BoneCast

CSA Edition

Vertebroplasty in osteoporosis

Prof Bernard Cortet, Lille, France

IOF
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Osteoporosis
Foundation

Vertebroplasty in osteoporosis

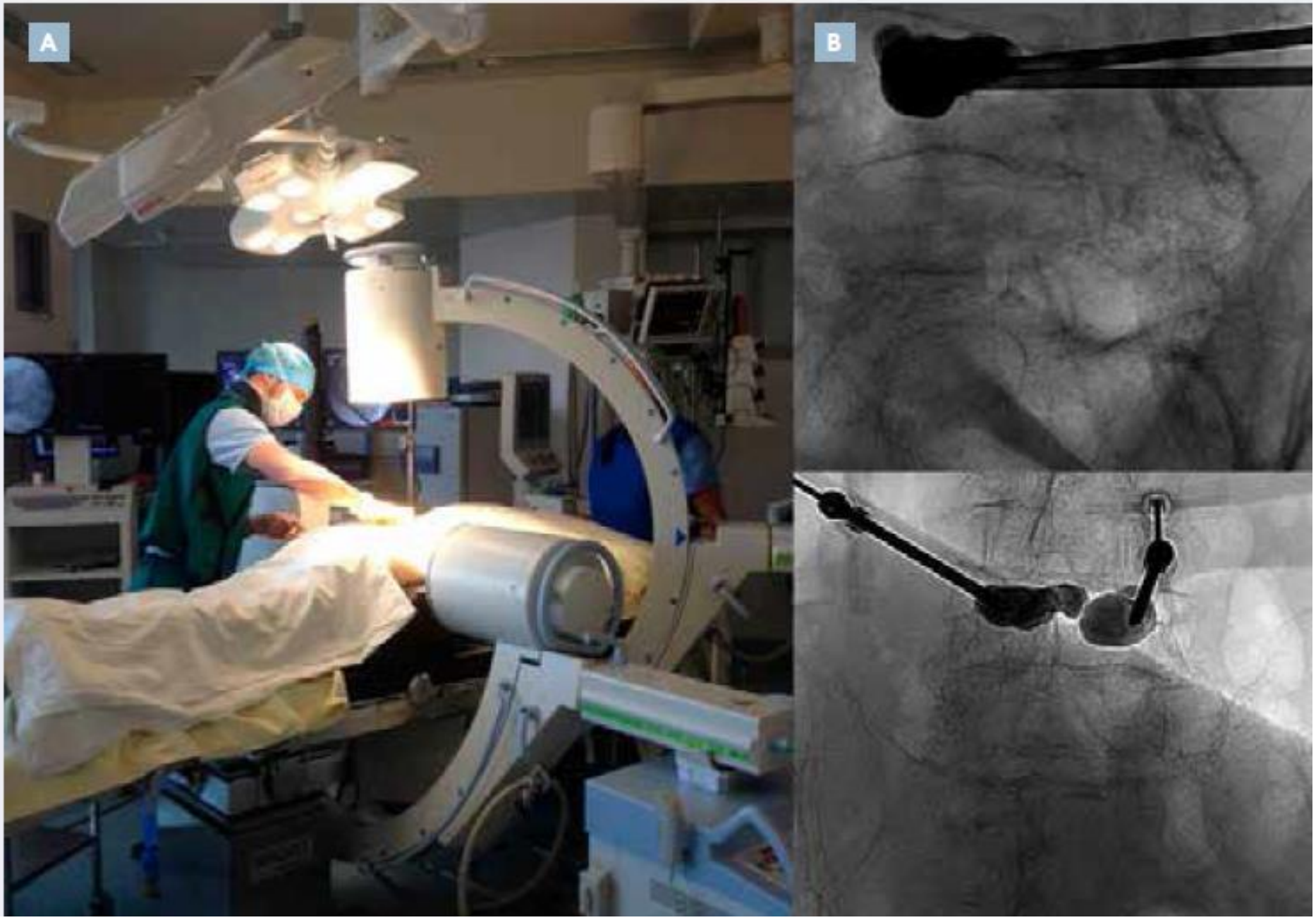
Bernard Cortet

Department of Rheumatology & ULR 4490
University-Hospital of Lille
59000 LILLE, France

Disclosures

Occasional interventions as an expert or speaker for

Alexion, Amgen, Expansience, Ferring, Kyowa-Kirin, Lilly, Mylan, MSD, Novartis, Theramex, UCB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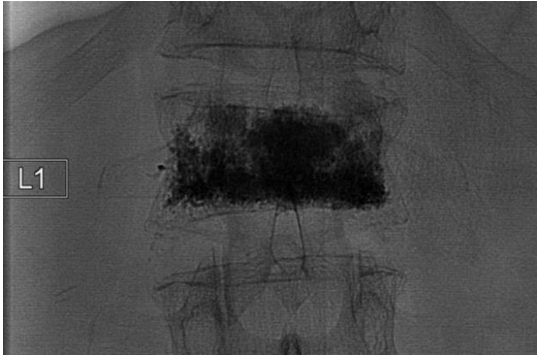
Introduction

Percutaneous vertebroplasty

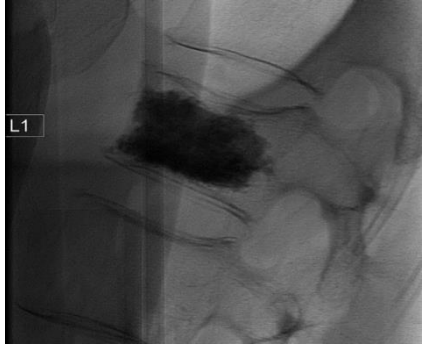
⇒ Cement injection (usually PMMA in the vertebral body)

⇒ Goals :

- To improve bone strength
- To decrease pain



Context



- ✓ Vertebroplasty (VP) has been commonly practiced for 30 years and yet the debate is still raging today in the field of osteoporossis
- ✓ VP was initialy developed by a French neuroradiologist Pr Hervé Deramond and a neurosurgeon, Pr Galibert for treating aggressive vertebral hemangiomas
- ✓ Due to the potential interest of VP therafter other indications have been proposed: bone metastases and VF due to osteoporosis
- ✓ My purpose will be to :
  - Present the main data from the literature
  - Express some reservations about "negative" studies
  - Explain "positive" studies by going beyond randomized studies.
  - Specify the place of the VP in the field of osteoporosis

The Efficacy and Safety of Vertebral Augmentation: A Second ASBMR Task Force Report

Peter R Ebeling,[1] Kristina Akesson,[2] Douglas C Bauer,[3] Rachelle Buchbinder,[4] Richard Eastell,[5] Howard A Fink,[6] Lora Giangregorio,[7] Nuria Guanabens,[8] Deborah Kado,[9] David Kallmes,[10] Wendy Katzman,[11] Alexander Rodriguez,[1] Robert Wermers,[12] H Alexander Wilson,[13] and Mary L Bouxsein[14]

[1]Department of Medicine, School of Clinical Sciences, Monash University, Melbourne, Australia
[2]Department of Clinical Sciences, Lund University, Malmö, Sweden
[3]Department of Medicine, University of California, San Francisco San Francisco CA, USA
[4]Department of Clinical Epidemiology, Cabrini Institute, and Department of Epidemiology and Preventive Medicine, School of Public Health and Preventative Medicine, Monash, Monash University, Melbourne, Australia
[5]Department of Human Metabolism, University of Sheffield, Sheffield, UK
[6]Veterans Affairs Medical Center, Geriatric Research Education and Clinical Center, and Department of Medicine, University of Minnesota, Minneapolis, MN, USA
[7]Department of Kinesiology and Schlegel Research Institute for Aging, University of Waterloo, Waterloo, Canada
[8]Department of Rheumatology, Hospital Clinic, University of Barcelona, Barcelona, Spain
[9]Department of Medicine, University of California, San Diego San Diego CA, USA
[10]Mayo Clinic, Rochester, MN, USA
[11]Department of Physical Therapy and Rehabilitation Science, University of California, San Francisco San Francisco CA, USA
[12]Division of Endocrinology, Mayo Clinic, Rochester, MN, USA
[13]Newport News, VA, USA
[14]Center for Advanced Orthopedic Studies, Beth Israel Deaconess Medical Center, Boston, MA, USA

Ebeling et al. JBMR 2019

ABSTRACT

Vertebral augmentation is among the current standards of care to reduce pain in patients with vertebral fractures (VF), yet a lack of consensus regarding efficacy and safety of percutaneous vertebroplasty and kyphoplasty raises questions on what basis clinicians should choose one therapy over another. Given the lack of consensus in the field, the American Society for Bone and Mineral Research (ASBMR) leadership charged this Task Force to address key questions on the efficacy and safety of vertebral augmentation and other nonpharmacological approaches for the treatment of pain after VF. This report details the findings and recommendations of this Task Force. For patients with acutely painful VF, percutaneous vertebroplasty provides no demonstrable clinically significant benefit over placebo. Results did not differ according to duration of pain. There is also insufficient evidence to support kyphoplasty over nonsurgical management, percutaneous vertebroplasty, vertebral body stenting, or KIVA®. There is limited evidence to determine the risk of incident VF or serious adverse effects (AE) related to either percutaneous vertebroplasty or kyphoplasty. No recommendation can be made about harms, but they cannot be excluded. For patients with painful VF, it is unclear whether spinal bracing improves physical function, disability, or quality of life. Exercise may improve mobility and may reduce pain and fear of falling but does not reduce falls or fractures in individuals with VF. General and intervention-specific research recommendations stress the need to reduce study bias and address methodological flaws in study design and data collection. This includes the need for larger sample sizes, inclusion of a placebo control, more data on serious AE, and more research on nonpharmacologic interventions. Routine use of vertebral augmentation is not supported by current evidence. When it is offered, patients should be fully informed about the evidence. Anti-osteoporotic medications reduce the risk of subsequent vertebral fractures by 40–70%. © 2018 American Society for Bone and Mineral Research.

Ebeling et al. JBMR 2019

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Editorial

Plea for continuing but rational use of vertebroplasty for osteoporotic vertebral fractures

Bernard Cortet[a,*]
Patrick Chastanet[b]
Jean-Denis Laredo[c]
[a] *Service de Rhumatologie et EA 4490, CHU Lille et Université de Lille, 59000 Lille, France*

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.

Methods

- Pain < 12 months
- One or two recent vertebral fractures
- Genant classification ≥ grade 1
- MRI: Fracture, bone edema, or both.
- Vertebroplasty vs. sham procedure: introduction of the needle up to the blade.
- **Main criterion:**
  - Evolution of VAS at 3M
- **Secondary criteria:**
  - VAS D7and 6M
  - Qualeffo (41 items)
  - AQoL
  - EQ-5D
  - VAS resting and nocturnal pain
  - Questionnaire by 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)

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)	

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A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures

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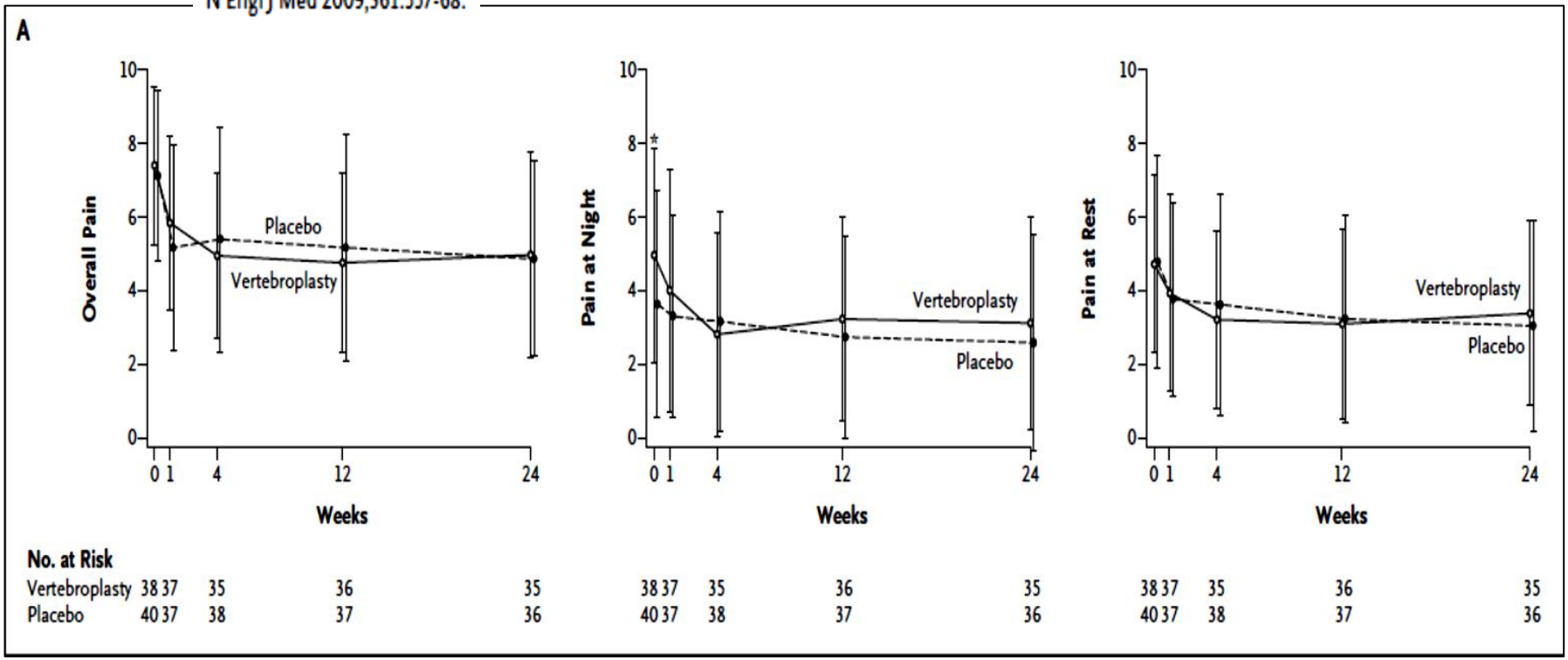
N Engl J Med 2009;361:557-68.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures

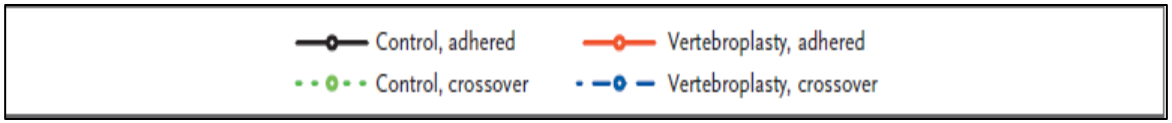
David F. Kallmes, M.D., Bryan A. Comstock, M.S., Patrick J. Heagerty, Ph.D., Judith A. Turner, Ph.D., David J. Wilson, F.R.C.R., Terry H. Diamond, F.R.A.C.P., Richard Edwards, F.R.C.R., Leigh A. Gray, M.S., Lydia Stout, B.S., Sara Owen, M.Sc., William Hollingworth, Ph.D., Basavaraj Ghdoke, M.D., Deborah J. Annesley-Williams, F.R.C.R., Stuart H. Ralston, F.R.C.P., and Jeffrey G. Jarvik, M.D., M.P.H.

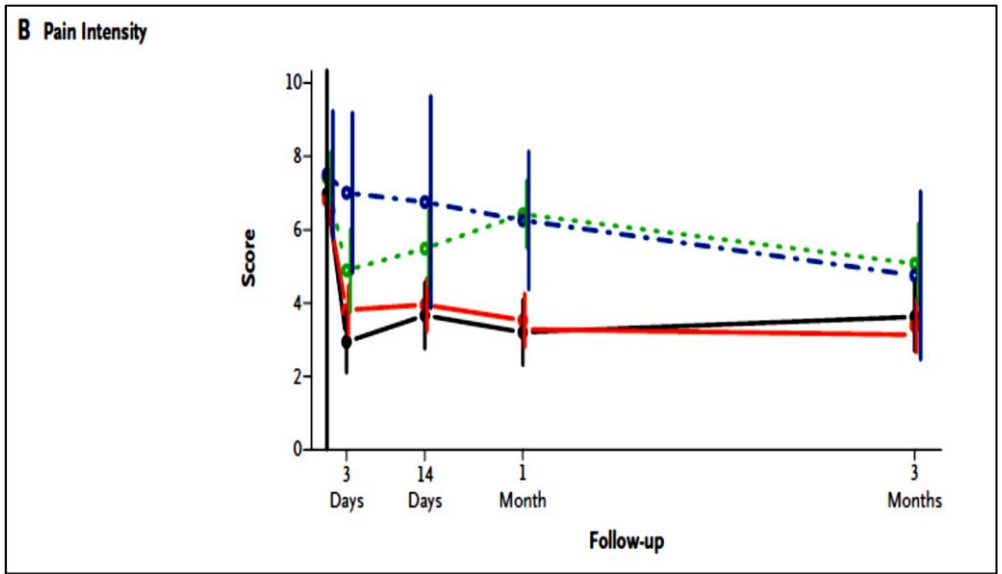
N Engl J Med 2009;361:569-79.

- Spinal pain < 12 months (126 days)
- 1 to 3 recent painful VFs
- VAS inclusion > 3 (VAS baseline = 7)
- MRI+ or bone scan+ in case of uncertainty about the age FV
- Sham procedure for controls

- Primary endpoint: pain on VAS at 1 month.

- 1813 eligible → 68 VP and 63 SP
  → 67 VP and 61 SP at 1 month





Comments about the 2 studies of the NEJM

- ✓ Small sample size
- ✓ Duration of pain, sometimes prolonged (up to 1 year)
- ✓ Not always indisputable signs of recent fracture
- ✓ Low level of pain in one of the 2 studies
- ✓ Sham procedure = it's not a real placebo (use of a local anesthetic)

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

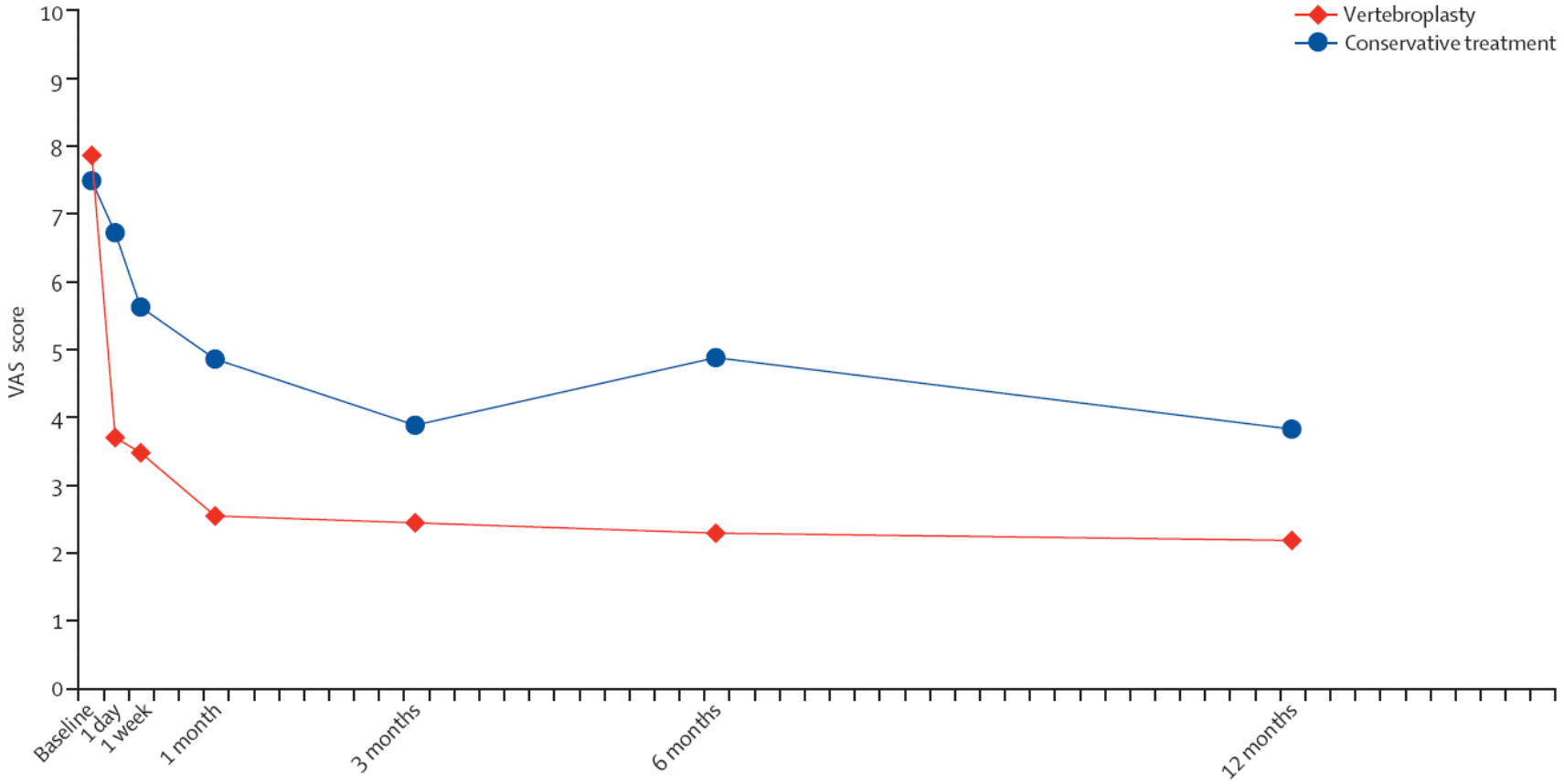
	Percutaneous vertebroplasty (n=101)	Conservative treatment (n=101)
Age (years)	75·2 (9·8)	75·4 (8·4)
Sex (female)	70 (69%)	70 (69%)
Duration of back pain (days)	29·3 (17·1)	26·8 (16·0)
Initial VAS score	7·8 (1·5)	7·5 (1·6)
Number of VCFs at baseline	2·4 (1·9)*	2·1 (1·5)*
Number and grading of VCFs with 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**

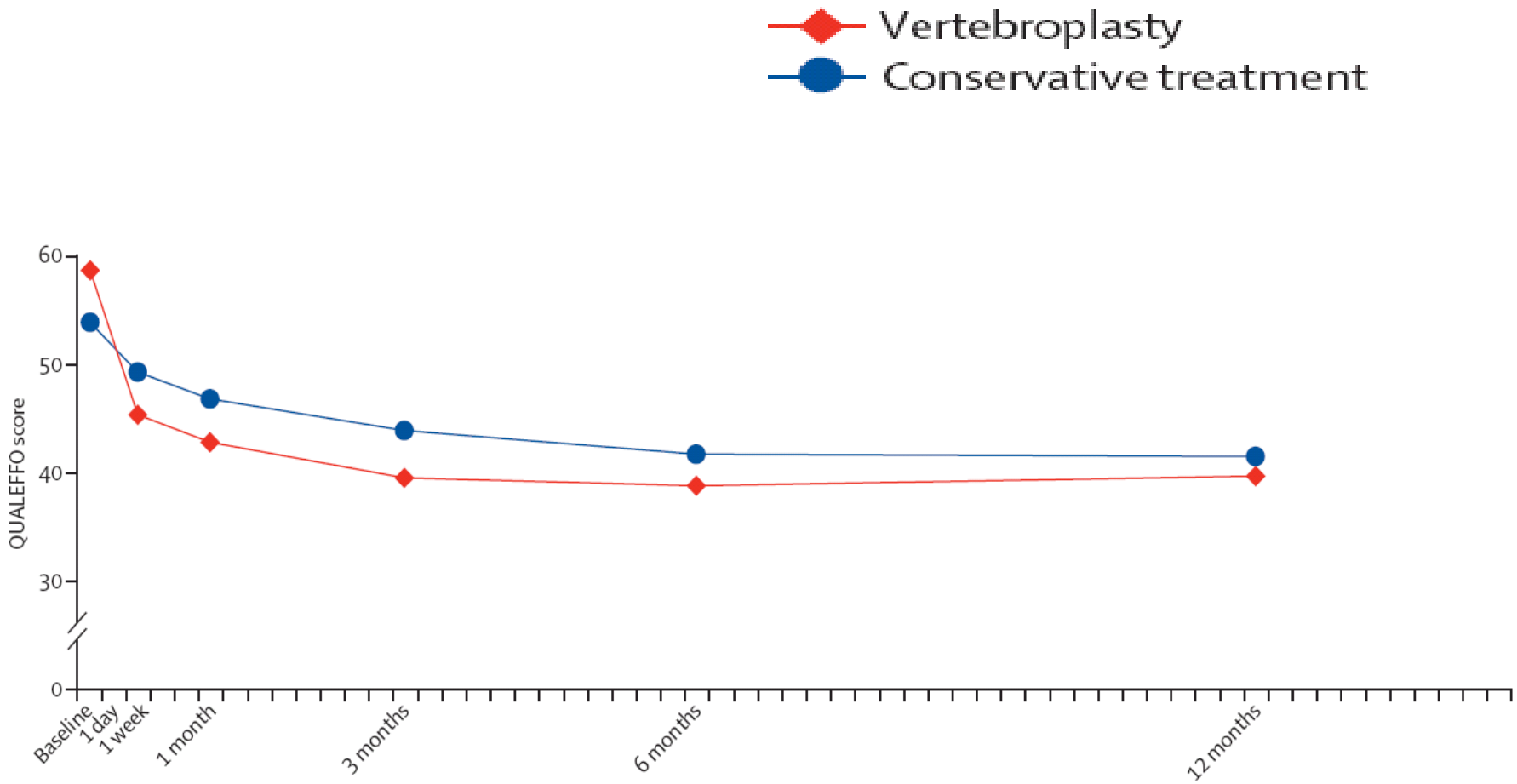
Pain ≥ 5 on VAS
MRI: bone edema on T2 weighted pictures

Klazen et al. Lancet 2010



VAS score

Klazen et al. Lancet 2010



Qualeffo score

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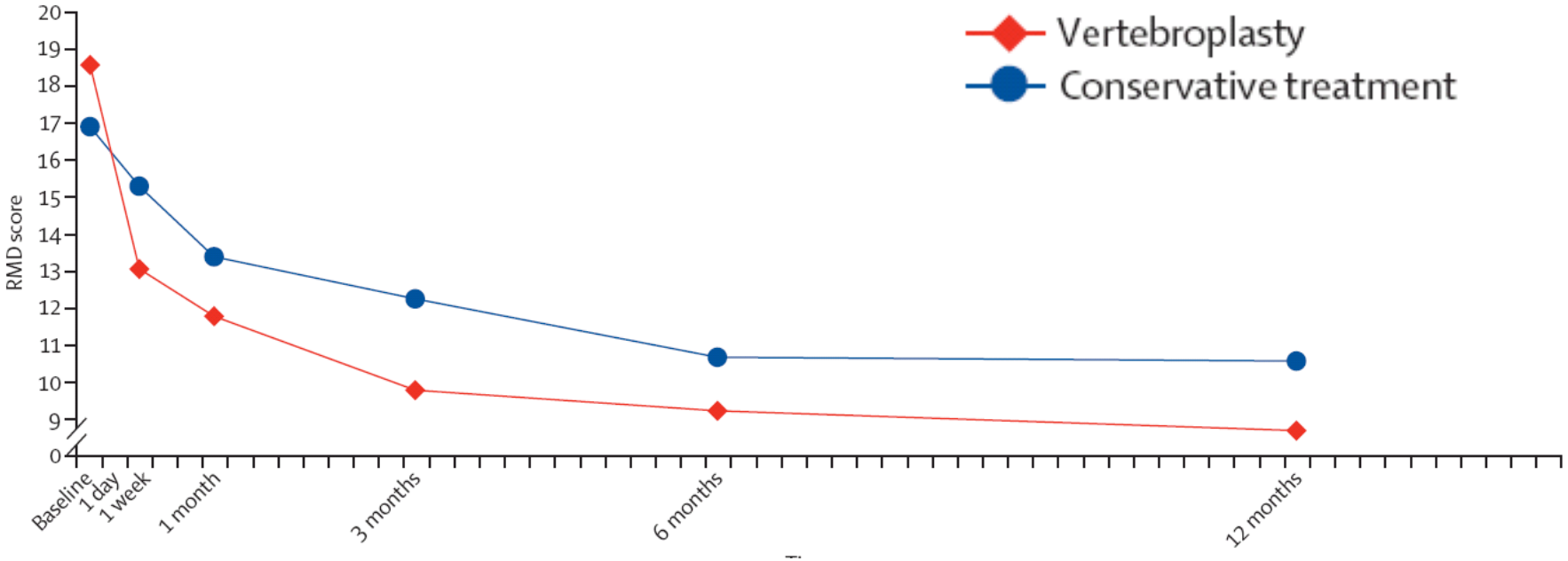


RMD score

Klazen et al. Lancet 2010

Randomized study VP vs sham procedure

- ✓ Inclusion criteria
  - ✓ NRS > 7
  - ✓ Pain < 6 weeks
- ✓ Main criterion for evaluation:
  - ✓Nb of patients with pain on NRS ≤ 4 at D 14

VAPOUR STUDY CLARCK et al. Lancet 2016

	Vertebroplasty (n=61)	Placebo (n=59)
Age (years)	80 (7)	81 (7)
Sex		
Male	13 (21%)	19 (32%)
Female	48 (79%)	40 (68%)
Hospital inpatient	34 (56%)	34 (58%)
Previous osteoporotic fractures	36 (62%)	32 (54%)
Medications for osteoporosis		
Any	48 (79%)	51 (86%)
Calcium or vitamin D	41 (70%)	48 (81%)
Bisphosphonates	29 (49%)	21 (36%)
Bone mineral density (T score)		
Lumbar spine	−4·1 (1·1)	−4·5 (0·9)
Femoral neck	−2·2 (0·7)	−2·2 (1·0)
Serum vitamin D (nmol/L)	70 (27)	73 (22)
Duration of fracture		
Mean (SD; weeks)	2·8 (1·6)	2·4 (1·4)
1–3 weeks	47 (77%)	48 (81%)
4–6 weeks	14 (23%)	11 (19%)
Spinal segment of fracture		
Thoracic (T4–T10)	19 (31%)	16 (27%)
Thoracolumbar (T11–L2)	37 (61%)	36 (61%)
Lumbar (L3–L5)	7 (12%)	10 (17%)
Vertebral body height loss (percentage points)	47 (15)	46 (15)
Genant grade (standing)		
Grade 1	3 (5%)	8 (14%)
Grade 2	13 (21%)	12 (20%)
Grade 3	45 (74%)	39 (66%)
Number of vertebral bodies treated		
1	51 (84%)	53 (90%)
2	10 (16%)	6 (10%)
Opioids for pain	53 (87%)	53 (90%)
Pain intensity during previous 24 h		
NRS score	8·6 (1·3)	8·6 (1·2)
VAS score	81 (18)	82 (15)
RDQ score	19·5 (3·5)	19·8 (3·7)
EQ-5D score	0·60 (0·07)	0·59 (0·06)
QUALEFFO score	65·4 (11·4)	67·7 (11·2)
Timed up-and-go score	26 (14)	29 (15)

Data are n (%) or mean (SD). Bone mineral density T score measured by quantitative computed tomography. NRS=Numeric Rating Scale pain. VAS=Visual Analogue Scale pain. RDQ=Roland-Morris Disability Questionnaire. EQ-5D=EuroQol five dimensions questionnaire. QUALEFFO=Quality of Life questionnaire of the European Foundation for Osteoporosis.

EVAPOUR STUDY CLARCK et al. Lancet 2016

	Vertebroplasty		Placebo		Difference (95% CI)	p value
	N	n (%) or mean (SD)	N	n (%) or mean (SD)		
Proportion of patients with NRS pain score <4						
3 days	58	18 (31%)	55	5 (9%)	22 (8 to 36)	0·004
14 days*	55	24 (44%)	57	12 (21%)	23 (6 to 39)	0·011
1 month	55	28 (51%)	57	10 (18%)	33 (17 to 50)	0·0002
3 months	53	29 (55%)	52	17 (33%)	22 (4 to 41)	0·023
6 months	51	35 (69%)	51	24 (47%)	22 (3 to 40)	0·027
Reduction in NRS pain score						
3 days	58	3·5 (2·6)	55	1·8 (2·3)	1·8 (0·8 to 2·7)	0·0003
14 days	55	4·2 (2·7)	57	3·0 (3·0)	1·2 (0·1 to 2·3)	0·026
1 month	55	4·6 (3·0)	57	3·2 (2·7)	1·4 (0·4 to 2·5)	0·010
3 months	53	5·4 (3·5)	52	4·1 (3·1)	1·3 (0 to 2·6)	0·047
6 months	51	6·1 (3·3)	51	4·8 (3·1)	1·3 (0 to 2·6)	0·043
Reduction in RDQ score						
3 days	58	4·5 (6·2)	55	2·9 (4·4)	1·6 (−0·4 to 3·6)	0·111
14 days	53	5·9 (5·8)	56	4·1 (6·3)	1·8 (−0·5 to 4·1)	0·121
1 month	55	6·9 (6·0)	54	4·3 (5·6)	2·6 (0·4 to 4·8)	0·021
3 months	53	9·6 (7·7)	50	6·4 (7·0)	3·2 (0·3 to 6·1)	0·031
6 months	49	11·7 (6·5)	51	7·4 (6·9)	4·2 (1·6 to 6·9)	0·0022
VAS pain score (patient reported)						
14 days	41	39 (28)	47	49 (28)	10 (−2 to 22)	0·096
6 months	42	23 (26)	46	34 (27)	11 (0 to 23)	0·050
VAS pain score (researcher observed)						
14 days	41	25 (23)	48	39 (29)	14 (3 to 26)	0·015
6 months	39	14 (21)	46	19 (20)	5 (−4 to 13)	0·301
QUALEFFO score						
14 days	48	49 (13)	54	55 (14)	6 (1 to 11)	0·029
1 month	48	49 (17)	52	52 (15)	4 (−3 to 10)	0·255
6 months	46	38 (15)	48	45 (16)	7 (1 to 13)	0·032
EQ-5D score						
3 days	58	0·69 (0·11)	52	0·65 (0·09)	−0·03 (−0·07 to 0·05)	0·091
14 days	49	0·69 (0·10)	56	0·68 (0·11)	−0·01 (−0·06 to 0·03)	0·471
1 month	47	0·75 (0·11)	51	0·70 (0·11)	−0·05 (−0·09 to 0)	0·043
3 months	51	0·75 (0·12)	49	0·71 (0·11)	−0·03 (−0·08 to 0·01)	0·164
6 months	47	0·80 (0·11)	50	0·74 (0·12)	−0·06 (−0·10 to −0·01)	0·012
Analgesic use						
3 days	59	57 (97%)	57	56 (98%)	2 (−4 to 7)	0·579
14 days	56	49 (88%)	57	52 (91%)	4 (−8 to 15)	0·520
1 month	55	41 (75%)	57	50 (88%)	13 (−1 to 28)	0·074
3 months	53	34 (64%)	53	44 (83%)	19 (2 to 35)	0·028
6 months	50	29 (58%)	51	39 (76%)	18 (1 to 36)	0·048

Data presented as mean (SD) were normally distributed. NRS=Numeric Rating Scale pain. RDQ=Roland-Morris Disability Questionnaire. VAS=Visual Analogue Scale pain. QUALEFFO=Quality of Life questionnaire of the European Foundation for Osteoporosis. EQ-5D=EuroQol five dimensions questionnaire. *Primary endpoint was the proportion of patients with an NRS pain score less than 4 at 14 days.

Table 2: Primary and secondary outcomes

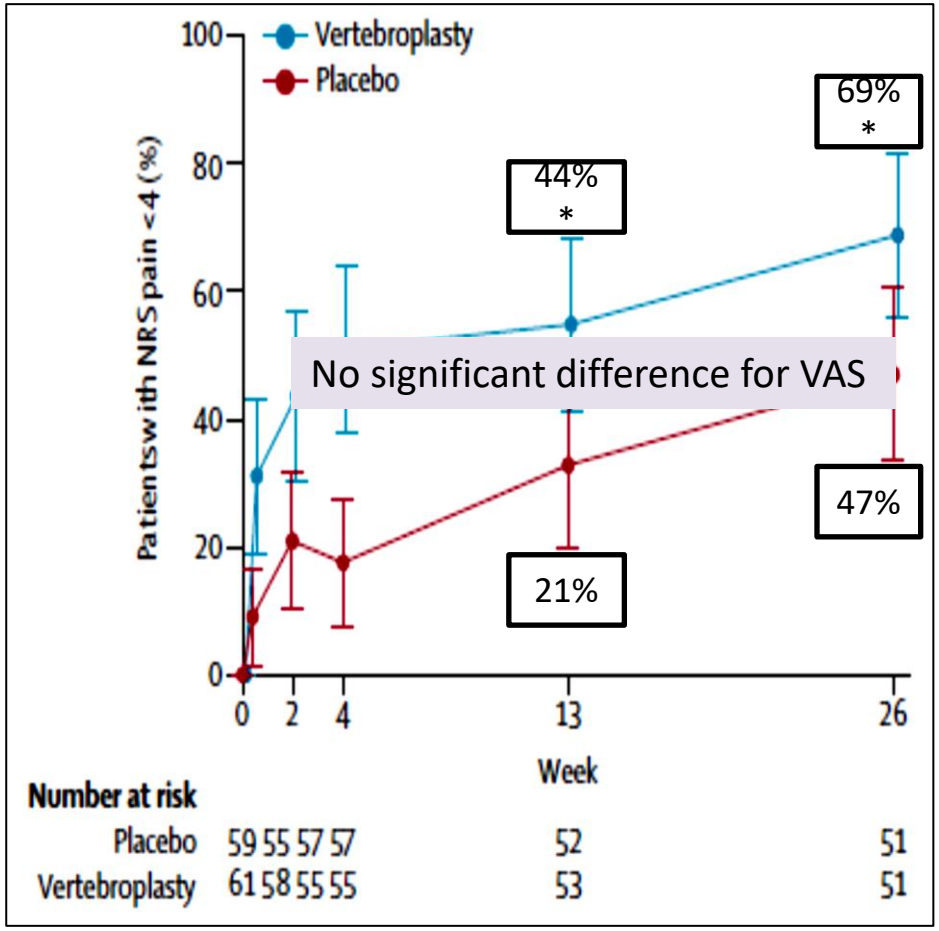
VAPOUR SUTDY – CLARCK et al. LANCET 2016

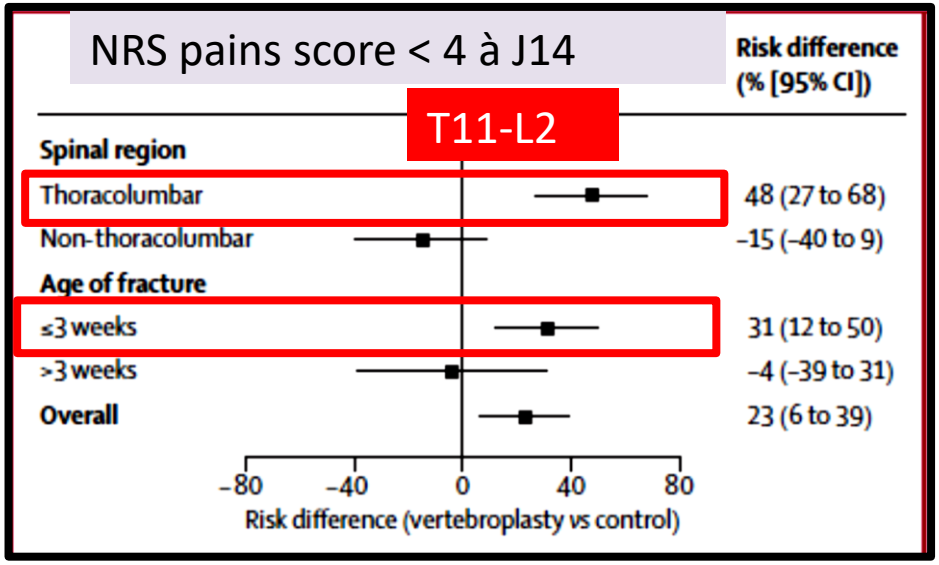
Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial

William Clark, Paul Bird, Peter Gonski, Terrence H Diamond, Peter Smerdely, H Patrick McNeil, Glen Schlaphoff, Carl Bryant, Elizabeth Barnes, Val Gebski

Lancet 2016; 388: 1408-16

- Spinal pain < 6 weeks (18.2 d)
- 1 to 2 recent VFs
- Numeric Rated Scale (NRS) pain score inclusion ≥ 7/10
- NRS = 8.6
- MRI+ SCAN
- Sham procedure for controls
- But, no cement smell and no periosteal contact.
- Main Criterion: NRS < 4 at D14
- 302 eligible → 61 VP and 59 SP
  → 55 VP and 57 SP at 14





Vertebroplasty versus sham procedure for painful acute osteoporotic vertebral compression fractures (VERTOS IV): randomised sham controlled clinical trial

Cristina E Firanescu,[1] Jolanda de Vries,[1,2] Paul Lodder,[2] Alexander Venmans,[1] Marinus C Schoemaker,[1] Albert J Smeet,[1] Esther Donga,[1] Job R Juttmann,[1] Caroline A H Klazen[3] Otto E H Elgersma,[4] Frits H Jansen,[5] Alexander V Tielbeek,[5] Issam Boukrab,[1] Karen Schonenberg,[1] Willem Jan J van Rooij,[1] Joshua A Hirsch,[6] Paul N M Lohle[1]

BMJ 2018;361:k1551 | doi: 10.1136/bmj.k1551

- Spinal pain ≤ 6 weeks then 9 weeks (39d)
- 1 to 3 recent painful VFs
- VAS inclusion ≥ 5
- Mean VAS at baseline = 7.8
- MRI+ SCAN
- Sham procedure for controls
- Primary endpoints: VAS pain at 1 week, 3 months and 12 months
- Secondary endpoints:
  - functional analysis measured on the modified Roland Morris scale (RMD), quality of life (QOL) measured with the QUALEFFO
  - Analgesics, secondary fractures, early and late complications
- 1280 eligible → 91 VP and 89 PCB
  → 90 VP and 86 PCBs at 12 months

Firanescu et al. BMJ 2018

Table 1 | Baseline characteristics of participants. Values are numbers (percentages) unless stated otherwise

Characteristics	Vertebroplasty (n=90)	Sham procedure (n=86)
Mean (SD) age (years)	74.7 (10.7)	76.9 (8.1)
Women	67 (74)	66 (77)
Median (interquartile range) No of days with back pain before procedure	43 (29-52)	36 (24-51)
Median (interquartile range) No of days from radiographic diagnosis to procedure	13 (7-18)	11 (7-17)
No of vertebral compression fractures at baseline	115	108
Type of fracture (Genant classification)*:		
Mild (20-25%)	37 (32)	30 (28)
Moderate (25-40%)	51 (44)	49 (45)
Severe (>40%)	27 (23)	30 (28)
Wedge	56 (49)	65 (60)
Biconcave	59 (51)	44 (40)
Initial pain treatment:		
None	4 (4)	8 (9)
Non-opioid drugs	78 (87)	65 (76)
Weak opioid derivatives	13 (14)	17 (20)
Strong opioid derivatives	42 (47)	25 (29)
Vertebral level with bone oedema:		
T5–T10	36 (31)	24 (22)
T11–L2	59 (51)	69 (64)
L3–L5	20 (17)	15 (14)
No of spinal levels treated†:		
1	70 (78)	67 (78)
2	15 (17)	15 (17)
3	5 (6)	4 (5)
Drugs for osteoporosis	42 (47)	49 (57)
Osteonecrosis	24 (27)	17 (20)
Mean (SD) bone density T score	−2.4 (1.0)	−2.4 (0.9)
Mean (SD) initial VAS score‡	7.7 (1.4)	7.9 (1.6)
Mean (SD) QUALEFFO score§	68.4 (17.1)	69.7 (17.9)

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Main Evaluation Criteria

Table 2 | Mean visual analogue scale (VAS) scores for vertebroplasty and sham procedure groups at each time point

	Mean VAS scores (95% CI)*		
Time points	Vertebroplasty (n=90)	Sham procedure (n=86)	Group difference†
Baseline	7.72 (7.21 to 8.24)	7.92 (7.40 to 8.45)	0.20 (−0.53 to 0.94)
1 day	5.24 (4.73 to 5.76)	4.82 (4.29 to 5.34)	−0.43 (−1.17 to 0.31)
1 week	4.38 (3.86 to 4.90)	4.27 (3.74 to 4.79)	−0.11 (−0.85 to 0.63)
1 month	3.32 (2.80 to 3.84)	3.73 (3.20 to 4.26)	0.41 (−0.33 to 1.15)
3 months	2.69 (2.16 to 3.21)	2.90 (2.35 to 3.44)	0.21 (−0.54 to 0.96)
6 months	3.02 (2.48 to 3.55)	3.41 (2.86 to 3.96)	0.39 (−0.37 to 1.15)
12 months	2.72 (2.18 to 3.26)	3.17 (2.60 to 3.75)	0.45 (−0.37 to 1.24)
Difference between baseline and 12 months	5.00 (4.31 to 5.70)	4.75 (3.93 to 5.57)	0.13 (−0.41 to 0.66)

Average pain scores for each group are similar

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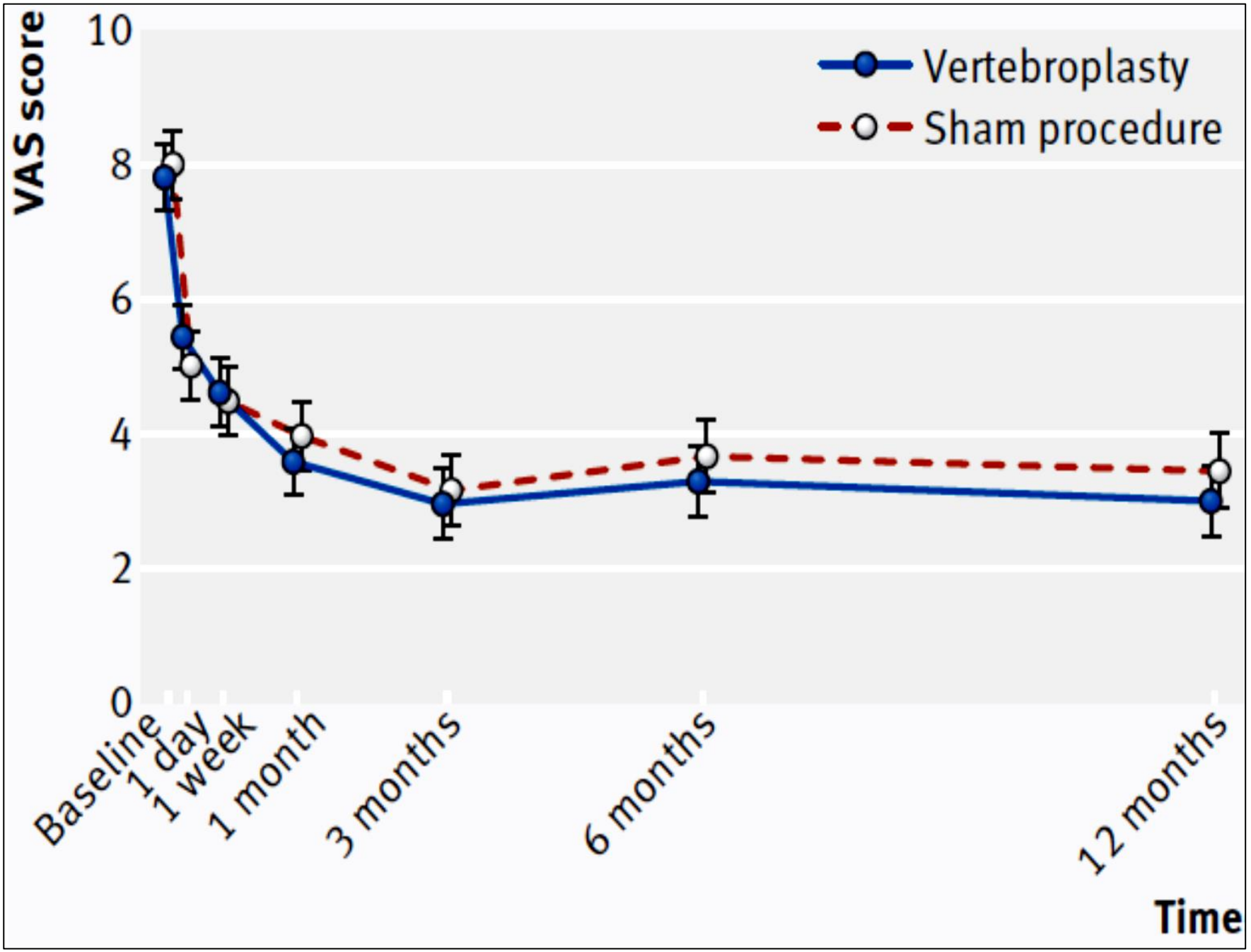

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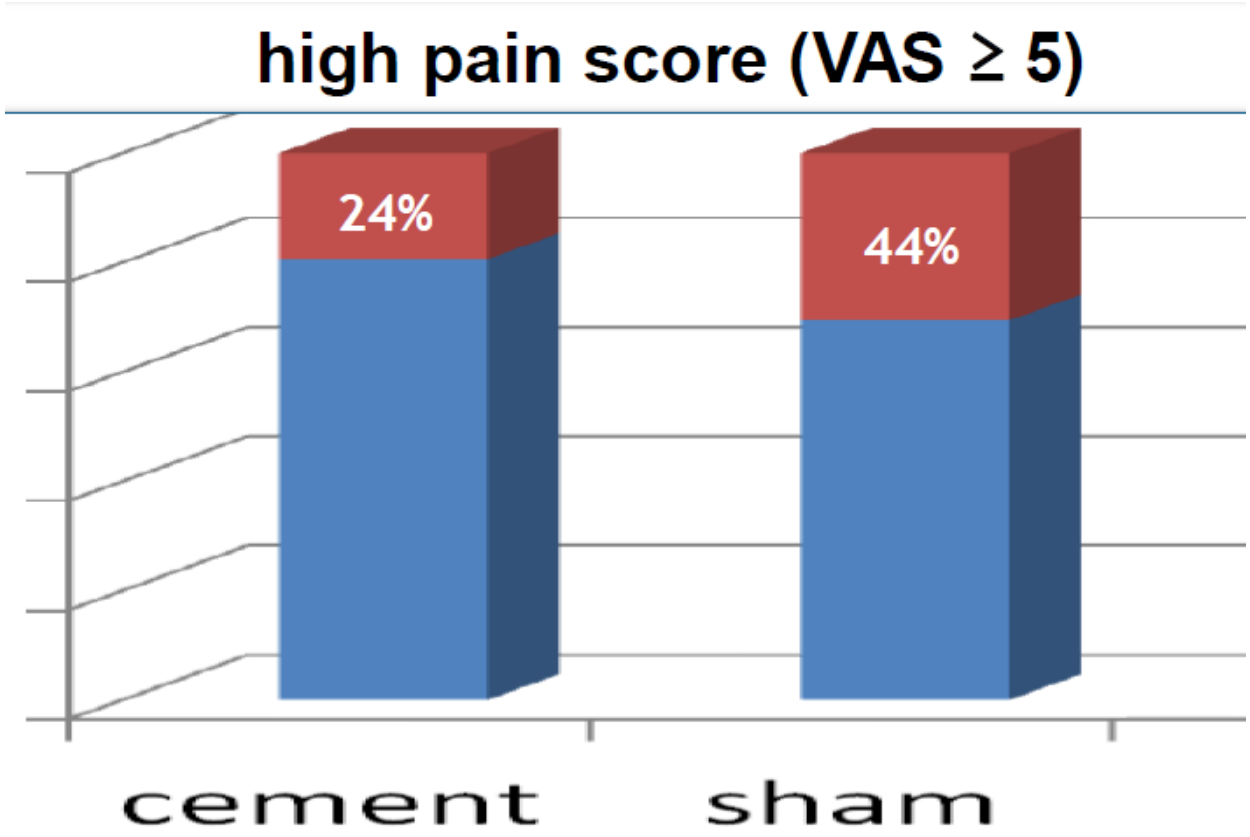
Secondary analyses

Subgroup analysis shows a higher % of patients in the control group with a VAS ≥ 5 to 12 months (P = 0. 009)



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Differences between the study by Clarck and Finaranescu

- The mean age was older in the study by Clarck
- A majority of patients from the study by Clarck were hospitalized for vertebral fracture whereas all the patients from the study of Finarescu were outpatients
- The level of pain at baseline was higher in the study by Clark
- The sham procedure was not the same into the 2 studies

Clarck et al. Lancet 2016
Firanescu et al. BMJ 2018

NIH U.S. National Library of Medicine

ClinicalTrials.gov

A Trial of Vertebroplasty for Painful Chronic Osteoporotic Vertebral Fractures :

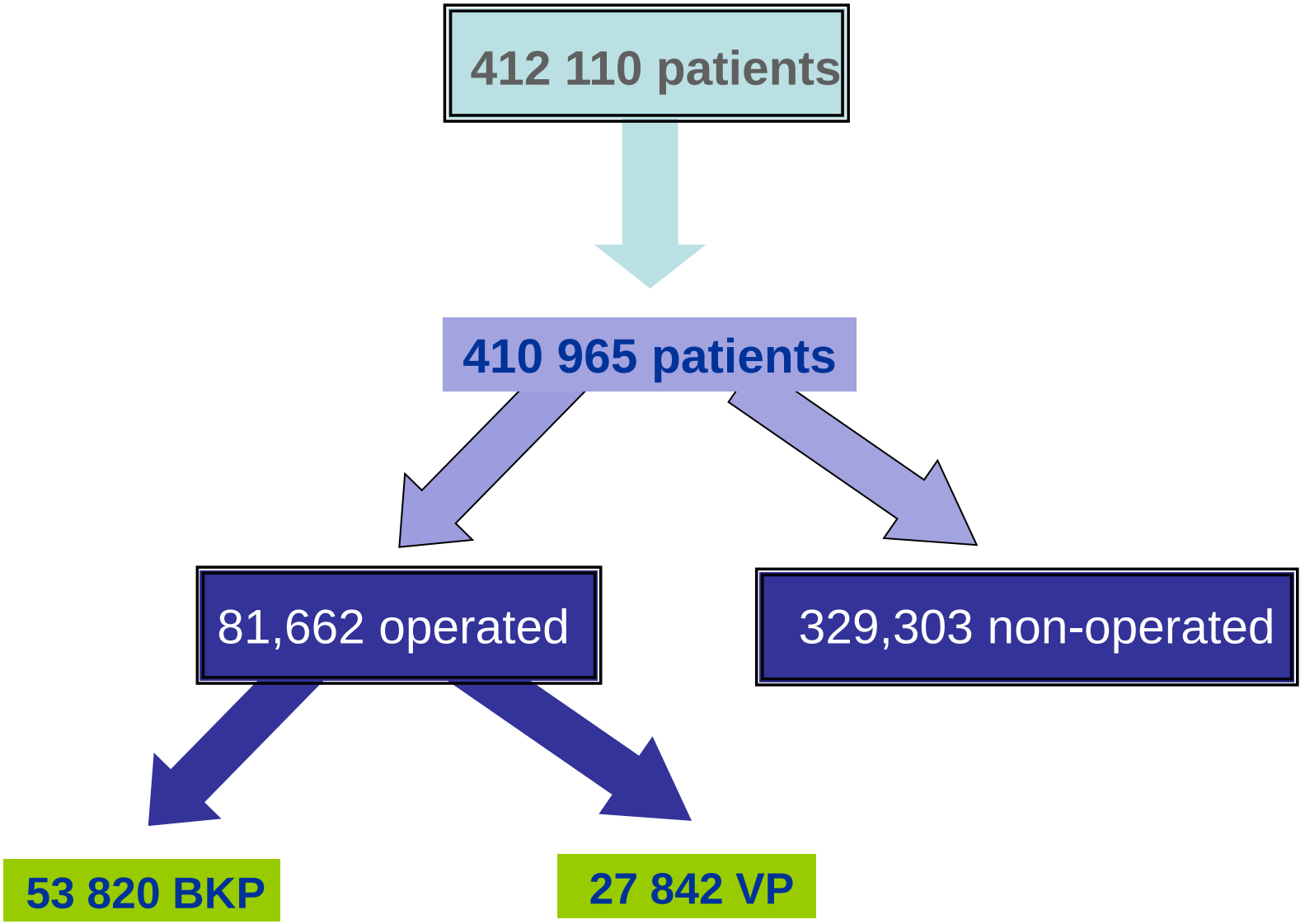
VERTOS V

- Objective To compare pain **relief after PV** with a **sham intervention** in selected **patients with a chronic osteoporotic VCF** (three months or longer) using the same strict inclusion criteria as in VERTOS II an IV. Secondary outcome measures are back pain related disability and quality of life.
- Methods The VERTOS V study is a **prospective RCT with pain relief as primary endpoint**. Inclusion criteria are a VCF of thoracic level 5 or lower with focal tenderness at fracture level, assessed by an internist on physical examination and a Visual Analogue Scale (VAS) score ≥ 5 for three months or longer, decreased bone density defined as T score ≤ -1 and age 50 years or older. 94 patients will be included, 47 in each arm. **Crossovers are not allowed**. Follow-up is at regular intervals during one year period with VAS score for pain as primary endpoint. Secondary endpoints are back pain related disability and quality of life measured with the Quality of Life Questionnaire of the European Foundation for Osteoporosis and physical function measured with the Roland Morris Disability questionnaire.

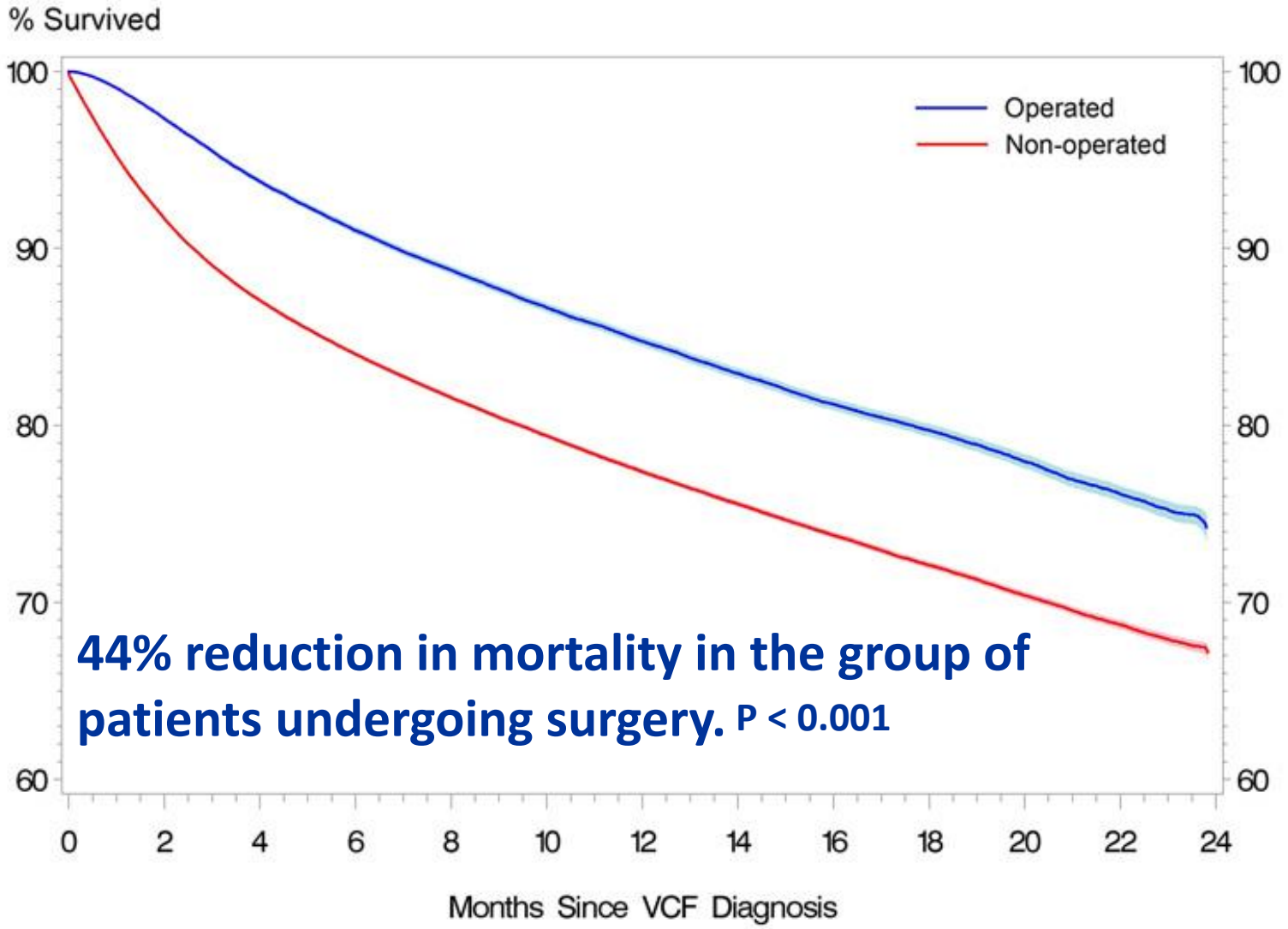
Mortality of operated (kyphoplasty/vertebroplasty) versus non-operated patients in non-traumatic vertebral fractures (NVTF): about a cohort of 410,965 patients

Eddidin et al JBMR 2011

Number of patients



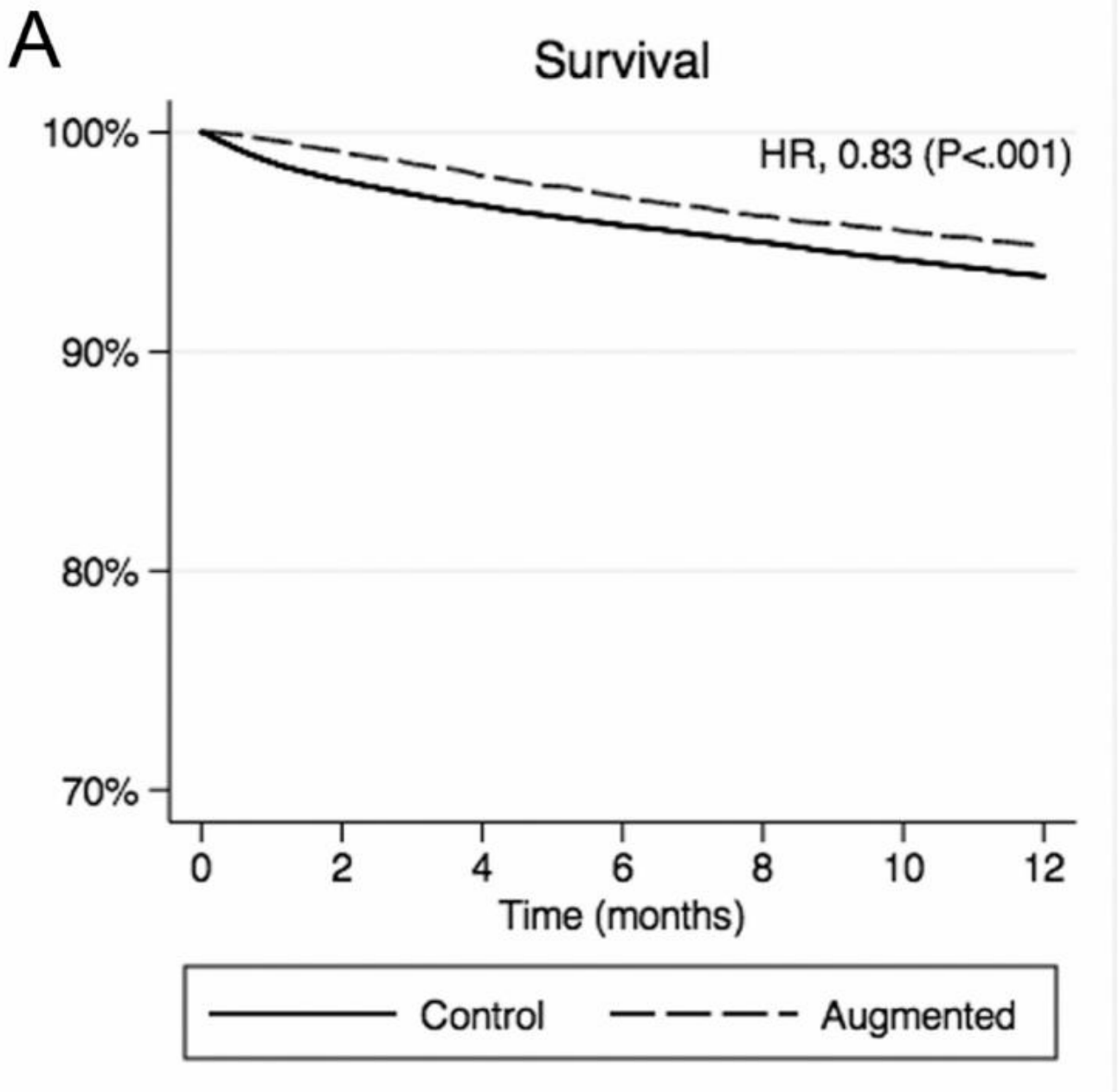
Crude survival: comparison of operated and non-operated patients



44% reduction in mortality in the group of patients undergoing surgery. $P < 0.001$

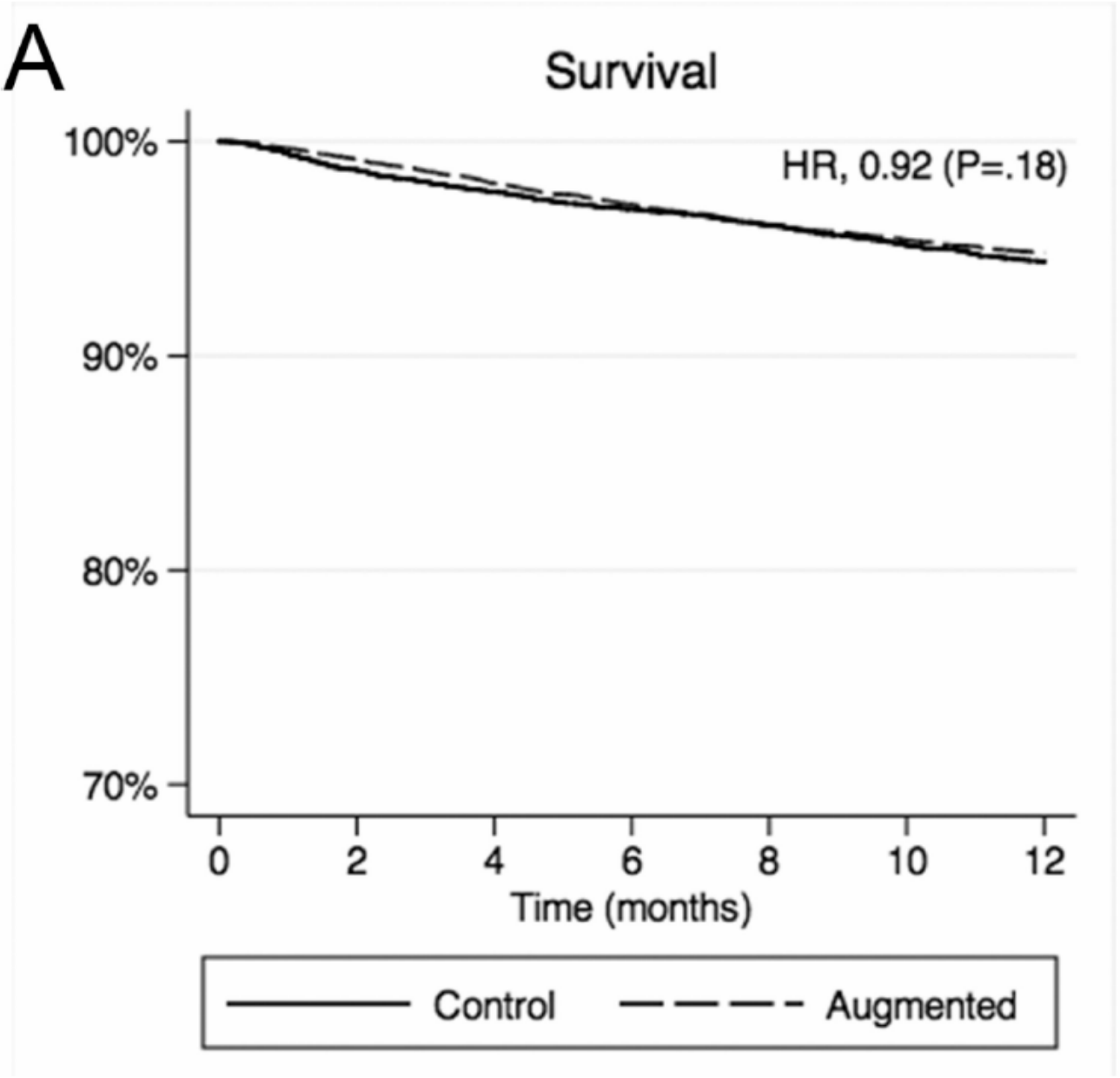
Eddidin et al JBMR 2011

Retrospective study: 20% MEDICARE 2002-2006



McCullough et al.
JAMA Intern Med 2013

Retrospective study: 20% MEDICARE 2002-2006



McCullough et al.
JAMA Intern Med 2013

Retrospective study: 100% MEDICARE 2005-2014

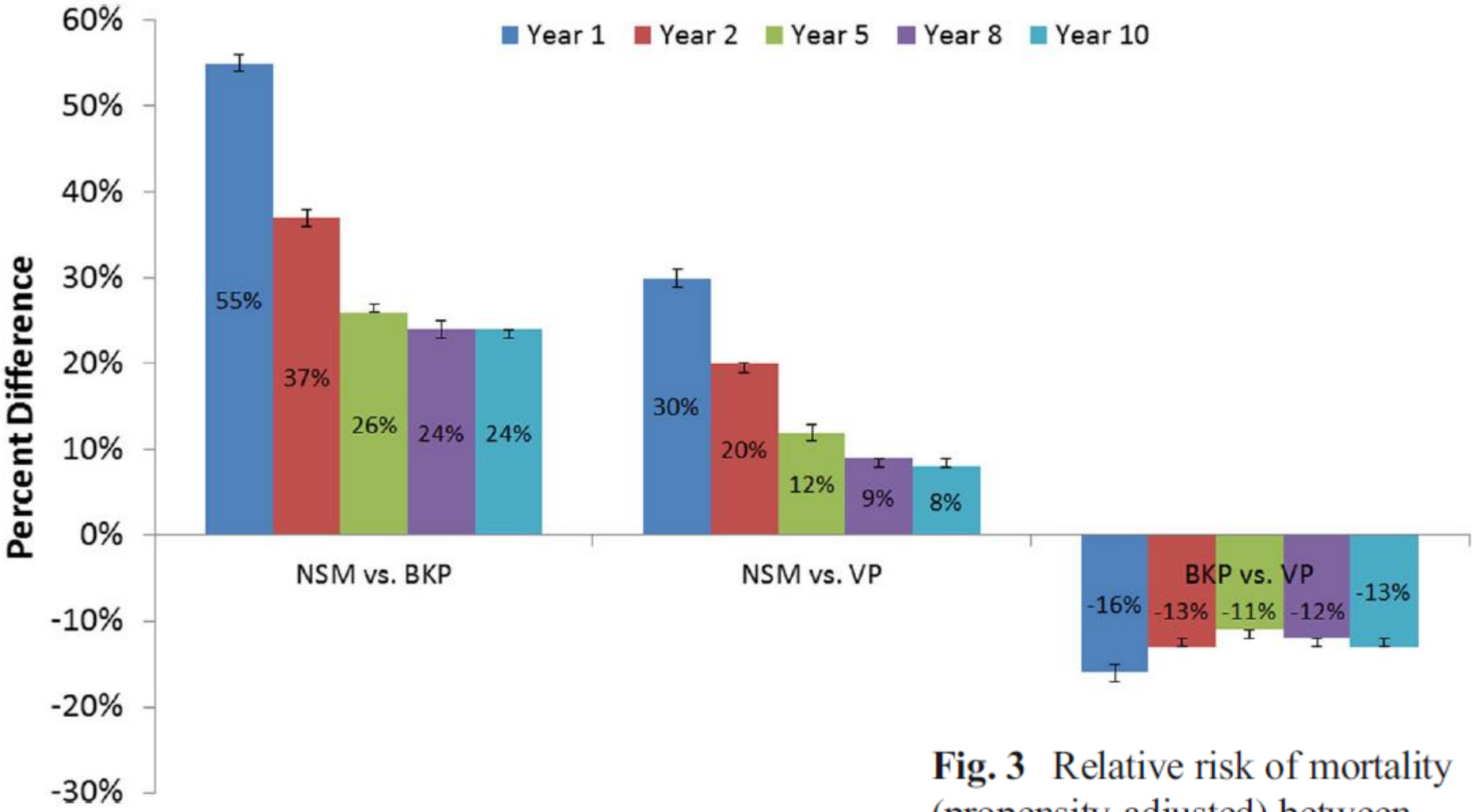


Fig. 3 Relative risk of mortality (propensity-adjusted) between NSM, BKP, and VP cohorts ($p < 0.001$ for all)

Ong et al. OI 2018

Retrospective study: 100% MEDICARE 2005-2014

- Impact of the two 2009 NEJM studies on mortality
- 20% VP+KP/all VF in 2005
- 24% in 2008
- 14% in 2014
- Rate of death (propensity score) after VF = 4% higher in 2010-2014 vs. 2005-2009

Ong et al. OI 2018

Meta-analysis

Table 1: Literature Review Search Strategies

Database	Date of Search	Search Terms	No. of Studies
PubMed	14/4/2018	MeSH terms: spinal fracture, vertebroplasty, kyphoplasty, mortality	14
PubMed	14/4/2018	General terms: vertebral augmentation, mortality	50
PubMed	15/4/2018	General terms: vertebroplasty, kyphoplasty, mortality	87
EMBASE	15/4/2018	General terms: vertebral augmentation AND mortality	37
EMBASE	15/4/2018	PICO search strategy: P-osteoporotic vertebral compression fracture OR vertebral compression fracture I-vertebral augmentation OR percutaneous vertebroplasty OR kyphoplasty C-conservative treatment O–mortality OR survival	7
Cochrane	16/4/2018	General search terms: vertebroplasty AND kyphoplasty AND mortality OR survival AND osteoporotic	33

Hind et al. Radiology 2020

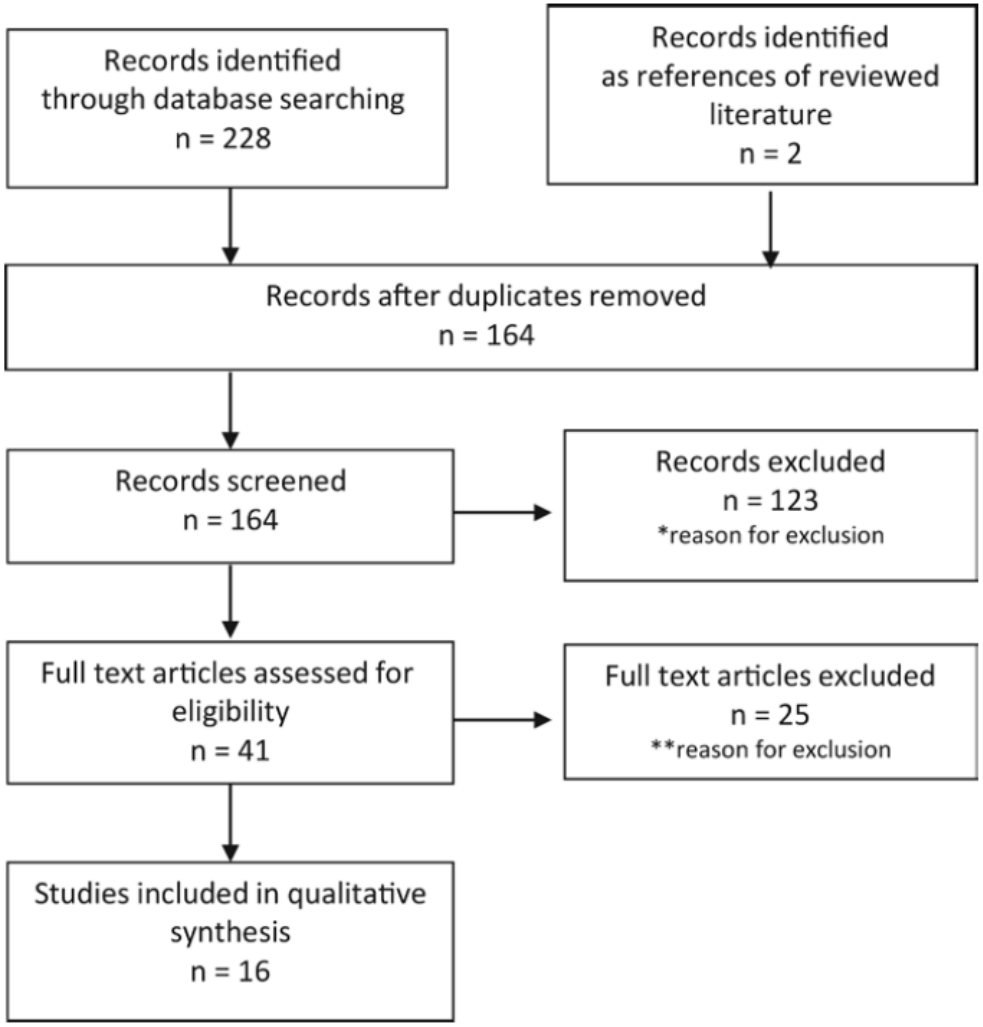


Figure 1: Systematic literature review flow diagram. * Review article *n* = 34; no vertebral fractures, *n* = 19; no mortality data, *n* = 13; case report, *n* = 13; pathologic fractures, *n* = 10; technical study, *n* = 9; commentary article, *n* = 8; no nonsurgical management comparator, *n* = 7; no vertebral augmentation, *n* = 6; unable to find abstract, *n* = 2; nonhuman research, *n* = 2. **No nonsurgical management comparator, *n* = 3; review article, *n* = 6; preliminary research of a later publication, *n* = 3; commentary article, *n* = 4; no mortality data, *n* = 9.

Hind et al. Radiology 2020

Study or Subgroup	log[Hazard Ratio]	SE	Surgical Total	Non-surgical Total	Weight	Hazard Ratio IV, Random, 95% CI
Diamond 2006	0.068	0.48	88	38	2.8%	1.07 [0.42, 2.74]
Gerling 2011	-0.051	0.552	46	129	2.2%	0.95 [0.32, 2.80]
Klezl 2012	-0.528	0.439	53	51	3.3%	0.59 [0.25, 1.39]
Lange 2014	-0.538	0.096	598	3009	22.0%	0.58 [0.48, 0.70]
Lin 2017	-0.33	0.125	1773	5324	18.4%	0.72 [0.56, 0.92]
McDonald 2011	0.02	0.108	524	367	20.5%	1.02 [0.83, 1.26]
Ong 2018	-0.198	0.003	378988	1698956	30.7%	0.82 [0.82, 0.83]
Total (95% CI)			**382070**	**1707874**	**100.0%**	**0.78 [0.66, 0.92]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 18.67$, df = 6 (P = 0.005); $I^2 = 68\%$

Test for overall effect: Z = 2.98 (P = 0.003)

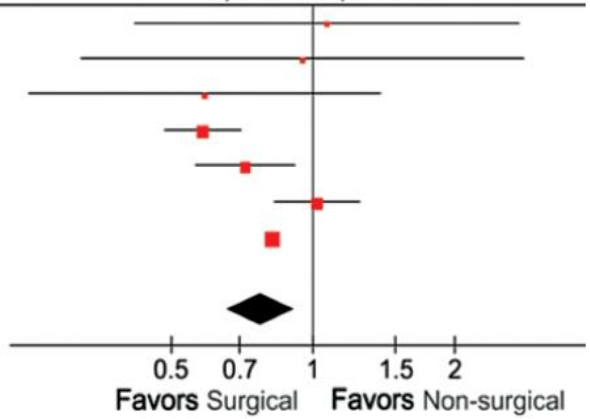


Figure 2: Pooled meta-analysis of hazard ratios in studies comparing mortality outcomes of patients with osteoporotic vertebral compression fractures receiving vertebral augmentation versus nonsurgical management. SE = standard error, IV = inverse variance, CI = confidence interval.

Hind et al. Radiology 2020

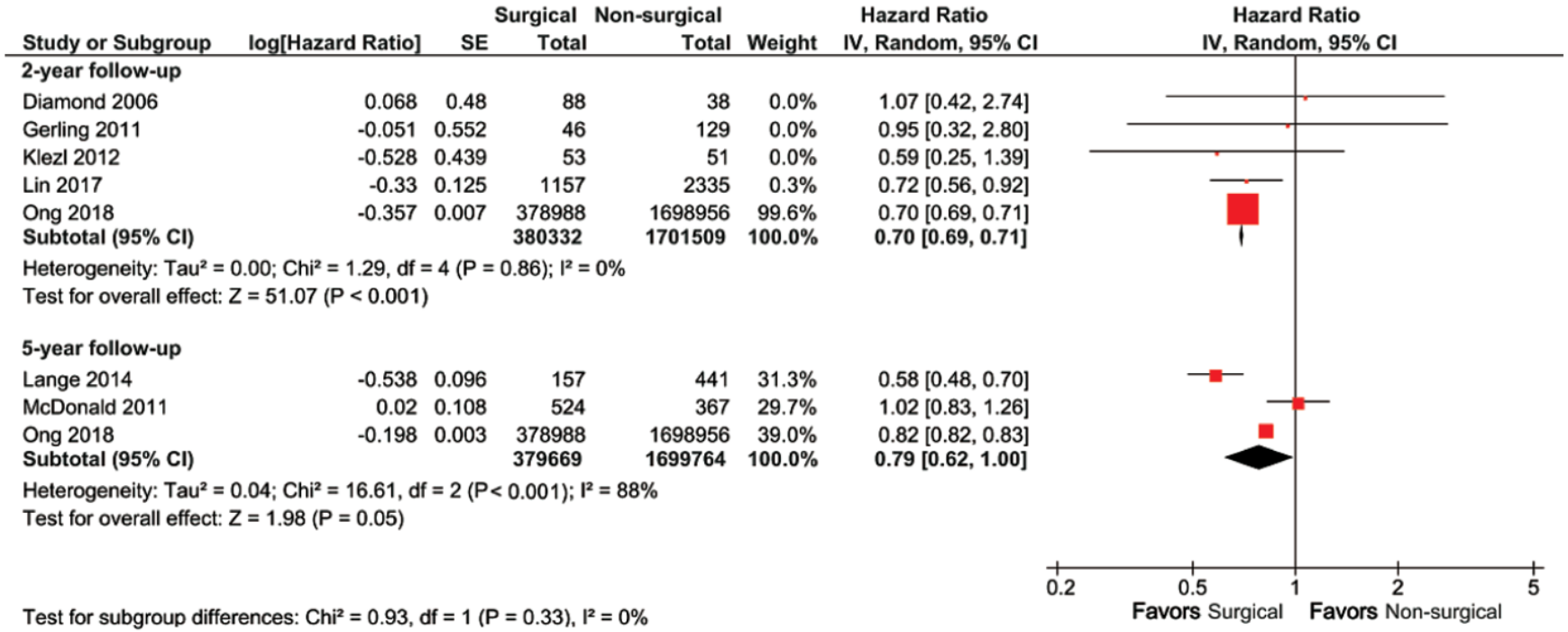


Figure 3: Pooled meta-analysis of hazard ratios comparing mortality outcomes of patients with osteoporotic vertebral compression fractures receiving vertebral augmentation versus nonsurgical management analyzed by extent of follow-up . SE = standard error, IV = inverse variance, CI = confidence interval.

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Table 3: Sensitivity Analysis

Study Removed and Year	Pooled Hazard Ratio*	*P* Value	I^2 Value (%)
None	0.78 (0.66, 0.92)	.003	68
Diamond et al 2006	0.77 (0.65, 0.91)	.003	73
Gerling et al 2011	0.77 (0.65, 0.92)	.004	73
Klezl et al 2012	0.78 (0.66, 0.93)	.006	72
Lange et al 2014	0.84 (0.76, 0.92)	.002	18
Lin et al 2017	0.79 (0.65, 0.97)	.02	72
McDonald et al 2011	0.72 (0.60, 0.88)	.001	66
Ong et al 2018	0.77 (0.58, 1.00)	.05	69

* Data in parentheses are 95% confidence intervals

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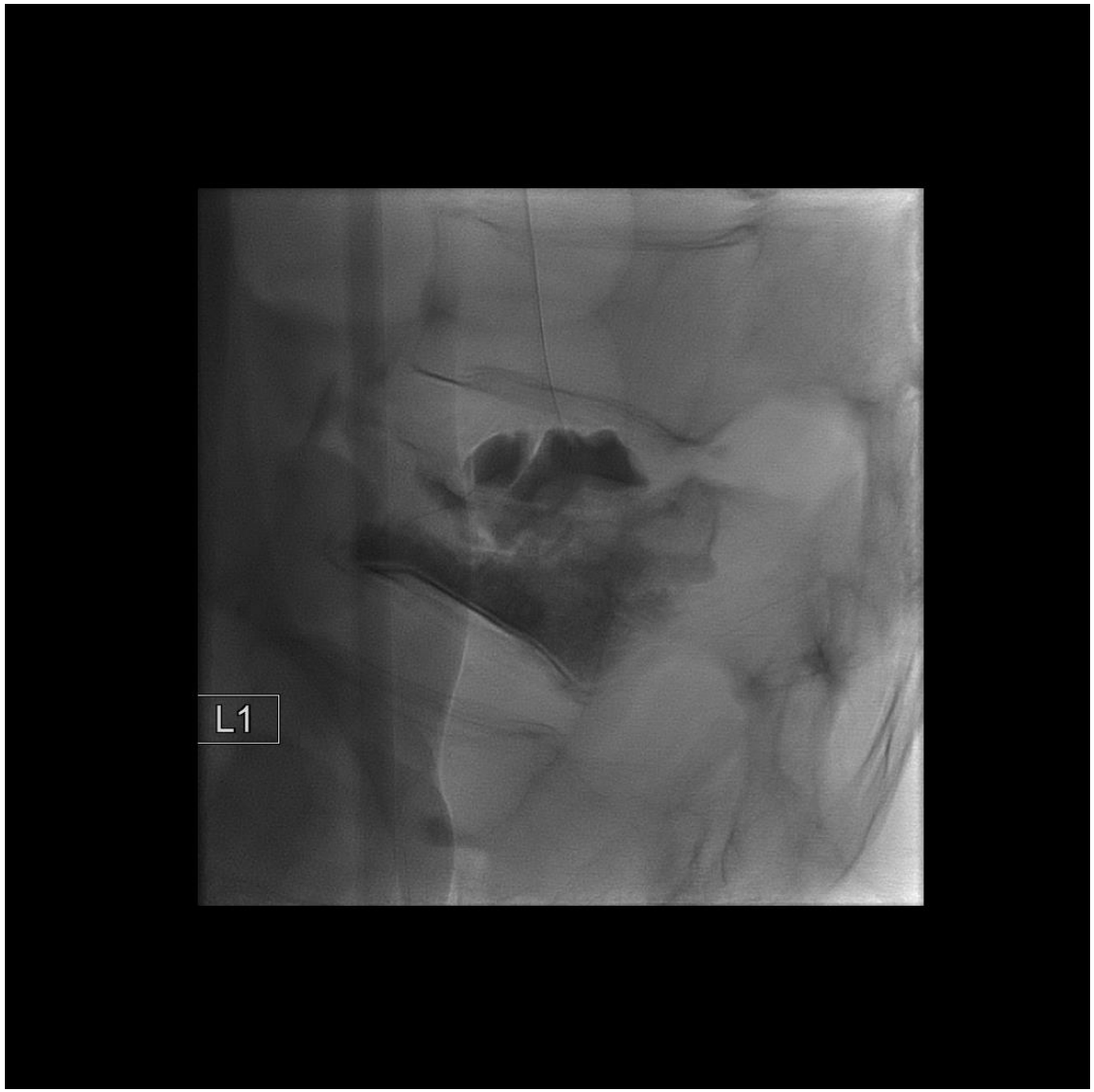
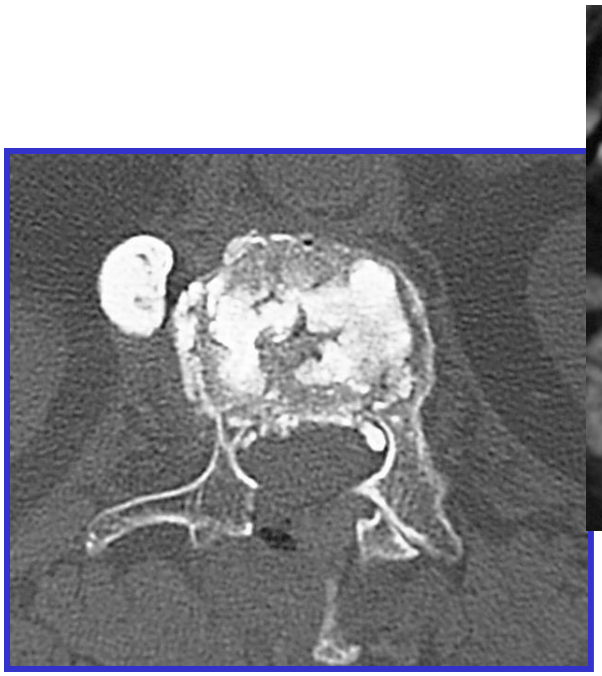
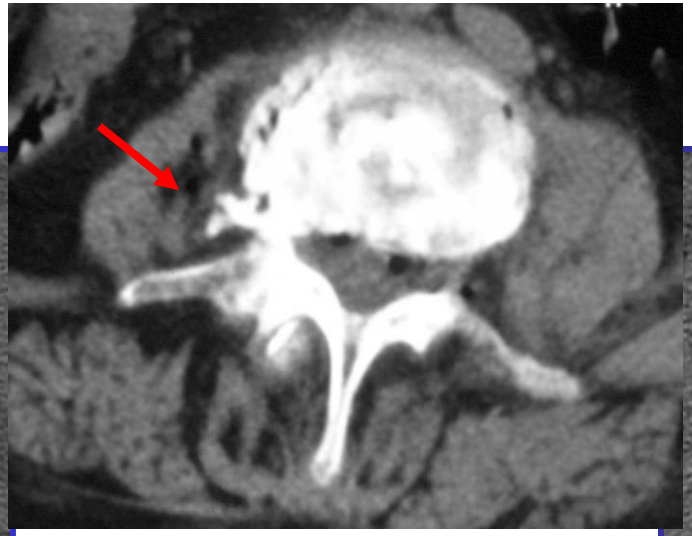
Safety

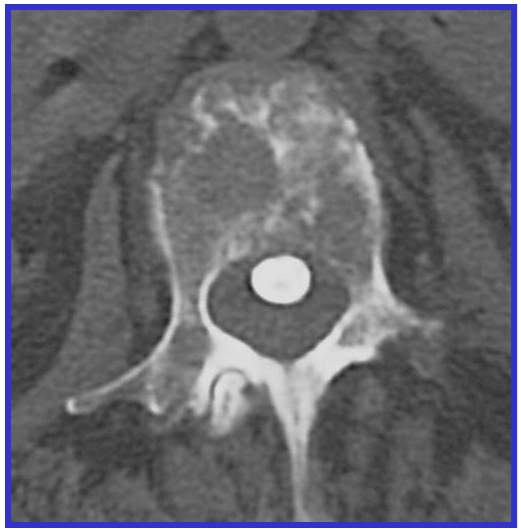
Leaks of cement

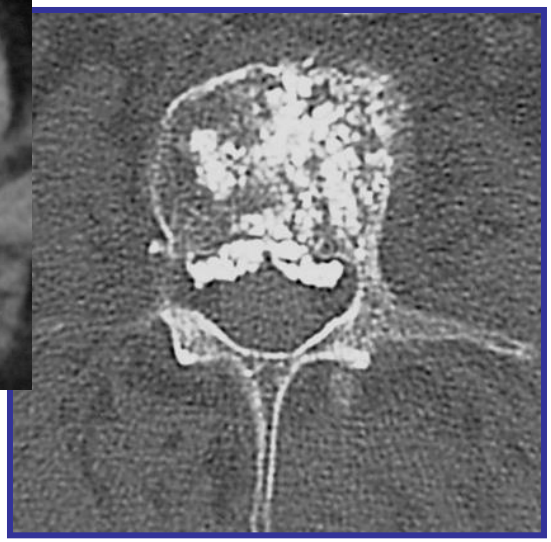


Leaks of cement

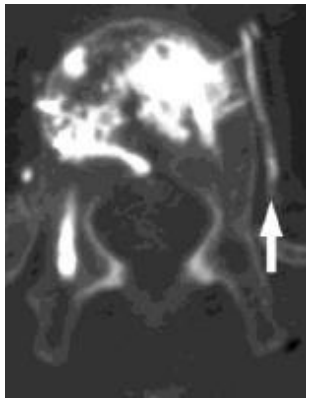






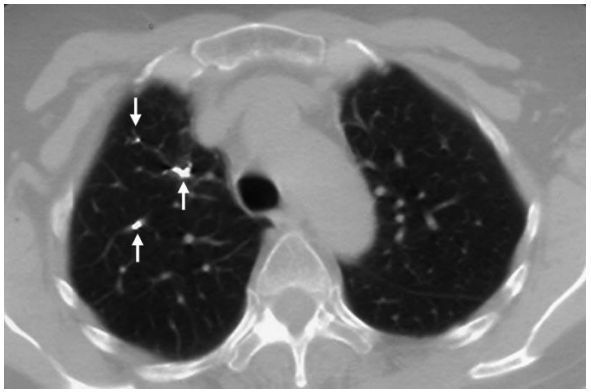


VERTOS 4



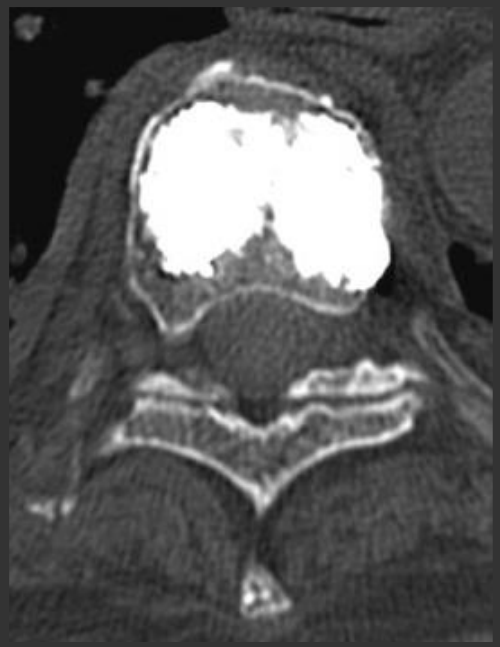
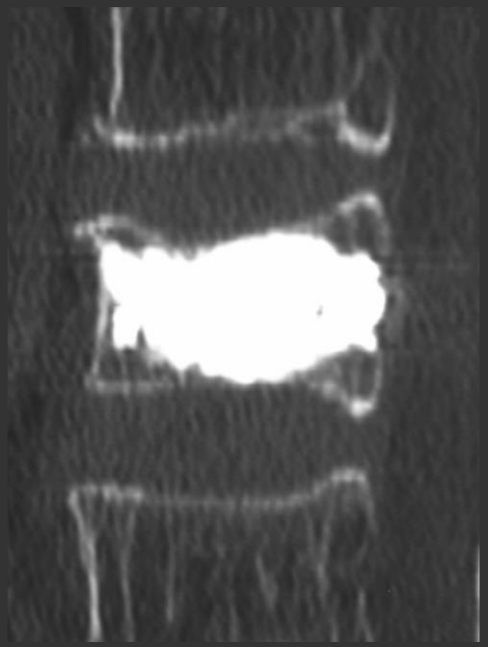
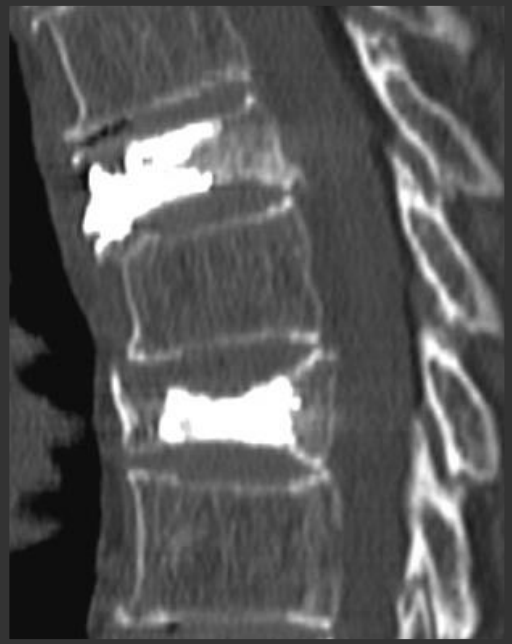
- 64.8% of the CT-scans showed a cement leak

- All these patients remained asymptomatic
  - paravertebral vein 41 (25. 8%)
  - intervertebral disc 21 (13. 2%)
  - pulmonary system 7 (4%)



- no other complications during or after the procedure

FREQUENCY OF ADJACENT VERTEBRAL FRACTURES

- **For Grados et al: RR = 2.27 [1.1-4.6] vs. RR = 1.44 [0.82-2.55] for incident VF in the vicinity of a fractured uncemented vertebra.**
- **Kim et al. Acta Radiol 2004 106 patients, 212 VP**

  Risk factors: degree of restoration spinal height, location (TL hinge), proximity/treated vertebrae
- **Relative risks of 3 [1.6-5.6] and 2 [1.1-3.8] for Abbad et al. Press Med 2016**

- Mean follow-up: 11.4 months (1-24) - 15 patients (18 VF)/91 for VP vs. 21 patients (30 VF)/85 for conservative treatment (p=0.44)

- Mean time to onset: 4.6 ± 5.4 months (PV) vs. 6.1 ± 5.9 when conservative treatment (p=0.48)

Table 2: Distribution of new VCFs

Distribution	PV (n = 91)	Conservative Therapy (n = 85)	P Value
Adjacent	7	11	.23
Between	4	3	
Distant	7	16	

Klazen et al. AJNR 2010

Secondary results

- Mean 10-month follow-up (median = 12; range 1-12)
- 31 new fractures were found in 15 VP patients.
- 28 new fractures in 19 patients in the control group

- No significant difference between the two groups at 3, 6 and 12 months (P = 0.60) for the occurrence of new vertebral fractures.

- Vertebroplasty does not cause new fractures.

Firanescu et al. BMJ 2018

Secondary results

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

- Vertebroplasty protects against the risk of vertebral further compression ➔ possible protection from increased kyphosis

Firanescu et al. BMJ 2018

Table 3 Subgroup analyses for the rate of new vertebral fractures

Variable	Number of trials	Number of patients	Statistical method	Effect size (95% CI)	Heterogeneity (I^2)	Test for subgroup differences
Different types of fractures						
Clinical fractures	5	788	Risk ratio (IV, random, 95% CI)	0.93 [0.58, 1.49]	32%	$p = 0.83$
Radiological fractures	6	619	Risk ratio (IV, random, 95% CI)	1.03 [0.48, 2.20]	74%	
Different duration of follow-up						
6 months	2	505	Risk ratio (IV, random, 95% CI)	1.29 [0.08, 20.78]	68%	$p = 0.76$
12 months	7	768	Risk ratio (IV, random, 95% CI)	1.07 [0.62, 1.82]	68%	
24 months	2	134	Risk ratio (IV, random, 95% CI)	0.56 [0.11, 3.01]	63%	
Different types of study design						
Sham injection	4	403	Risk ratio (IV, random, 95% CI)	1.00 [0.73, 1.36]	0%	$p = 0.95$
Conservative therapy	7	1004	Risk ratio (IV, random, 95% CI)	1.03 [0.45, 2.34]	74%	

Lou S. Osteoprosos Int 2019

Safety (summary)

- In expert hands there are no more serious complications.
- The risk of vertebral fracture adjacent to the cemented vertebra is not found in recent studies.
- On the other hand, a cemented vertebral fracture is never progressive.

Conclusion

- VP is useful in some patients with osteoporotic vertebral fractures (not all, of course).
- In the acute phase, efficacy in elderly patients with a high level of pain, numerous comorbidities, especially if they are hospitalized.
- After 12 weeks VP is probably useful if pain persists and if there is edema on MRI on T2-weighted pictures.

Q&A

THANK YOU

On behalf of IOF, we thank you for your participation in this webinar

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BoneCast

CSA Edition Webinar

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Our vision is a world without fragility fractures,
in which healthy mobility is a reality for all.

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