

Balloon Kyphoplasty in the Treatment of Vertebral Compression Fractures in Cancer Patients

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Abstract

Patients with cancer are at increased risk of painful vertebral compression fractures (VCFs). The Cancer Patient Fracture Evaluation (CAFE) trial was the first randomised controlled study to compare the safety and effectiveness of balloon kyphoplasty (BKP – a minimally invasive procedure) with non-surgical fracture management in the treatment of VCFs in patients with cancer. Data from the CAFE trial demonstrated that BKP is a safe and effective treatment option that quickly reduces pain and improves physical function and vertebral body height in patients with cancer and painful VCFs. Data from peer-reviewed published studies support the CAFE trial findings.

Keywords

Balloon kyphoplasty, vertebral compression fracture, cancer, safety, effectiveness, pain, risk

Disclosure: Leonard Bastian has received honoraria for consulting for Medtronic Spine LLC.

Acknowledgement: Medical writing support was provided by Dr Richard Barry (Quintiles Medical Communications) and was funded by Medtronic Inc.

Received: 19 April 2012 **Accepted:** 8 May 2012 **Citation:** *European Oncology & Haematology*, 2012;8(3):144–7 DOI: 10.17925/EOH.2012.08.3.144

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Support: The publication of this article was funded by Medtronic Inc. The views and opinions expressed are those of the author and not necessarily those of Medtronic Inc.

Patients with cancer are at increased risk of painful vertebral compression fractures (VCFs), loss of mobility, neurological deficits and reduced quality of life (QoL).^{1,2} VCFs can occur as a direct consequence of cancer or as an indirect consequence of the cancer therapy and are prevalent in patients with multiple myeloma or secondary metastases (in particular from breast and prostate carcinoma).³ Indeed, the risk of developing a VCF is five times higher in women with breast cancer than in women without breast cancer.⁴ Furthermore, the presence of one VCF is frequently associated with an increased risk of future vertebral fractures⁵ that can lead to further deteriorations in health and wellbeing. Thus, the long-term consequences of VCFs include progressive spinal deformity and pain as well as substantial impairments in physical, psychological and social functioning.⁶

Painful VCFs are usually treated using either non-surgical management or surgical methods. The aims of non-surgical management, which uses analgesics, bed rest, radiation therapy and antiresorptive therapy, are to reduce pain, improve functional status and prevent future fractures.⁷ However, non-surgical management often proves to be of limited effectiveness. Furthermore, as patients with VCFs often have poor bone quality, conventional open surgery may not always be the optimum treatment choice and is normally reserved for individuals with neurological impairment.⁸ Balloon kyphoplasty (BKP) represents a minimally invasive surgical treatment option.

About Balloon Kyphoplasty

BKP involves percutaneous augmentation of the fractured vertebra by orthopaedic balloon dilation and injection of bone cement under low

manual pressure. It is a minimally invasive procedure that has been used worldwide to treat over one million patients with VCFs in all indications. It aims to restore the anatomic shape of the vertebral body, decrease spinal deformity, reduce pain and improve physical function. The procedure usually takes less than one hour per fracture level and requires little or no post-operative rehabilitation. The different steps of a BKP procedure are shown in *Figure 1*. More information about BKP can be found on the Medtronic website.⁹

The Cancer Patient Fracture Evaluation (CAFE) Trial

The Cancer Patient Fracture Evaluation (CAFE) trial was the first study designed to compare the safety and efficacy of BKP with non-surgical management for the treatment of painful VCFs in patients with cancer. Data from this trial were published by Berenson and colleagues in *The Lancet Oncology*⁷ and were also presented at several oncology congresses by Professor Leonard Bastian, CAFE trial Investigator and author of this article.

Study Design and Included Patients

In total, 22 sites across Europe, the US, Canada and Australia participated in the CAFE trial. The study was a randomised controlled trial in patients ≥ 21 years of age with cancer and painful VCFs. Each patient had between one and three VCFs and reported considerable pain (10-point numerical rating scale score ≥ 4) and disability (Roland–Morris disability questionnaire [RMDQ] score ≥ 10) at baseline. The primary endpoint was back-specific functional status measured by the RMDQ score at one month. Enrolled patients were randomised

Figure 1: Stages of the Balloon Kyphoplasty Procedure



Steps 1–2: During the procedure, two orthopaedic balloons are inserted into the fractured vertebra through small cannulae.
 Step 3: The balloons are inflated to reduce the fracture and restore vertebral body height.
 Steps 4–5: The balloons are removed and the voids created are carefully filled with bone cement to stabilise the fracture.

1:1 to receive either BKP or non-surgical management. Patients in the non-surgical (control) group were allowed to cross-over to receive BKP after one month.

Clinical and Radiographic Findings

In total, 134 patients were enrolled in the study and assigned to either BKP (n=70) or non-surgical management (n=64). At one month after surgery, patients treated with BKP (n=65) showed a significant (p<0.0001) mean improvement (-8.3 points) in functional status (RMDQ score) from baseline compared with those who received non-surgical management (n=52; mean improvement in functional status 0.1 points). Significantly (p=0.0018) fewer patients treated with BKP required analgesics at one month compared with the control group (see Figure 2A). BKP also provided significantly (p<0.0001) greater pain relief in the two-week period leading up to the one-month time-point compared with non-surgical care (see Figure 2B). Benefits to patients in terms of pain relief and physical function were reflected in improvements in overall QoL. At one month, patients treated with BKP showed significant (p<0.0001) improvements in Short Form-36 Physical Component Summary (SF-36 PCS) scores compared with those who received non-surgical care.

When assessing Karnofsky performance status (KPS) in patients with cancer, the minimal clinically important difference estimate is approximately five points; in the CAFE trial, at one month, a mean 16-point increase in KPS scores from baseline was observed in the BKP-treated patients (see Figure 3). Furthermore, at one month, 75 % of patients in the BKP group had a KPS score of at least 70 (a score of 70 in the KPS represents the clinically meaningful threshold from which patients have the ability to care for themselves).

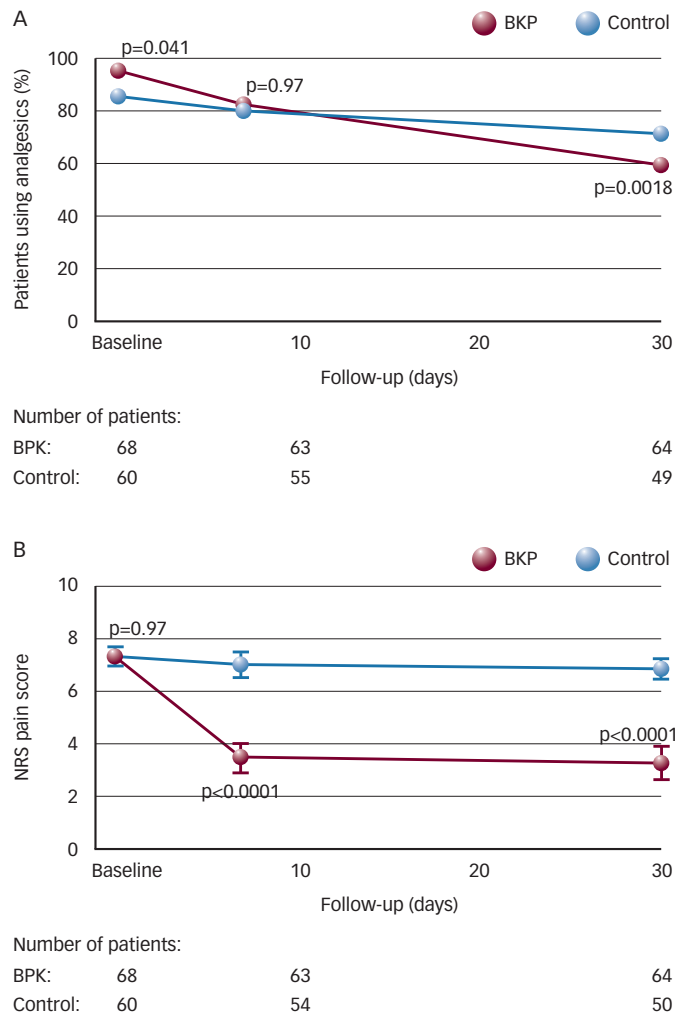
Berenson et al. reported that the improvements observed in disability, physical functioning and pain at one month in patients treated with BKP were sustained throughout the 12-month follow-up period.

Finally, one-month radiographic data showed that BKP provided significant (p<0.05) vertebral body height restoration for mid-thoracic (except for the anterior body measurement) and transition zone vertebrae compared with non-surgical care.

Adverse Events

The incidence of adverse events was similar between the two treatment groups. The most common adverse events in the first month were back pain (four patients in the BKP group and five patients in the control group) and symptomatic vertebral fracture (two patients in the BKP group and three patients in the control group).

Figure 2: Back Pain and Pain Management During the First Month After Surgery

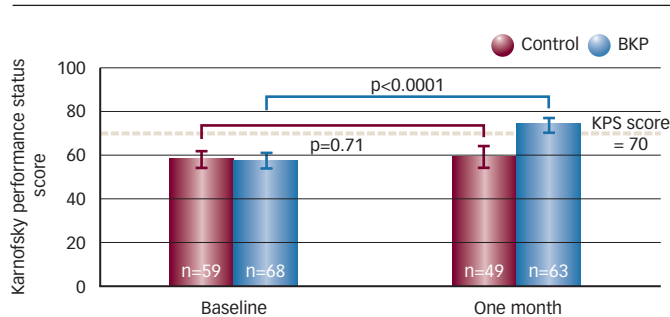


A: Proportion of patients using analgesics for back pain at each time point.
 B: Group mean and 95 % confidence intervals of numerical rating scale (NRS) pain scores (scale 0–10). In both panels, lower values are associated with an improvement.
 BKP = balloon kyphoplasty.
 Source: reprinted from The Lancet Oncology, Vol. 12.3, James Berenson, Robert Pflugmacher, Peter Jarzem, et al., Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial, 225–235, Copyright 2012, with permission from Elsevier.

Conclusions from the CAFE Trial

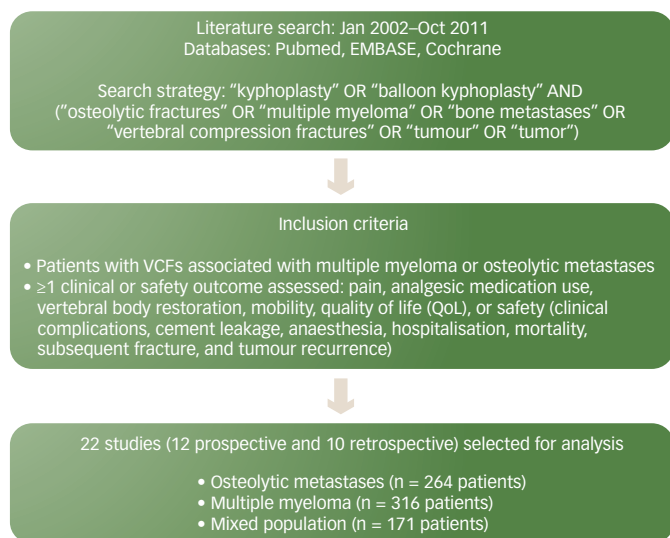
The data from the CAFE trial demonstrated that BKP is a safe and effective procedure that quickly reduces pain and also improves physical function and vertebral body height in patients with cancer

Figure 3: Karnofsky Performance Status Scores at Baseline and at One Month



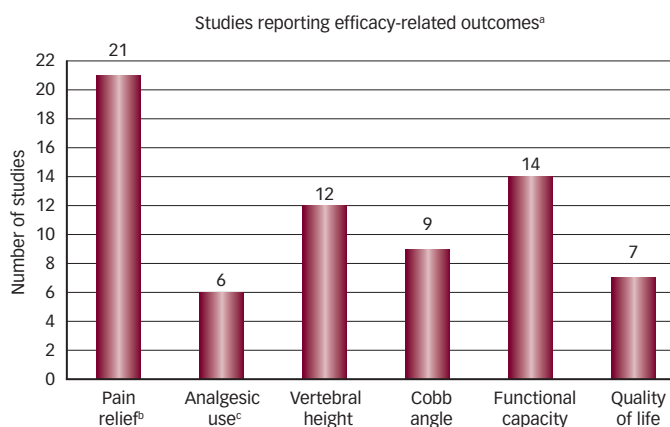
Patients with available KPS scores at baseline and at one month. Group means and 95 % confidence intervals are shown. A higher score indicates an improvement. A KPS score of 70 denotes the clinically meaningful threshold from which patients have the ability to care for themselves. BKP = balloon kyphoplasty; KPS = Karnofsky performance status.

Figure 4: Literature Review



QoL = quality of life; VCF = vertebral compression fracture.

Figure 5: Efficacy-related Outcomes in Patients with Cancer Treated with Balloon Kyphoplasty for Vertebral Compression Fractures (22 studies)^{7,10-30}



^a Efficacy-related outcomes defined as: sustained relief from pain, reduction in analgesic medication use, vertebral height restoration (stabilised), kyphotic angle correction (stabilised), improved physical functioning (long-term) and improved quality of life.

^b No long-term data were available in two studies.

^c A significant reduction was observed in two studies, complete cessation in one study, adapted to pain severity (no opiates required) in one study and unspecified in one study.

Box 1: Studies Selected for Analysis in the Literature Review^{7,10-30}

- Berenson J et al., *Lancet Oncol*, 2011;12:225–35⁷
- Ashamalla H et al., *Int J Radiat Oncol Biol Phys*, 2009;75:836–42¹⁰
- Astolfi S et al., *Eur Spine J*, 2009;18 Suppl 1:115–21¹¹
- Cardoso ER et al., *J Neurosurg Spine*, 2009;10:336–42¹²
- Dalbayrak S et al., *J Clin Neurosci*, 2010;17:219–24¹³
- Dudeney S et al., *J Clin Oncol*, 2002;20:2382–7¹⁴
- Eleraky M et al., *J Neurosurg Spine*, 2011;14:372–6¹⁵
- Fourney DR et al., *J Neurosurg*, 2003;98:21–30¹⁶
- Gerszten PC et al., *J Neurosurg Spine*, 2005;3:296–301¹⁷
- Gerszten PC et al., *Neurosurg Focus*, 2009;27:E9¹⁸
- Huber FX et al., *Clin Lymphoma Myeloma*, 2009;9:375–80¹⁹
- Khanna AJ et al., *Osteoporos Int*, 2006;17:817–26²⁰
- Köse KC et al., *J Natl Med Assoc*, 2006;98:1654–8²¹
- Lane JM et al., *Clin Orthop Relat Res*, 2004;49:53–22²²
- Lieberman I et al., *Clin Orthop Relat Res*, 2003;415S:S176–86²³
- Pflugmacher R et al., *Z Orthop Ihre Grenzgeb*, 2007;145:39–47²⁴
- Pflugmacher R et al., *Eur Spine J*, 2008;17:1042–8²⁵
- Qian Z et al., *J Clin Neurosci*, 2011;18:763–7²⁶
- Sandri A et al., *Radiol Med*, 2010;115:261–71²⁷
- Vrionis FD et al., *Tech Reg Anesth Pain Manag*, 2005;9:39²⁸
- Zhao J et al., *J Clin Rehabil Tissue Eng Res*, 2008;12:7089–92²⁹
- Zou J et al., *J Surg Oncol*, 2010;102:43–7³⁰

and painful VCFs. Professor Leonard Bastian commented: "This study demonstrates BKP should be considered when painful vertebral compression fractures occur in patients with cancer. It is an additional therapy which can really add to the patient's quality of life".

Systematic Literature Review of Balloon Kyphoplasty Treatment in Patients with Vertebral Compression Fractures Associated with Multiple Myeloma or Osteolytic Metastases

Data from peer-reviewed published studies¹⁰⁻³⁰ extend the findings from the CAFE trial⁷ and confirm that BKP is an effective treatment option for VCFs in patients associated with multiple myeloma or osteolytic metastases.

BKP is a recognised treatment option for VCFs in patients with osteoporosis, but the potential benefits of the procedure in patients with cancer and VCFs are less well known. Clinical findings from the CAFE trial demonstrated the beneficial effects of BKP in patients with cancer compared with non-surgical management. To establish whether the CAFE trial findings were consistent with those of other published studies in patients with cancer and VCFs, a systematic review of the literature was performed (see Figure 4).

An analysis of health and clinical outcomes data from the 22 studies that were included in the review of the literature (see Box 1)^{7,10-30} demonstrated that BKP is an effective treatment option for VCFs in patients with cancer. Patients benefited from significant long-term pain relief with reduced analgesic medication use, vertebral body height and kyphosis (Cobb angle) were stabilised, and patients had improved mobility and QoL (see Figure 5). As highlighted in the CAFE study, BKP was performed safely – there were few major complications and no procedure-related deaths across studies in this group of patients, who are subject to significant morbidity and mortality. In one study, one patient with

multiple myeloma experienced asystole after BKP and required cardiopulmonary resuscitation.²⁸

The data highlighted in this literature review are consistent with that from the study of BKP in patients with osteoporotic VCFs who do not have a history of cancer.⁸

Summary

Data from 22 published studies (including the CAFE study)^{7,10-30} showed that BKP is a safe and effective treatment option that quickly reduces pain, stabilises vertebral body height and kyphosis, and improves physical function and QoL in patients with cancer and painful VCFs. ■

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