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REVIEW

Appropriateness criteria for treatment of osteoporotic vertebral compression fractures

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Abstract

The purpose of this study was to review and summarise the literature on appropriateness criteria for treatment of osteoporotic vertebral compression fractures (OVCF), with appropriateness defined as a treatment where the expected benefits outweigh the expected harms, confirmed by available evidence and expert opinion. A comprehensive search of peer-reviewed publications (PubMed, EMBASE) and grey literature was performed. To be included for analysis, documents had to be a review article (e.g. clinical guideline or meta-analysis), focus on OVCF and make a statement on treatment appropriateness. Eleven publications fulfilled the eligibility criteria. Among the five publications that made recommendations about non-surgical management (NSM), there is agreement that conservative methods are appropriate in OVCF patients who have low level of pain, and that the majority of patients should be treated with conservative methods before other treatments are initiated. All publications made recommendations about vertebral augmentation procedures (VAP), i.e. vertebroplasty (VP) and/or balloon kyphoplasty (BKP). VAP are mostly considered appropriate in patients with high level of pain who do not respond to NSM. However, results cannot be generalised due to heterogeneity of treatment recommendations and patient selection. Although there is a consensus that NSM should be considered as the first-line treatment, there is more heterogeneity in treatment recommendations for VAP. This could most likely be explained by an insufficient clinical evidence base for VAP and heterogeneity of OVCF patients, leading to greater reliance on expert opinion affecting the quality of evidence in the primary sources.

Keywords Appropriateness · Balloon kyphoplasty · Osteoporotic vertebral compression fractures · Vertebral augmentation · Vertebroplasty

Introduction

Vertebral compression fractures are a common problem of osteoporosis, with an estimated incidence of half a million symptomatic fractures sustained in Europe each year [1, 2] affecting 1.1% women and 0.6% men in the age group 50–79 years [3]. Incidence of osteoporotic vertebral compression fracture (OVCF) increases as people age, although at all ages, more women than men are affected [3]. Symptomatic OVCF can cause significant pain and decrease a patient's mobility with substantial impact on a patient's quality of life (QoL) [4], both in the short and long term [5].

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Short-term treatment goals for patients who suffered an OVCF are pain relief, restoration of mechanical stability and mobility improvement. To this end, patients may receive either non-surgical (conservative) management (NSM) in terms of narcotic analgesics, bed rest and bracing, or they may undergo vertebral augmentation [6, 7]. As the acute fracture heals, the initial pain caused by the fracture subsides in a majority of patients, usually within a couple of weeks [8, 9]. Still, up to one third of patients experience insufficient response and/or intolerance to conservative treatment [10]. Also, in the elderly patient population, NSM increases the risk for adverse outcomes associated with the use of narcotics and prolonged inactivity. Hence, vertebral augmentation procedure (VAP) has become a widespread treatment option for many OVCF patients. As such, both vertebroplasty (VP) and balloon kyphoplasty (BKP) are minimally invasive procedures where cement is injected into the affected vertebra in order to stabilise the vertebra and reduce pain caused by the fracture. The procedures differ in the way that VP uses needles

to deliver the cement to the vertebra while BKP first expands the vertebra with a balloon, before cement is injected. Utilisation data show that in the USA, more than 300,000 inpatient VAPs were performed between 2005 and 2010, with BKP accounting for almost three in four procedures [11].

Because published evidence about the effectiveness and safety of VAP in the treatment of OVCF is limited (see e.g. [12–14]), more research is needed to fully understand the benefits and harms of VAP. Further, for more than a decade, the scientific and clinical community has been stressing the need for "establishing which patients are most likely to benefit and at which point after their fracture PVA [percutaneous vertebral augmentation] becomes appropriate" [15]. After many years of study, there is still no consensus pertaining to these questions. Appropriateness is commonly defined as a treatment where the expected benefits outweigh the expected harms by a sufficiently wide margin [16]. The term is often seen within other disease areas and has leveraged the development and dissemination of so-called Appropriate Use Criteria (AUC) — sometimes referred to as Appropriateness Criteria —, most prominently in the treatment of cancer (e.g. [17, 18]) and cardiovascular disease (e.g. [19, 20]). In the area of OVCF, two AUC documents [21, 22] and one study on the applicability of AUC have been published to date [23]. However, guidance on appropriateness of treatment may also be found in other types of publications such as clinical practice guidelines, systematic reviews and position statements. AUC definitions as used by professional associations concerned with the diagnosis and treatment of diseases of the spine are summarised in Table 1. Using these definitions as guidance, appropriateness criteria was defined as literature making treatment recommendations based on available evidence and collective judgement from experts. This paper seeks to systematically review the available literature on appropriateness criteria for treatment of OVCF.

Material and methods

Review protocol

The review methodology was predefined in a full protocol in accordance with the requirements of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement [28]. Only minor amendments were made to the protocol. However, after study selection, we abandoned the idea of performing a quality assessment of included studies using the Appraisal of Guidelines for Research and Evaluation (AGREE) II [29]. This decision was based on the fact that most identified publications were not clinical practice guidelines, for which this tool was developed and validated.

Study identification

A comprehensive, systematic search of the databases PubMed and EMBASE was run on January 18, 2017, using the search terms[1]: osteoporo*, vertebral, spinal, compression, fracture*, appropriate*, criteria, guideline, guidance, "position statement", standard*, consensus, recommend*, "patient selection" and indication. Only publications reported in English between the years 2000 and 2016 were included. In addition, websites linked to professional associations, patient organisations, health technology assessment (HTA) bodies and databases of practice guidelines were searched during January 2017. This grey literature search was restricted to Europe's "Big Five" (Germany, the UK, France, Italy and Spain), North America and Australia.

Selection of studies

After removal of duplicates, all references were screened for inclusion based on their title and abstract. The following inclusion criteria were applied: the publication (1) is an overview article such as an Appropriateness Criteria document, clinical practice guideline, consensus/position statement, meta-analysis or HTA, (2) is concerned with the treatment of vertebral compression fractures caused by osteoporosis (not by malignancy or trauma) and (3) makes recommendations on the appropriateness of one or more treatments in this patient group (not merely reviewing efficacy, safety or treatment indications). Subsequently, the full-text manuscripts of eligible publications were reviewed for inclusion by two independent reviewers (SL and JW).

Data extraction

Relevant data from the publications were extracted by both reviewers (SL and JW) using a standardised data extraction form, with any discrepancy resolved by discussion. The primary outcome measure was appropriateness criteria for the treatment of OVCF. Other extracted data was scope, method, patient population, treatment options, strength of recommendation, country/region for recommendation, publication type and publisher. Definition of appropriateness in the

[1] Search strings: PubMed; (osteoporo*[tiab] AND (vertebral[tiab] OR spinal[tiab]) AND compression[tiab] AND fracture*[tiab]) AND (appropriate*[tiab] OR criteria[tiab] OR guideline[tiab] OR guidance[tiab] OR "position statement"[tiab] OR standard*[tiab] OR consensus[tiab] OR recommend*[tiab] OR "patient selection" [tiab] OR indication) AND (("2000/01/01"[PDat]: "2016/12/31"[PDat]) AND English[lang])

EMBASE; osteoporo*:ab,ti AND vertebral:ab,ti AND ('compression'/exp. OR compression:ab,ti) AND ('fracture'/exp. OR fracture:ab,ti) AND (appropriate*:ab,ti OR criteria:ab,ti OR guideline:ab,ti OR guidance:ab,ti OR 'position statement':ab,ti OR standard*:ab,ti OR consensus:ab,ti OR recommend*:ab,ti OR 'patient selection':ab,ti OR indication:ab,ti) AND [2000–2016]/py AND [english]/lim AND ([article]/lim OR [article in press]/lim OR [conference paper]/lim OR [review]/lim)

Table 1 Definitions of Appropriate Use Criteria

Spinal Intervention Society (SIS) [24]	Appropriate Use Criteria (AUC) specify in which circumstances it is appropriate to perform a procedure. In an effort to foster clinical decision-making, AUC developers integrate the best available scientific evidence and the collective judgement of experts to generate statements regarding the appropriateness of performing a procedure at the level of patient-specific symptoms, medical history and test results.
American Academy of Orthopaedic Surgeons (AAOS) [25]	Appropriate Use Criteria (AUC) specify when it is appropriate to use a procedure. An "appropriate" procedure is one for which the expected health benefits exceed the expected health risks by a wide margin. Often, sound data is not available or does not provide evidence that is detailed enough to apply to the full range of patients seen in everyday clinical practice. Nevertheless, physicians must make daily decisions about when to use or not use a particular procedure. AUCs facilitate these decisions by combining the best available scientific evidence with the collective judgement of physicians in order to determine the appropriateness of performing a procedure.
American College of Radiology (ACR) [26]	The ACR Appropriateness Criteria® (AC) are evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition. Employing these guidelines helps providers enhance quality of care and contribute to the most efficacious use of radiology.
North American Spine Society (NASS) [27]	[…] Regardless of established levels of evidence, spine care providers must regularly make decisions about indications for procedures/treatment. While higher level evidence is preferred, in those areas where evidence is sparse, appropriate use criteria (AUCs) indicate reasonable care based on available evidence combined with a rigorous, transparent recommendation process and well-defined scenarios.

publications and evidence base used to support conclusions drawn was extracted when readily available. This information is provided in Table 2.

Data analysis

Appropriateness criteria were grouped by treatment option and publication type and summarised narratively in text form. No statistical analyses were performed.

Results

Study identification and selection

Details of the flow of studies included at each step of the review are specified in the PRISMA flow diagram (Fig. 1). A systematic search of the PubMed and EMBASE databases yielded 374 and 339 hits, respectively. Of the total of 713 references, 289 duplicates were removed. Based on title and abstract review of the remaining 424 records, 321 references were excluded. Additional references ($n = 18$) of potential relevance for this review were identified from websites of professional associations, patient organisations, HTA bodies and practice guideline databases. In total, 121 records were screened for eligibility. Of these, eight publication studies could not be obtained. Following detailed examination of the remaining 113 articles, 102 citations were excluded for not meeting the eligibility criteria. Most of these references were excluded because they were lacking statements on the appropriateness of a certain treatment. Eleven studies met the eligibility criteria and were included for data extraction.

List of included articles

A complete list of articles and their study characteristics, including publishers' assessed level of evidence when readily available, is provided in Table 2. We included two recently published documents regarding Appropriate Use Criteria [21, 22], two position statements or consensus papers [31, 39] and six guidelines or technology assessments [40–42, 47–49]. Further, we included one systematic review [50], which also performed a meta-analysis on the data. No apparent biases linked to type of publication or publisher have been identified.

Appropriateness of non-surgical management

Five publications made treatment recommendations on NSM [21, 39, 40, 48, 49] (Table 3). As regards place in therapy, conservative therapy has been recommended as first-line

Table 2 List of publications included in the review

Publication	Body/ publisher	Patient population	Treatments*	Methods/ evidence base
Appropriate Use Criteria				
Anselmetti et al. (2013) [21]	European multi-disciplinary panel of 12 experts	OVCF and absence of neurological symptoms or contra--indications	NSM, VP, BKP	Review of literature and expert panel; review performed to select 7 clinical variables relevant to treatment choice. Then, an expert panel assessed appropriateness for 128 scenarios using RAND/UCLA Appropriateness Method (RAM). Final recommendations were formulated in December 2011.
McConnell et al. (2014) [22]	Specialty society (ACR)	VCF due to osteoporosis and malignancy	NSM, VP, BKP	Review of literature and expert panel; based on 74 reviews, experimental studies, and observational studies published between 1991 and 2014 [30], and modified Delphi method by a multidisciplinary expert panel. Paper authors rank study quality between 1 and 4 for each publication; 1 for well-designed studies and 4 for studies not useful as primary source.
Position statements and consensus papers				
Barr et al. (2014) [31]	Specialty societies and associations**	OVCF	VP, BKP	Review of literature and position of Societies; based especially on the 6 RCTs available of VAP versus NSM or sham therapy [32–38].
Brunton et al. (2005) [39]	Primary Care Consortium (PCECTAFP)	OVCF	NSM, VP, BKP	Review of literature and panel members' clinical experience. Publication authors provided no information about how reviewed literature was identified and selected.
Guidelines and technology assessments				
AAOS (2010) [40]	Specialty society (AAOS)	OVCF	NSM, VP, BKP	Review of literature and AAOS work group; review based on 50 articles published between 1966 and 2009. Recommendations and their strength were voted on using the nominal group technique (NGT). Draft guidelines were peer-reviewed and sent for public commentary. Final recommendations were formulated in February 2010. Each recommendation was written using language that accounts for the final strength of the recommendation; strong, moderate, limited, inconclusive or consensus (the opinion of the work group).

Table 2 (continued)

Publication	Body/ publisher	Patient population	Treatments*	Methods/ evidence base
Karliner (2009) [41]	Specialty society (CTAF)	VCF due to osteoporosis, trauma, and pathology	BKP	Review of literature and CTAF criteria; literature published until April 2009, results prompted by the RCT [38], but also based on 13 non-randomised comparison studies, and 49 case series. The MEDLINE, EMBASE, and Cochrane clinical trials database, Cochrane reviews database and the Database of Abstracts of Reviews of Effects (DARE) were searched for relevant references. The CTAF voted to accept the recommendation as presented in the publication.
NICE (2013) [42]	Government (NICE)	OVCF	VP, BKP	NICE multiple technology appraisal process; review of literature published until 22 November 2011 [7], which included 9 RCTs reported in eleven publications [32–38, 43–46]. Searches in 7 databases were performed, including e.g. MEDLINE (Ovid), EMBASE, and the Cochrane Library. Quality and strength of evidence was assessed by expert consensus. Recommendations were formulated by expert consensus.
NICE (2003) [47]	Government (NICE)	VCF due to osteoporosis and malignancy	VP	NICE interventional procedure guidance process; review of literature and advisor's opinion. Literature including totally 41 studies. A systematic search of MEDLINE, PREMEDLINE, EMBASE, Current Contents, PubMed, Cochrane Library and Science Citation Index using Boolean search terms for literature published until October 2002 was conducted. Totally 41 studies (32 case series, 6 case reports, 2 non-randomised comparative studies, and 1 systematic review) were found.
OHTAC (2010) [48]	Advisory Committee (OHTAC)	OVCF	VP	Deliberations of OHTAC based on review of five RCTs; two comparing VP with sham procedure [32, 34], two comparing VP with conservative treatment [36, 46] and one comparing VP with BKP [45]. The quality of the evidence according to the GRADE working group was

Table 2 (continued)

Publication	Body/ publisher	Patient population	Treatments*	Methods/ evidence base
				considered "High" for the two blinded RCTs [32, 34] and "Moderate" for the two open RCTs [36, 46] and the study comparing VP with BKP [45].
OHTAC (2010) [49]	Advisory Committee (OHTAC)	OVCF	BKP	Deliberations of OHTAC based on review of two RCTs; one comparing BKP with VP [45] and one comparing BKP with non-surgical care [38]. The quality of the evidence according to the GRADE working group was considered as "Moderate" for both trials.
Systematic literature reviews and meta-analyses				
Buchbinder et al. (2015) [50]	Cochrane review	OVCF	VP	Review of literature and authors' conclusions; literature published until 12 November 2014. CENTRAL, MEDLINE and EMBASE were searched for studies assessing benefits and harms of VP. Totally eleven RCTs and one quasi-RCT conducted in various countries were included: two RCTs of VP versus placebo [32, 34], six comparing VP and usual care [33, 35, 36, 43, 46, 51], and four comparing VP and BKP [45, 52–54]. The placebo-controlled trials were judged to be at low overall risk of bias [32, 34]. The other included trials were generally considered to be at high risk of bias.

*This column lists all OVCF treatments that the publication was primarily concerned with based on title and/or abstract. Please note that some publications may not make recommendations for all treatments listed here (e.g. [22]). Likewise, some publications make recommendations for or against treatments not included in their main focus (e.g. [48, 49]). These recommendations are, however, included in the results section of this paper.

**SIR, AANS, CNS, ACR, ASNR, ASSR, CIRA, SNIS

AANS, American Association of Neurological Surgeons; *AAOS*, American Academy of Orthopaedic Surgeons; *ACR*, American College of Radiology; *ASNR*, American Society of Neuroradiology; *ASSR*, American Society of Spine Radiology; *BKP*, balloon kyphoplasty; *CIRA*, Canadian Interventional Radiology Association; *CNS*, Congress of Neurological Surgeons; *CTAF*, California Technology Assessment Forum; *NICE*, National Institute for Health and Care Excellence; *NSM*, non-surgical management; *OHTAC*, Ontario Health Technology Advisory Committee; *OVCF*, osteoporotic vertebral compression fracture; *PCECTAFP*, Primary Care Education Consortium, Texas Academy of Family Physicians; *RCT*, randomised controlled trial; *SIR*, Society of Interventional Radiology; *SNIS*, Society of NeuroInterventional Surgery; *VAP*, vertebral augmentation procedure; *VCF*, vertebral compression fracture; *VP*, vertebroplasty

treatment option in a range of patient groups, starting from all patients with OVCF [48, 49], to those with low level of pain, disability, or deformity [39] or negative magnetic resonance imaging (MRI) [21]. In a panel study, Anselmetti and colleagues assessed the appropriateness of different treatment options for OVCFs in 128 hypothetical patient profiles, which were derived by permutations of seven clinical factors (time since fracture, MRI findings, mobility limitation, severity of

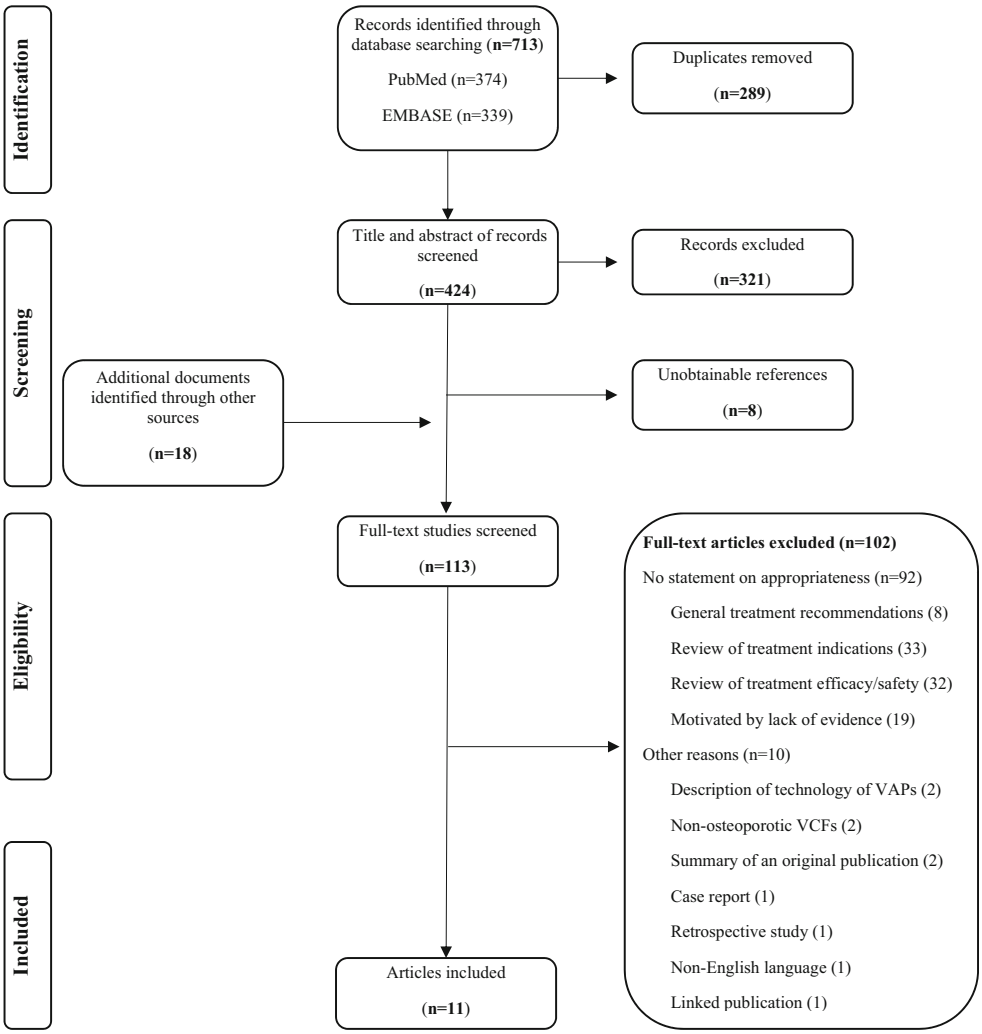

Fig. 1 Study flow diagram

pain, spinal deformity, proof of ongoing fracture process, presence of pulmonary and/or gastrointestinal dysfunction) [21]. The authors conclude that NSM is usually appropriate in patients who lack MRI evidence of fracture and MRI-positive patients without other unfavourable factors, but recommend against NSM in patients with proof of ongoing fracture process and two or more other unfavourable factors [21]. Specific recommendations for subtypes of conservative therapy are available from the American Academy of Orthopaedic Surgeons' (AAOS) clinical practice guideline for OVCF treatment [40]. For patients with acute OVCF, the guidelines suggest calcitonin treatment (AAOS strength of recommendation: moderate) and consider L2 nerve block as an option (AAOS strength of recommendation: limited), but are unable to recommend for or against other types of conservative therapy such as bed rest, analgesics and bracing (AAOS strength of recommendation: inconclusive) [40]. Across the majority of publications, NSM is considered an appropriate first-line treatment option for OVCF.

Appropriateness of vertebral augmentation procedures

Two publications made statements on the appropriateness of VAP (either VP or BKP) in general [31, 39], without differentiating between the two techniques, and one publication made the same recommendations for both procedures [42] (Table 4). In fact, motivated by a lack of evidence for the superiority of one procedure over the other, some even regard "kyphoplasty and vertebroplasty as generally interchangeable techniques for the performance of percutaneous vertebral augmentation" [31]. Across the included publications, vertebral augmentation is considered as an appropriate treatment option for OVCF patients with high level of pain, who do not respond to non-operative therapy. Uncertainty remains, however, what constitutes a failure of NSM. Barr and colleagues propose to define failure of conservative medical therapy based on the patient's pain level, response to analgesic drugs and

Table 3 Recommendations made for non-surgical management

Appropriate Use Criteria
- Recommended in patients with negative MRI [21]
- Recommended in patients with positive MRI and no other unfavourable conditions [21]
- Recommended against NSM in patients with proof of ongoing fracture process and two or more other unfavourable factors [21]

Position statements and consensus papers
- For patients with low level of pain, disability or deformity [39]

Guidelines and technology assessments
- Calcitonin treatment for 4 weeks is suggested in patients who present with OVCF on imaging with correlating clinical signs and symptoms suggesting an acute injury (0–5 days after identifiable event or onset of symptoms) and who are neurologically intact (AAOS strength of recommendation: moderate, based on 4 studies) [40]
- L2 nerve root block is an option in patients who present with OVCF at L3 or L4 on imaging with correlating clinical signs and symptoms suggesting an acute injury and who are neurologically intact (AAOS strength of recommendation: limited, based on 1 study) [40]
- Unable to recommend for or against bed rest, complementary and alternative medicine, opioids/analgesics, brace, supervised or unsupervised exercise program, or electrical stimulation for patients who present with OVCF on imaging with correlating clinical signs and symptoms and who are neurologically intact (AAOS strength of recommendation: inconclusive, based on 1 study) [40]
- Recommended conservative treatment which allows the fracture to heal as first-line treatment [48, 49]

functional status [31], acknowledging that individual differences in these variables preclude stringent cut-off values. Likewise, there is no hard-and-fast time period for a fracture to heal with NSM before VAPs may be offered. Even if Brunton and colleagues suggest to wait up to 6 weeks for symptoms to improve [39], Barr and colleagues found no support for the concept of a mandatory waiting time [31], and the National Institute for Health and Care Excellence (NICE) [42] does not discuss time since fracture in their recommendations. In general, VAP is the recommended treatment option in patients who have severe pain despite optimal pain management.

Table 4 Recommendations made for vertebral augmentation procedures

Position statements and consensus papers
- Appropriate therapy for treatment of painful VCFs refractory to non-operative medical therapy [31]
- For patients with low level of pain, disability or deformity who do not respond to NSM within 6 weeks [39]
- For patients with high level of pain, disability or deformity [39]

Guidelines and technology assessments
- Recommended as options only in people who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management and in whom the pain has been confirmed to be at the level of the fracture by physical examination and imaging (type of evidence not specifically stated) [42]

Appropriateness of vertebroplasty

In total, seven publications included statements on the appropriateness of VP in treating OVCF patients [21, 22, 40, 42, 47, 48, 50] (Table 5). A recent Cochrane review by Buchbinder and colleagues of 11 RCTs and one quasi-RCT of VP in patients with OVCF concludes that "current literature does not support the likelihood of identifying subsets of patients who would benefit from vertebroplasty" [50]. Further, Buchbinder concludes that their review does not support a role for VP in routine practice and that no demonstrable clinically important benefits of VP compared with a sham procedure were identified [50]. Similarly, the American Academy of Orthopaedic Surgeons (AAOS) makes only recommendations against the procedure. Based on five studies [32, 34, 36, 46, 55], they conclude that "By making a strong recommendation against the use of vertebroplasty we are expressing our confidence that future evidence is unlikely to overturn the results of these trials." [40].

Others express a slightly less stringent approach towards VP. The Ontario Health Technology Advisory Committee (OHTAC) base their recommendations on the same studies as AAOS ([32, 34, 36, 46]) except for one ([45]) instead of [55]) and recommend only against VP as first-line treatment [48]. Similarly, in the guidelines developed by the ACR based on analysis of current literature and expert opinion, McConnell and colleagues conclude that VP should be used for patients who have failed or cannot tolerate conservative or traditional management [22]. This recommendation is also supported by the NICE guidelines [42, 47]. Across the included publications, VP is considered an appropriate treatment option in patients who have failed NSM or cannot tolerate NSM.

Appropriateness of balloon kyphoplasty

Five publications made statements about the appropriateness of BKP [21, 22, 40–42] (Table 6). Based on five studies [38, 45, 56–58], the AAOS recommend BKP as an option for patients with an OVCF on imaging (limited strength of recommendation) [40]. This recommendation was downgraded from "moderate" to "limited" due to lack of evidence for VP and the technical similarities between VP and BKP. Recommendations by Karliner [41], published by the California Technology Assessment Forum (CTAF), are mainly based on results from one study [38]. Karliner suggests that it is important that patients considering BKP start with a trial of NSM given that the procedure carries some risk and that the mean age of the fracture was 5–6 weeks in the analysed RCT [38]. Most patient selection criteria are similar between VP and BKP in the reviewed publications. BKP has, however, been suggested to be advantageous in complex cases (e.g. several unfavourable factors or burst fractures).

Table 5 Recommendations made for vertebroplasty

Appropriate Use Criteria
- Recommended in patients with positive MRI, time since fracture ≥ 6 weeks and no spinal deformity [21]
- Recommended in patients who have failed or cannot tolerate conservative or traditional management [22]

Guidelines and technology assessments
- Recommend against VP for patients who present with OVCF on imaging with correlating clinical signs and symptoms and who are neurologically intact (AAOS strength of recommendation: strong, based on 5 studies) [40]
- Recommended as options only in people who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management and in whom the pain has been confirmed to be at the level of the fracture by physical examination and imaging (type of evidence not specifically stated) [42]
- Should be limited to patients whose pain is refractory to more conservative treatment [47]
- Not recommended as first-line treatment [48]

Systematic literature reviews and meta-analyses
- No role in the treatment of OVCF in routine clinical care (based upon moderate quality evidence) [50]

Discussion

Despite the significant burden of OVCFs, there are currently no universally accepted treatment pathways for this condition. Of the two main treatment options, which are NSM (conservative) and VAP, conservative therapy is considered by many as the first-line treatment option, see e.g. [22, 48, 49, 59]. This is mainly due to the fact that conservatively treated OVCF patients had sufficient pain relief within a couple of weeks [8, 9]. However, conservative treatment fails in a significant number of patients who continue to experience severe pain [10], which is when VAP may become a relevant treatment alternative. This paper reviewed and summarised the available literature on appropriateness criteria in the treatment of OVCFs to assess whether patient groups that may benefit the most from either NSM or VAP can be identified. To give an idea of possible conflict of interest, we have looked at type of publication and publisher. For example, one could presume that spine societies might have a subconscious bias to have a more favourable view toward spine interventions. However, we did not identify any noticeable bias linked to either type of publication or publisher.

Table 6 Recommendations made for balloon kyphoplasty

Appropriate Use Criteria
- Recommended in patients with ongoing fracture process [21]
- Recommended in patients with positive MRI and ≥ 1 other unfavourable factor [21]
- In complex cases (e.g. burst fractures with neuro-logical compromise) or fractures in which height restoration or deformity correction may be beneficial [22]

Guidelines and technology assessments
- Option for patients who present with OVCF on imaging with correlating clinical signs and symptoms and who are neurologically intact (AAOS strength of recommendation: limited, based on 5 studies) [40]
- Recommended for the treatment of recent (< 3 month old) OVCF confirmed by MRI [41]
- Recommended against the treatment of chronic (> 3 month old) osteoporotic, traumatic or pathologic vertebral compression fractures [41]
- Recommended as options only in people who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management and in whom the pain has been confirmed to be at the level of the fracture by physical examination and imaging [42]

Overall, there is a consensus that the majority of patients who have sustained an acute OVCF should be treated with NSM before other treatments are initiated. This is because the majority of patients with OVCF who are managed conservatively gradually improve. Primary candidates for conservative therapy include patients with negative imaging evidence of fracture and those who are not impaired by either severe pain, immobility or vertebral deformity [21, 39]. Controversy remains, however, about the length of a qualifying period of NSM before considering alternative treatment such as VAP, with suggested waiting time up to 6 weeks [39] or that "the appropriate timing in relation to the age of the fracture could be left for clinicians to judge" [42] . Although NSM is recommended in the first weeks after fracture, some evidence suggests that VP and BKP are most effective when completed within a few weeks of fracture [60].

The findings emerging from this review should be considered along with some limitations. The primary limitation is the lack of publications concerning treatment recommendations or appropriateness criteria for OVCF, possibly leading to heterogeneity among included studies meeting the pre-defined eligibility criteria. The study results could probably be improved by including more studies, e.g. non-English publications that may have been overlooked.

Another main limitation is the heterogeneity of patients and the heterogeneity of treatment recommendations in the included publications. Since the analysis is dependent on the quality of each of the individual studies, the accuracy and reliability of the pooled results in the source papers may have been influenced. This can probably be explained by limited clinical evidence of VAP, making the impact of expert judgement in each publication more important. An improved clinical evidence base for VAPs would be required to reduce the impact of opinion bias and provide better consistency between treatment recommendations and guidelines. One of the main reasons for variability in treatment recommendations is because the clinical data on the benefits and harms of VAPs compared to NSM or with each other is an area of controversy. For example, the two randomised controlled trials, comparing VP with a sham procedure involving the paraspinal injection of an anaesthetic, found no difference in terms of the primary outcome measure — pain relief [32, 34]. These studies, contradicting previous literature which was biased to favour VAP because of a

placebo effect, spurred debate and concerns among both physicians and payers regarding the effectiveness of VP and why these two studies differed from the vast majority of the previous literature [61–66]. Thus, improving the understanding of the effectiveness of VAP is the most important area for further research in this field.

Beyond the uncertainty related to the clinical effectiveness of VAP, another important area for further research is the appropriate timing of VAP and the appropriate patient selection. Currently, there is a clear gap between the study populations in the main VAP clinical trials (patients with recent fracture) and treatment recommendations (e.g. patients that fail NSM). Also, optimal treatment for OVCF may differ between subgroups (e.g. elderly, comorbidities, level of spine deformity).

There will undoubtedly be a continued role for NSM for most patients and the future emphasis will likely include a refined pathway that uses the best clinical evidence to provide treatment guidelines. The production and collection of high quality clinical data analysing the treatments for OVCFs is of importance and this should include well-designed RCTs as well as on-label studies and an OVCF treatment registry. The assimilation of a larger body of data will promote appropriate treatment of patients with OVCFs.

In conclusion, there is reasonably good agreement in the scientific community that NSM is considered appropriate for patients with low level of pain and during the first weeks since fracture, and that VAP is appropriate for patients suffering severe pain who do not tolerate medical treatment or who do not respond to conservative therapy in a given time frame. However, the evidence to support consensus about use of VAP is limited and it is still very difficult to predict which patients will fail pain management. More research is needed to adequately identify the appropriate patient that would benefit the most from VAP.

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Compliance with ethical standards

Conflict of interest F. Borgström is employed by and owns stock in Quantify Research AB, a contract research organisation within health economics and outcomes research. S. Luthman and J. Widén are employed by Quantify Research AB.

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