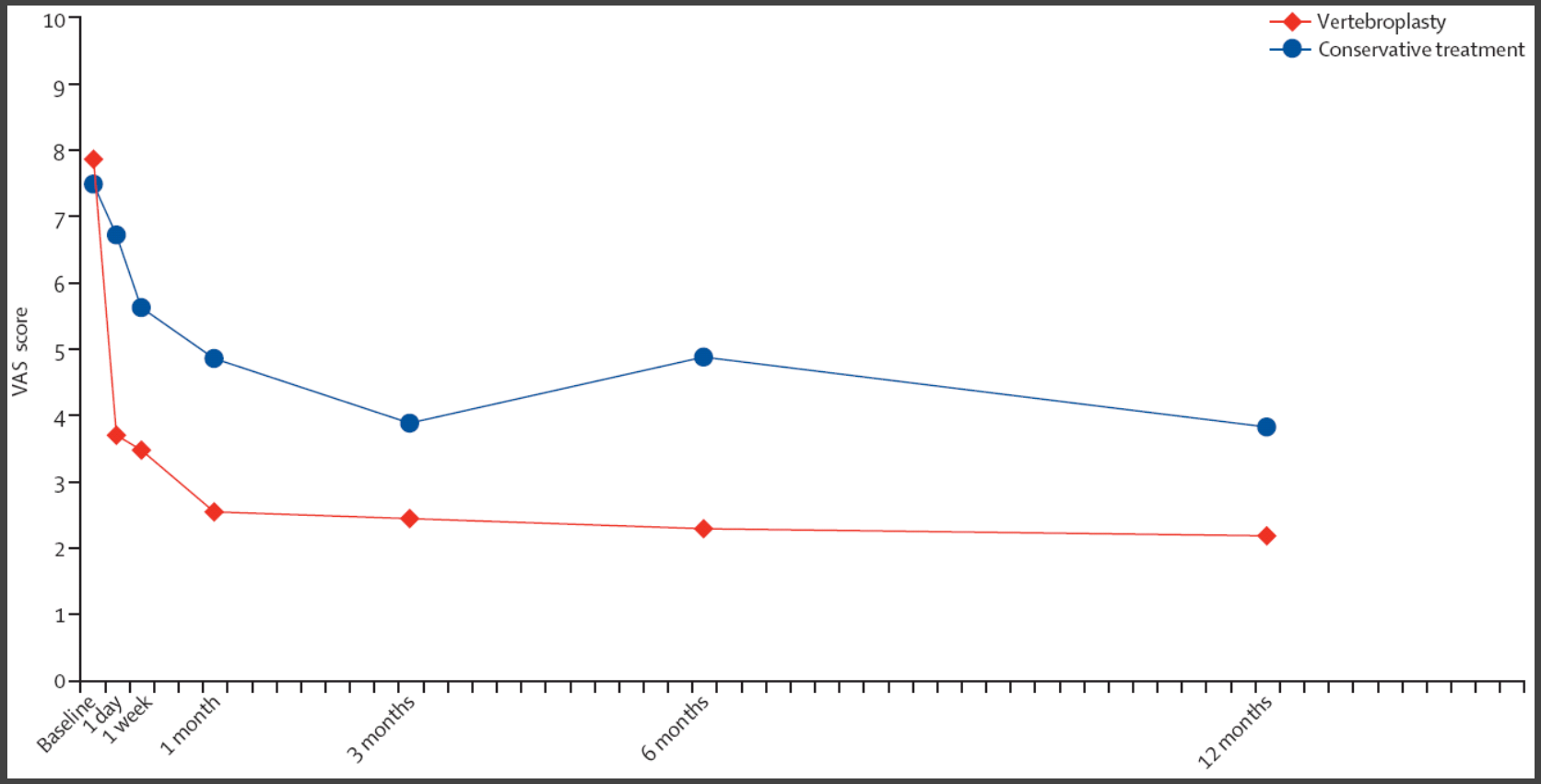
	Percutaneous vertebroplasty (n=101)	Conservative treatment (n=101)
Age (years)	75·2 (9·8)	75·4 (8·4)
Sex (female)	70 (69%)	70 (69%)
Duration of back pain (days)	29·3 (17·1)	26·8 (16·0)
Initial VAS score	7·8 (1·5)	7·5 (1·6)
Number of VCFs at baseline	2·4 (1·9)*	2·1 (1·5)*
Number and grading of VCFs with bone oedema†		
Mild (10–20%)	57 (42%)	55 (46%)
Moderate (20–40%)	58 (43%)	45 (38%)
Severe (>40%)	21 (15%)	20 (17%)
Wedge	90 (66%)	97 (81%)
Biconcave	46 (34%)	23 (19%)
Crush	0	0
Initial pain treatment		
None	5 (5%)	7 (7%)
Non-opiate drugs	40 (40%)	43 (43%)
Weak opiate derivatives	31 (31%)	22 (22%)
Strong opiate derivatives	19 (19%)	20 (20%)
Vertebral level with bone oedema		
Th5–Th10	19 (14%)	32 (25%)
Th11–L2	91 (65%)	66 (52%)
L3–L5	29 (21%)	28 (22%)
Use of osteoporosis drugs	24 (24%)	26 (26%)
Bone density T score	−3·0 (1·17)	−3·0 (1·05)
EQ-5D score	0·27 (0·03)	0·38 (0·03)
QUALEFFO score	58·7 (13·5)	54·7 (14·4)
RMD score	18·6 (3·6)	17·2 (4·2)

Data are mean (SD) or number (%). VAS=visual analogue scale. VCF=vertebral compression fracture. EQ-5D=EuroQol-5 dimensions. QUALEFFO=Quality of Life Questionnaire of the European Foundation for Osteoporosis. *Range 1–5. †Percentages are proportion of total number of VCFs (136 in percutaneous vertebroplasty group, 120 in conservative treatment group).

Table 1: **Baseline characteristics**

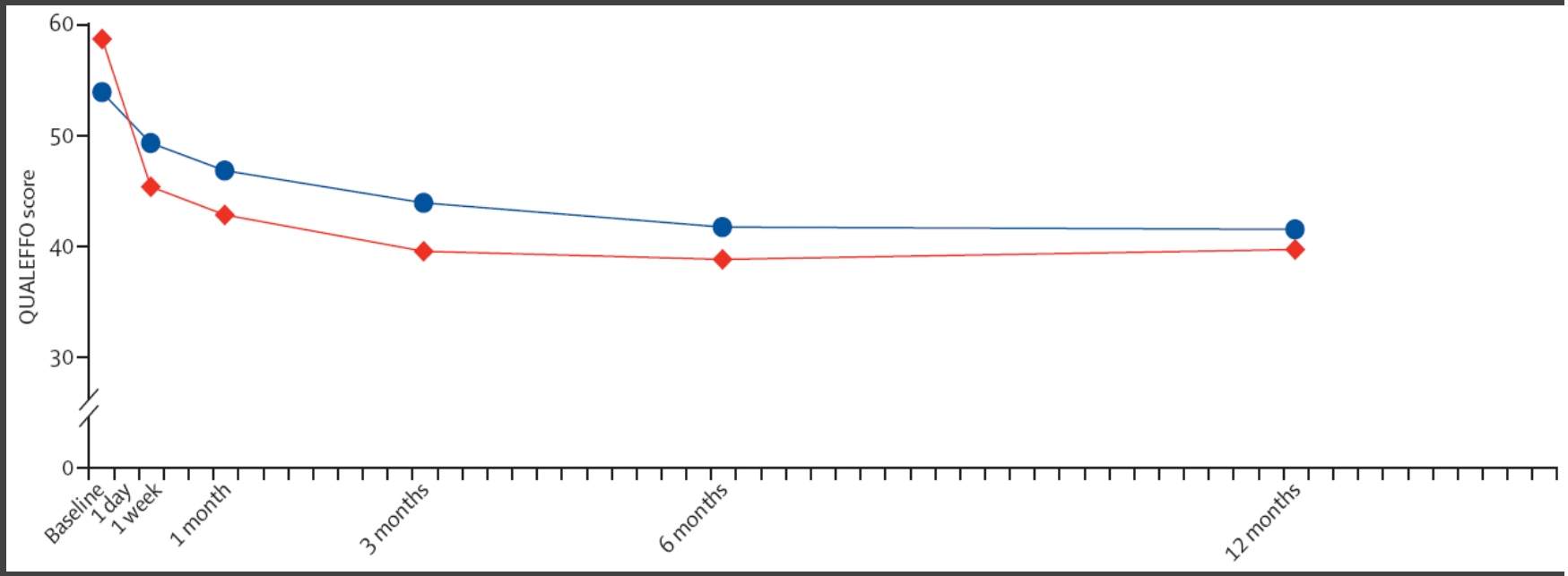
Douleur ≥ 5
IRM: modification de signal

Klazen et al. Lancet 2010



VAS score

Klazen et al. Lancet 2010



Qualeffo score

Klazen et al. Lancet 2010

Vertebroplasty IS IT REALLY EFFECTIVE?

- Buchbinder, R., et al., *A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures.* N Engl J Med, 2009. **361**(6): p. 557-68.

- Kallmes, D.F., et al., *A randomized trial of vertebroplasty for osteoporotic spinal fractures.* N Engl J Med, 2009. **361**(6): p. 569-79.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 6, 2009 VOL. 361 NO. 6

A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures

Rachelle Buchbinder, Ph.D., Richard H. Osborne, Ph.D., Peter R. Ebeling, M.D., John D. Wark, Ph.D., Peter Mitchell, M.Med., Chris Wriedt, M.B., B.S., Stephen Graves, D. Phil., Margaret P. Staples, Ph.D., and Bridie Murphy, B.Sc.

Method

patients:

Pain <12 months

Presence of one or two recent vertebral fractures

Genant's method: ≥ grade 1

MRI: Fracture, bone edema, or both.

Vertebroplasty versus simulated procedure: introduction of the needle to the blade

Main Judgment : 3M AVS

Secondary criteria:

- AVS 1S, 3M, 6M
- Qualeffo (41 items)
- AQoL
- EQ-5D
- EVA resting and nocturnal pain
- Rolland Morris : 23 items

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Vertebroplasty (N = 38)	Placebo (N = 40)
Age — yr	74.2±14.0	78.9±9.5
Female sex — no. (%)	31 (82)	31 (78)
Duration of back pain — wk		
Median	9.0	9.5
Interquartile range	3.8–13.0	3.0–17.0
Duration of symptoms <6 wk — no. (%)	12 (32)	13 (32)
Body-mass index†	25.6±5.5	24.6±5.7
Duration of corticosteroid use — yr‡		
Median	3.0	2.0
Interquartile range	0.3–10.8	0.3–12.5
Pain score§		
Overall	7.4±2.1	7.1±2.3
At rest	4.5±2.3	4.8±2.8
In bed at night	4.8±3.0	3.6±3.2
QUALEFFO total score¶	56.9±13.4	59.6±17.1
AQoL score‖	0.33±0.25	0.27±0.26
RDQ score**	17.3±2.8	17.3±2.9
EQ–5D score††	0.30±0.32	0.28±0.33
Timed Up and Go test — sec‡‡	20.5±8.8	23.9±13.8
Medication for osteoporosis — no. (%)		
Any	35 (92)	37 (92)
Calcium supplements	27 (71)	25 (62)
Vitamin D	14 (37)	18 (45)
Bisphosphonates	31 (82)	32 (80)
One or more previous vertebral fractures — no. (%)	18 (47)	21 (52)
Opioids for pain — no. (%)	30 (79)	34 (85)

Table 2. Outcomes at 1 Week and at 1, 3, and 6 Months, According to Intervention Group.*

Outcome Measure	1 Week			1 Month		
	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)†	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)†
Pain score‡						
Overall	1.5±2.5	2.1±2.8	−0.7 (−1.8 to 0.4)	2.3±2.6	1.7±3.3	0.5 (−0.8 to 1.7)
At rest	0.8±3.0	1.3±3.9	−0.2 (−1.5 to 1.1)	1.4±2.9	1.2±4.0	0.5 (−0.9 to 1.8)
In bed at night	0.9±2.7	0.4±2.8	−0.1 (−1.3 to 1.1)	1.9±2.8	0.5±3.3	0.8 (−0.5 to 2.1)
QUALEFFO total score§	−0.5±7.4	3.6±9.2	−4.0 (−7.8 to −0.2)	2.8±9.3	2.4±12.3	0.9 (−4.2 to 6.0)
AQoL score¶	0.0±0.2	0.0±0.2	0.0 (−0.1 to 0.1)	0.0±0.2	0.1±0.3	0.0 (−0.1 to 0.1)
RDQ score‖	1.8±5.0	4.0±6.8	−2.1 (−5.2 to 0.9)	4.4±6.6	3.1±6.8	1.7 (−1.8 to 5.2)
EQ–5D score**	0.1±0.3	0.1±0.3	0.0 (−0.1 to 0.2)	0.1±0.3	0.1±0.3	0.0 (−0.1 to 0.1)
	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI) ††	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI)††
Perceived pain — no. (%)‡‡						
Better	6 (16)	13 (35)	0.5 (0.2 to 1.1)	12 (34)	9 (24)	1.5 (0.7 to 3.0)
No change	26 (70)	23 (62)		21 (60)	20 (53)	
Worse	5 (14)	1 (3)		2 (6)	9 (24)	

Outcome Measure	3 Months			6 Months		
	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)†	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)†
Pain score‡						
Overall	2.6±2.9	1.9±3.3	0.6 (−0.7 to 1.8)	2.4±3.3	2.1±3.3	0.1 (−1.2 to 1.4)
At rest	1.4±3.4	1.5±3.7	0.1 (−1.1 to 1.4)	2.0±3.2	0.9±3.2	0.3 (−0.9 to 1.5)
In bed at night	1.6±2.9	0.8±3.4	0.2 (−0.9 to 1.3)	1.5±3.6	1.6±3.6	−0.2 (−1.6 to 1.1)
QUALEFFO total score§	6.0±9.6	6.1±13.7	0.7 (−4.4 to 5.7)	6.4±13.4	6.1±13.4	0.6 (−5.1 to 6.2)
AQoL score¶	0.0±0.2	0.1±0.3	0.0 (−0.1 to 0.1)	0.0±0.3	0.1±0.3	0.1 (−0.1 to 0.2)
RDQ score‖	3.7±5.4	5.3±7.2	−1.5 (−4.8 to 1.7)	4.1±5.8	3.7±5.8	0.0 (−3.0 to 2.9)
EQ–5D score**	0.2±0.3	0.2±0.4	0.0 (−0.1 to 0.2)	0.2±0.4	0.2±0.4	0.0 (−0.1 to 0.2)
	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI)††	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI)††
Perceived pain — no. (%)‡‡						
Better	14 (39)	12 (32)	1.2 (0.6–2.2)	16 (46)	15 (42)	1.1 (0.6 to 1.9)
No change	19 (53)	18 (49)		12 (34)	16 (44)	
Worse	3 (8)	7 (19)		7 (20)	5 (14)	

Conclusions

We found no beneficial effect of vertebroplasty as compared with a sham procedure in patients with painful osteoporotic vertebral fractures, at 1 week or at 1, 3, or 6 months after treatment.

VERTOS 4
Vertebroplasty versus sham procedure in recent fractures

Paul NM LOHLE

Cristina E Firanescu, Jolanda de Vries, Paul Lodder, Marinus C Schoemaker, Albert J Smeets, Alexander Venmans, Caroline A H Klazen, Otto E H Elgersma, Frits H Jansen, Alexander Tielbeek, Esther Donga, Job R Juttmann, Issam Boukrab, Karen Schonenberg, Willem Jan J van Rooij, JA Hirsch, Paul NM Lohle.

Depts Radiology & Internal Medicin ; Albert Schweitzer Dordrecht, Medisch Spectrum Twente, Catharina Eindhoven, St. Elisabeth Ziekenhuis & Tilburg University, Medical Clinical Psychology The Netherlands & Massachusetts General Hospital, Harvard Medical School, Boston USA

VERTOS IV study group. Trials. 2011 Apr 5;12:93.

VERTOS 4

- Randomized controlled prospective study against simulated N = 80
- The inclusion criteria:
  - acute spinal pain EVA ≥ 5
  - <6 weeks
  - intraosseous edema visible at MRI

- Pain relief defined as a decrease in VAS ≥ 3

- Primary objective :

AVS at 1 day, 1S, 3 and 12 months.

- Secondary objective:

Functional analysis, measured on the modified Roland-Morris scale (RMD), quality of life (QOL) measured on the questionnaire of the European Foundation for Osteoporosis (QUALEFFO)

- Analgesics, secondary fractures, early and late complications

VERTOS 4- inclusion day

Characteristics	PV group (N=90)	Sham group (N=86)
Age (years)	74.7 (10.7)	76.9 (8.1)
Sex (female)	67 (74%)	66 (77%)
Duration of back pain (days)	29.2 (16.3)	25.9 (13.8)
Mean days till procedure	14 (9.3)	14 (10.0)
Number of VCF's at baseline	115	108
Mild (10-20%) §	37 (32%)	30 (28%)
Moderate (20-40%)	51 (44%)	49 (45%)
Severe (>40%)	27 (23%)	30 (28%)
Wedge	56 (49%)	65 (60%)
Biconcave	59 (51%)	44 (40%)
Crush	0	0

No difference between groups

VERTOS 4 – inclusion day

None	4 (4%)	8 (9%)
Non-opiate drugs	78 (87%)	65 (76%)
Weak opiate derivatives	13 (14%)	17 (20%)
Strong opiate derivatives	42 (47%)	25 (29%)
Vertebral level with bone edema		
Th5-Th10	36 (31%)	24 (22%)
Th11-L2	59 (51%)	69 (64%)
L3-L5	20 (17%)	15 (14%)
No. of spinal levels treated ¶		
1	70 (61%)	66 (61%)
2	15 (26%)	15 (28%)
3	5 (13%)	4 (11%)
Use of osteoporosis drugs	42 (47%)	49 (57%)
Bone density T score	-2.4 (1.0)	-2.4 (0.9)
Initial VAS score ∞	7.7 (1.4)	7.9 (1.6)
QUALEFFO score ※	68.4 (17.1)	69.7 (17.9)
RMD score* *	18.0 (4.5)	17.8 (4.7)

No difference between groups

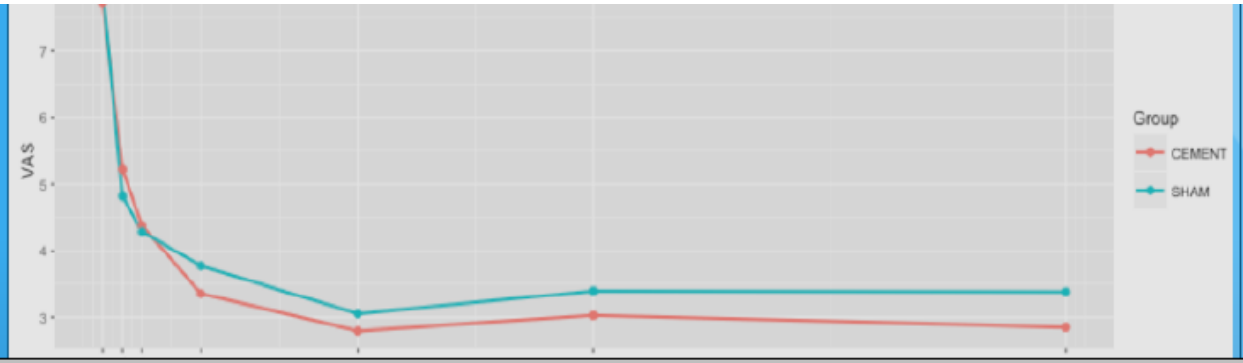
Primary objective

Table 2. Primary outcome- VAS score. (Intention- to- Treat Analyses)

Measure VAS*	PV group	Sham group	Treatment effect (95% CI)§	p value
At baseline	7.72 (1.41)	7.92 (1.56)	-.14 (-.43 / .16)	.37
At day1	5.22 (2.62)	4.82 (2.83)	.15 (-.15 / .45)	.32
At week 1	4.38 (2.5)	4.28 (2.84)	.03 (-.26 / .33)	.82
At 1 month	3.36 (2.63)	3.77 (2.91)	-.15 (-.45 / .15)	.32
At 3 months	2.79 (2.42)	3.05 (2.88)	-.1 (-.4 / .2)	.52
At 6 months	3.03 (2.61)	3.4 (2.59)	-.14 (-.44 / .16)	.35
At 12 months	2.85 (2.44)	3.38 (2.95)	-.2 (-.5 / .1)	.19

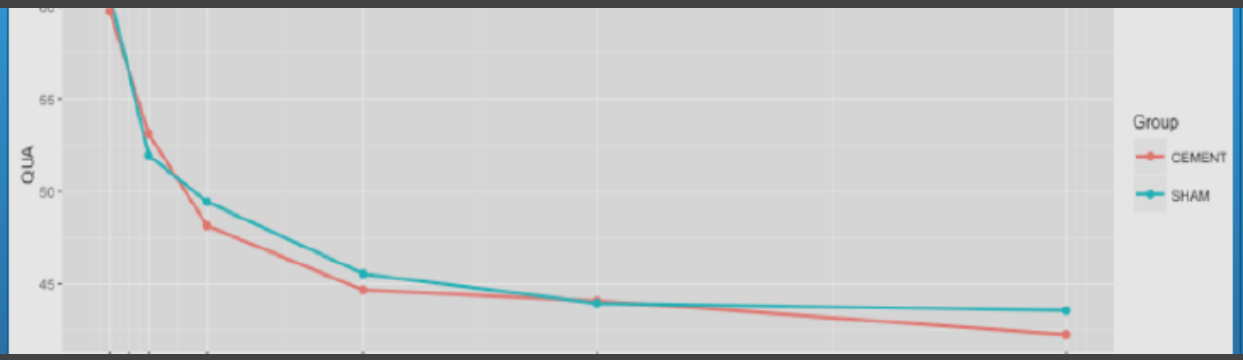
Les scores moyens de douleurs pour chaque groupe sont presque similaires

VAS



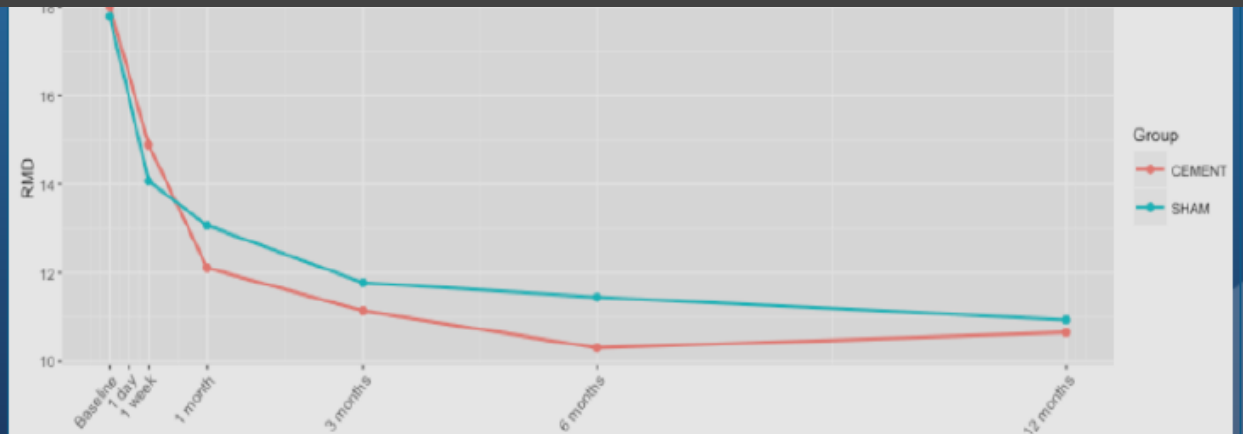
Les deux groupes ont montré une réduction significative des scores de l'EVA comparé à la baseline (p<.0001). Les deux groupes ne diffère pas significativement sur le EVA.

Qualeffo



Il n'y a pas de différence significative sur la qualité de vie.

RMD



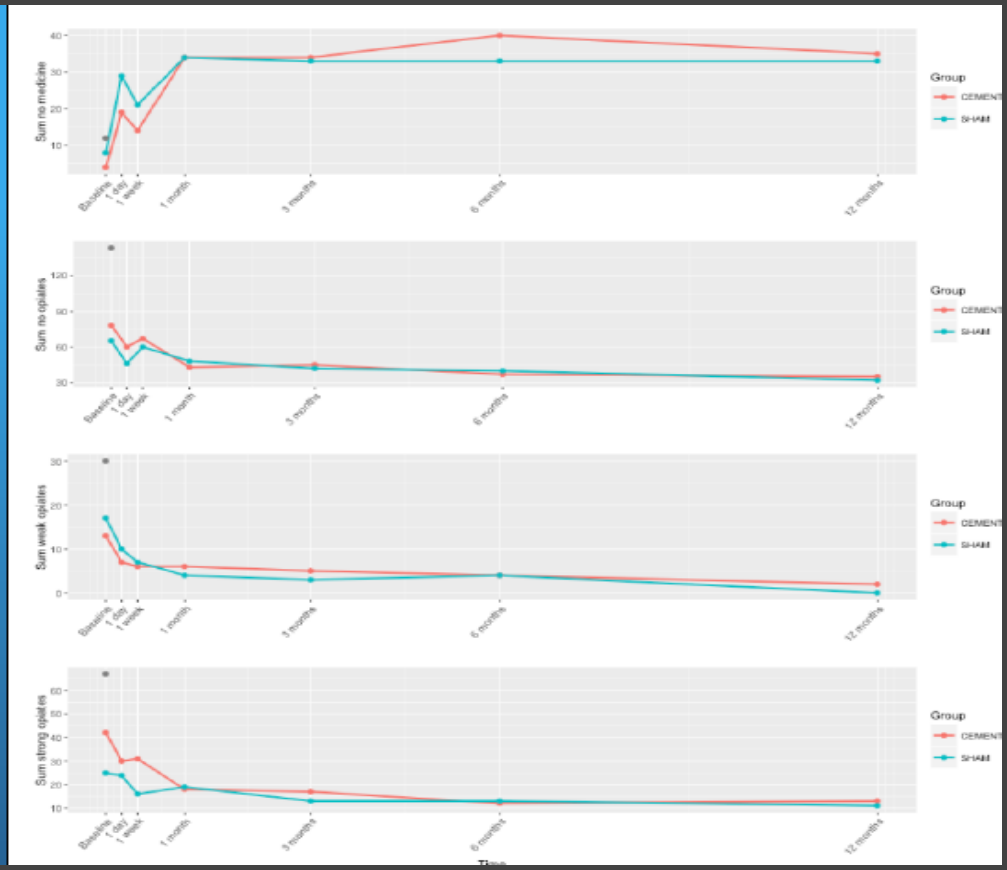
Secondary objective

no medication

NSAID's

weak opiates

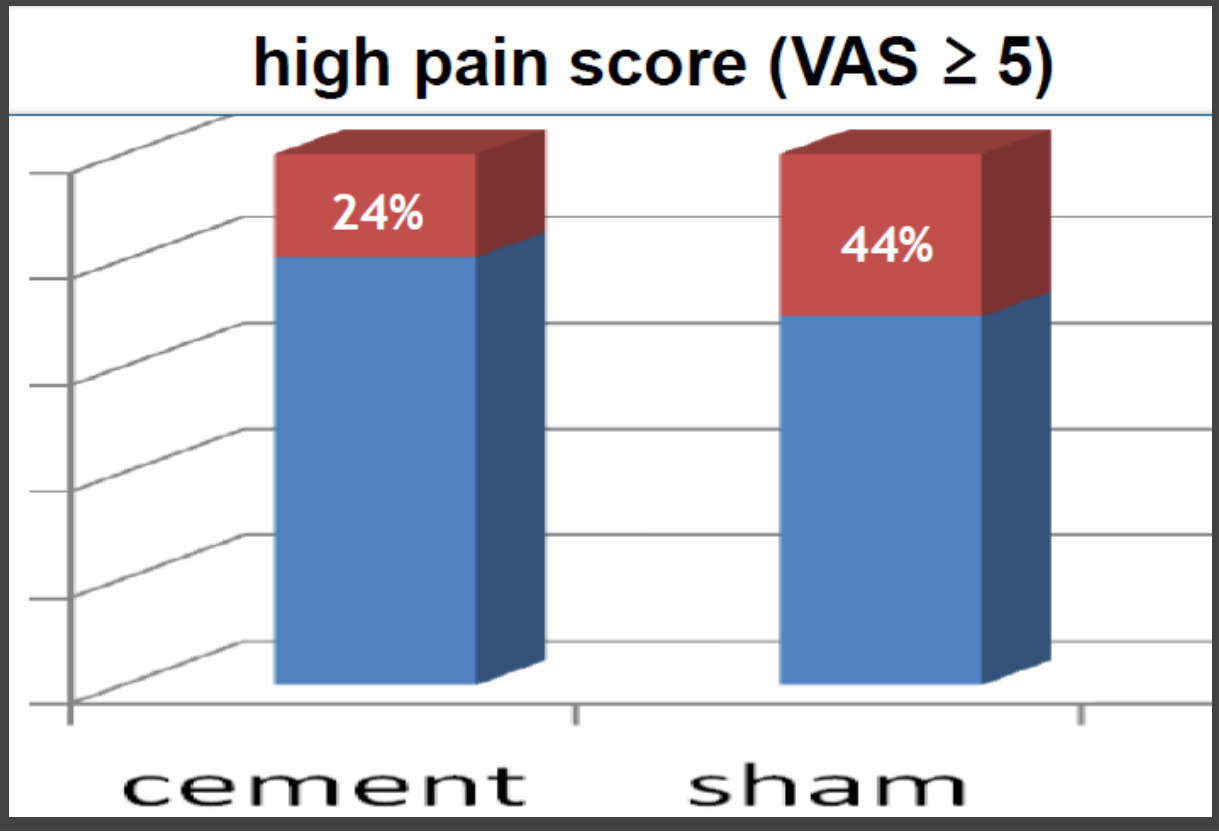
strong opiates



- Initially the class of drugs used for pain was similar in the 2 groups
- Drug use decreased significantly in both groups
- The largest reduction appears at one month three categories

Secondary objective

The analysis of the subgroups found a> % of patients in the control group with an EVA ≥ 5 to 12 months (P = 0. 009)



VERTOS 4 Conclusion

- Even if the sham procedure seems effective it is difficult to apply it in current practice (ethical, moral)

- local anesthetic infiltrations may be proposed in the acute phase as symptomatic treatment in the consolidation period but its effects remain unknown when to procedure is not simulated

VERTOS 5

Sham randomized Controlled Trial

Dennis FM Carli

A Venmans, I Boukrab, P Lodder, MC Schoemaker, AJ Smeets,
E Donga, CE Firanescu, WJJ van Rooij, J de Vries,
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Departments of Radiology Elisabeth Tweesteden ziekenhuis
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9 IÈME JOURNÉE EUROPÉENNE DE THÉRAPEUTIQUE VERTÉBRALE INTERVENTIONNELLE ET VERTÉBROPLASTIE , Paris 3 Février 2017

VERTOS 5

- Randomized controlled prospective study against simulated N = 80

- The inclusion criteria:
  - acute spinal pain EVA ≥ 5
  - > 12 weeks
  - MRI intraosseous edema
- Pain relief defined as a decrease in VAS ≥ 3

- Primary objective :

EVA at 1 day, 1S, 3 and 12 months.

- Secondary objective:

functional analysis, measured on the modified Roland-Morris scale (RMD), quality of life (QOL) measured on the questionnaire of the European Foundation for Osteoporosis (QUALEFFO)

- Analgesics, secondary fractures, early and late complications

Vertos 5

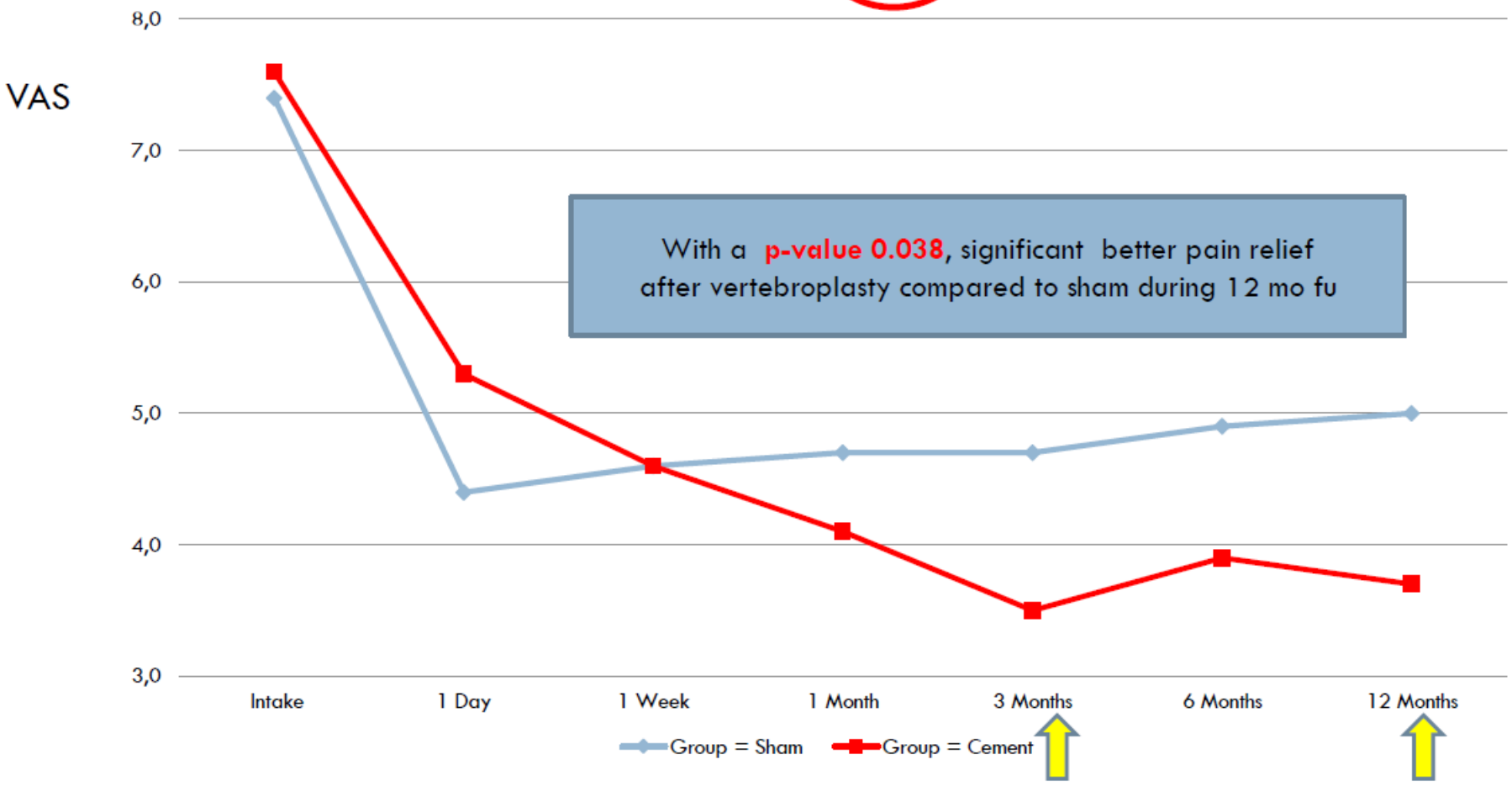
Baseline results, n = 53 treated (until 1-8-2016)

	Vertebroplasty	Sham
number of patients	27	26
mean age	68.8 ± 10.1	71.7 ± 10.3
female sex	20 (53%) ♀	18 (47%) ♀
initial VAS	7.6 (sd 1.5)	7.1 (sd 1.4)
bone density (T-score)	-2.1 (sd 1.1)	-2,1 (sd 1.1)
medication for osteoporosis (%)	87	100
number VCF treated	1.9 (sd 1.2)	1.9 (sd 1.1)

No differences between groups

Vertos 5

Preliminary pain results 53 patients in 2016



Vertos 5
study in sub-groups

AVS ≥ 5 at 12 months

VAS 5 or higher	Vertebroplasty	Sham
N = 29 involved	11	18
percentage	40 %	70 %
p- value	0.032	0.032

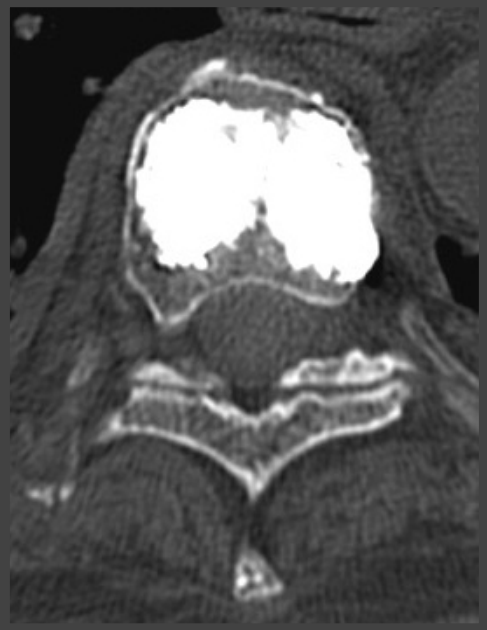
VERTOS 5 conclusion

VP on fractures evolving for more than 12 weeks more efficient tha sham procedures.

Study still ongoing (two thirds of patients included)

more information VERTOS 5 study protocol
→ visit Trials on http://www.clinicaltrials.gov NCT01963039

ADJACENT VERTEBRAL FRACTURES



Is Vertebroplasty safe
Rationnal

- **VP ↑ mechanical strength -> embrittlement of adjacent structures**
- **In addition the presence of a FVI ↑ the risk of FVP**
- **Role of cement leaks in the disc?**

Difficult to answer the questions because few randomized studies with large numbers and prolonged follow-up

- Grados et al. : RR = 2.27 [1.1-4.6] against RR = 1.44 [0.82-2.55] for an incident VF in the vicinity of a non-cemented fractured vertebra

VERTOS 4-Lohle et al. Secondary results

- Medium follow-up of 10 months (median = 12, ranging from 1 to 12)
  - 31 new fractures were found in 15 VP patients
  - 28 new fractures in 19 patients in the control group
- No significant difference between the 3, 6 and 12-month groups (P = 0.60) for the occurrence of new vertebral fractures

VP does not cause new fractures

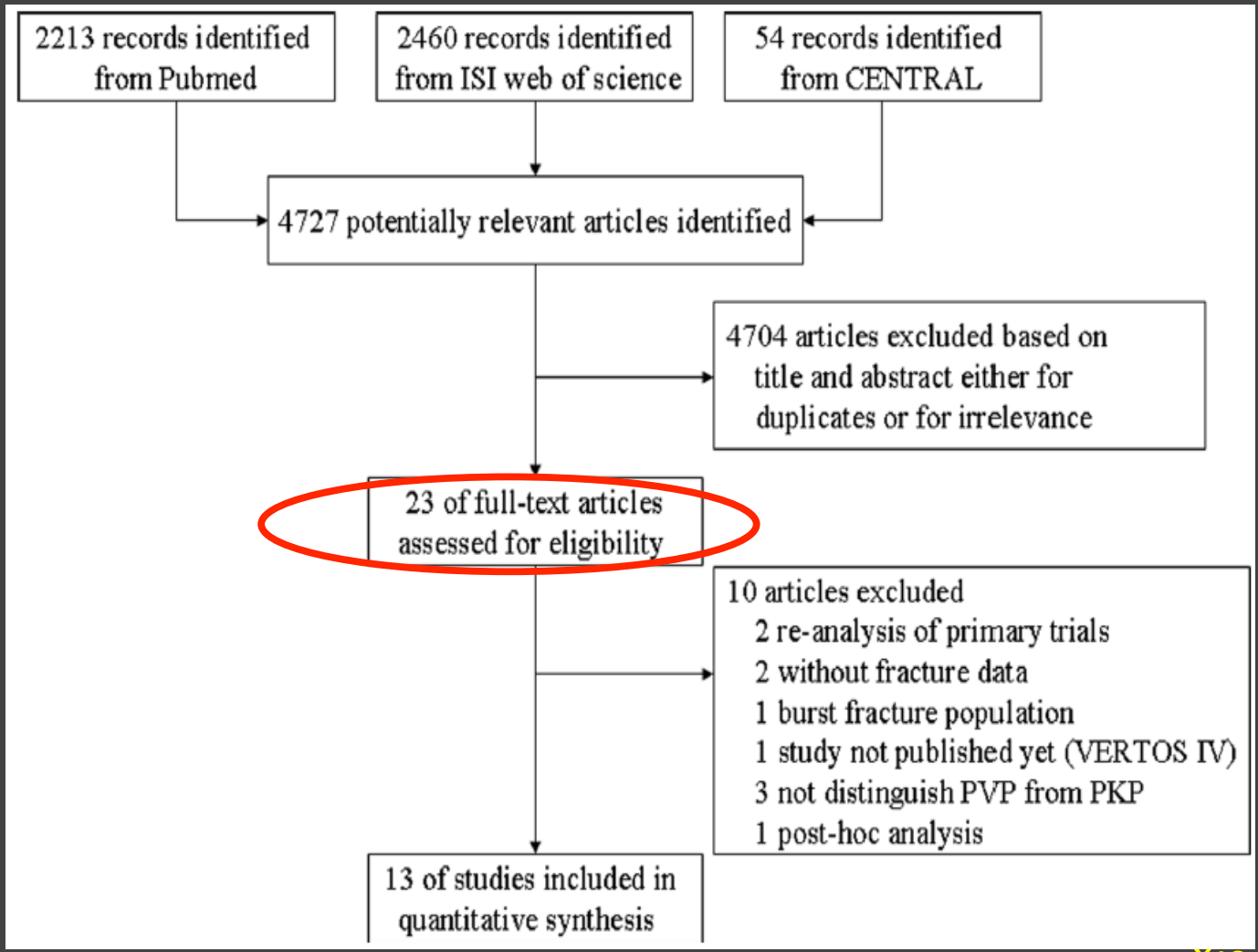
VERTOS 4-Lohle et al. Secondary results

- loss of vertebral height -> 7 patients in the VP group and 36 patients in the control group (P <. 001)

- Cimentoplasty protects against the risk of vertebral compression -> protection of kyphosis

META-ANALYSES

Flow diagram of study selection

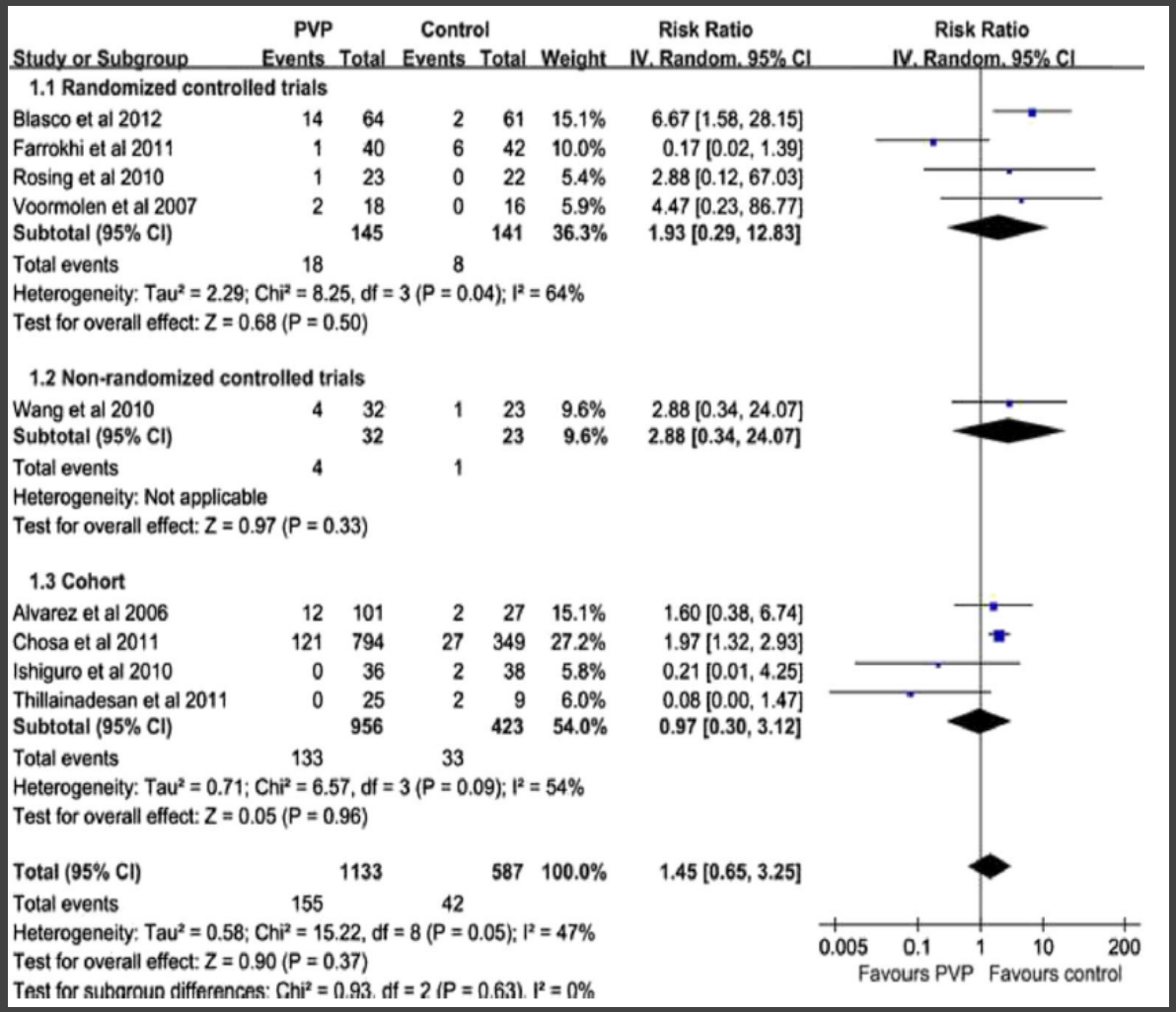


Han et al . OI 2014

Xie et al. Medicine 2016

Forest plot showing the association between percutaneous vertebroplasty and vertebral fracture.

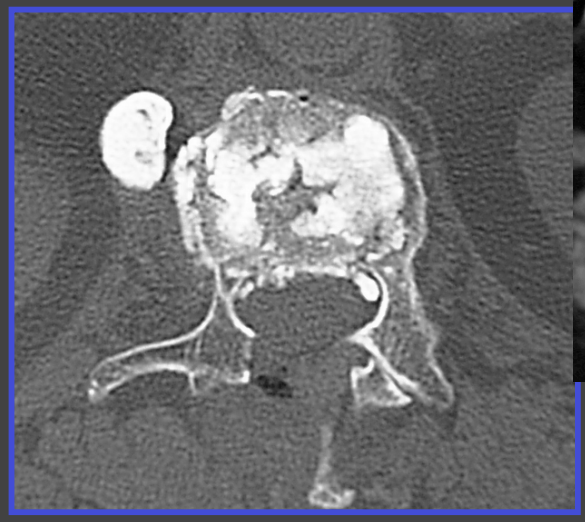
The combined RR demonstrated that PVP was not associated with increased risk of adjacent vertebral fracture



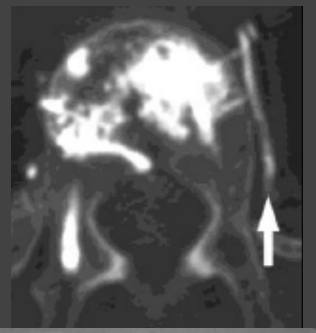
Dichotomous

Han et al . OI 2014

And what about the cement leaks



64. 8% of the scanner showed a cement leak



- All of these patients remained asymptomatic

- paravertebral vein 41 (25.8%)
- intervertebral disc 21 (13.2%)
- pulmonary system 7 (4%)

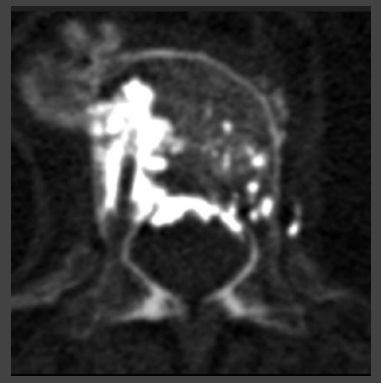
- no further complications during or after the procedure

Cement leak

ETUDES	TYPES D'ETUDE	% DE FUITE	EXAMEN D'EVALUATION DES FUITES
Heini et al *European Spine Journal 2000*	Prospective, non contrôlée	20	Radiographies
Yeom et al *The Journal of Bone and Joint Surgery 2003*	Rétrospective	63	Scanner et radiographies
Klazen et al (VERTOS II) *The Lancet 2010*	Prospective, randomisée, contrôlée et multicentrique	72	Scanner
Ding et al *European Spine Journal 2015*	Rétrospective	77,7	Scanner
Schmidt et al *European Spine Journal 2005*	Prospective, non contrôlée	81 34 48	Scanner Radiographies de face Radiographies de face et profil
STIC *2016*	**Prospective, randomisée, contrôlée et multicentrique**	**71,4**	**Scanner**

At least one leak of cement by the scanner for

- 85% of fractures classified Grade III according to annoying
- 66% for grade II
- 56% for grade I



(Grade 1, ~20-25%)

(Grade 2, ~25-40%)

(Grade 3, ~40%)

Cement leak

Discal leaks most often associated with height losses > 70%

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Predictors of Outcomes of Percutaneous Vertebroplasty for Osteoporotic Vertebral Fractures

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No influence of cement leakage on vertebroplasty results

VERTOS 2
Cement Pulmonary Embolism Risk

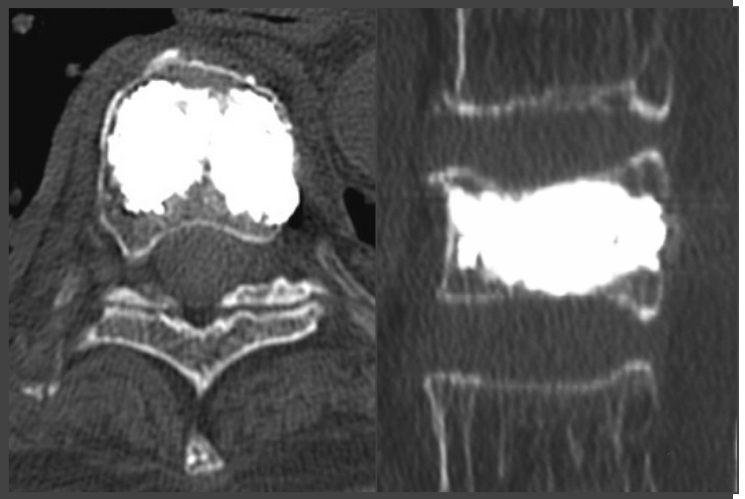
22-month follow-up of 54 patients of "Vertos"
CT to detect possible embolism.

14 pulmonary embolism (26%)
All patients were asymptomatic
The embolim were small and randomly distributed in small peripheral vessels
No changes in pulmonary parenchyma

Post-op CT or chest radiographs are not necessary in the follow up of VP

Venmans A, ***Klazen CA****, Mali WP.****AJNR Am J Neuroradiol****. **2010** Sep;31(8):1451-3.*

Conclusion



- Efficiency?
  - Not proven on fracture <6 weeks
  - Seem effective for fractures> 6 weeks
- Evolution of the spine
  - Decrease in the height of the vertebra -> protector
  - Fracture of other vertebrae -> no influence
- Complication : leaks-> Does not matter except for radicular pain