Management Pathway

Appropriate Management of Vertebral Fragility Fractures: Development of a Pathway Based on a Vertebral Compression Fracture Registry

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Background: The BenchMarket Medical (BMM) Vertebral Compression Fracture (VCF) Registry, now known as Talosix, is a collaborative effort between Talosix (the authorized registry vendor), Noridian Healthcare Solutions, and clinicians to gather outcomes evidence for cement augmentation treatments in patients with acute painful osteoporotic VCFs. The VCF Registry was designed to provide outcomes evidence to inform the Medicare payer's "coverage with evidence development" decision to authorize reimbursement for cement augmentation treatments.

Objectives: The purpose of this article was to present a pathway for appropriate use of vertebral augmentation based on the findings of the VCF Registry.

Study Design: Prospective observational data, including patient characteristics, diagnosis, process of care, and patient-reported outcomes (PROs) for pain and function, were collected from patients undergoing cement augmentation treatment. The PROs were collected at baseline, 1, 3, and 6 months following the procedure.

Setting: The VCF Registry is a national ongoing registry with no specified end time or designated sample size.

Methods: Primary outcomes were pain improvement measured using the Numeric Rating Scale and function improvement, measured using the Roland Morris Disability Questionnaire (RMDQ). Secondary outcomes included cement leakage, new neurologic deficits, adverse events, readmissions, and death.

Results: The VCF Registry delivered outcomes data to support Noridian's "coverage with evidence development" decision. A total of 732 patients were included in this study. Registry outcomes confirmed postmarket evidence of highly significant pain relief with mean pain score improvement of 6.5/10 points at 6 months. Function also improved significantly with mean RMDQ score change of 11.4/24 points 6 months after surgery. Results also showed the safety and reliability of cement augmentation.

Limitations: The nature of the registry data is that it contains nonrandomized, nonplacebo controlled data and should not be perceived as such. The real-world setting and the large number of patients within the dataset should increase the external validity of the findings.

Conclusions: Cement augmentation treatments of patients with acute painful VCFs reliably results in highly significant benefits of pain decrease and functional improvement for this Medicare population.

Key words: Vertebral compression fractures, osteoporosis, kyphoplasty, back pain, registry

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The management of acute or subacute symptomatic osteoporotic vertebral compression fracture (VCF) is somewhat controversial and has significant variability. Treatment includes use of bracing, opioid medications, activity modification, and interventional procedures, including cement augmentation (1,2). The development and implementation of registries for the study of processes of care and outcomes is a priority in the position statement on fragility fractures that was developed by the American Academy of Orthopaedic Surgeons, the American Orthopaedic Association, the Orthopaedic Trauma Association, and the International Geriatric Fracture Society to support optimal care of elderly patients (1). The purpose of this article was to present the outcomes of patients enrolled in the Talosix VCF Registry, and to form the basis for a pathway for the appropriate management of VCFs based on the registry findings.

The role of cement augmentation in the management of osteoporotic VCFs has been supported by multiple randomized controlled trials (RCTs) (3-12), meta-analyses (13,14), and registry outcomes (15,16). Other prospective clinical trials with sham controls have not demonstrated a significant advantage of vertebroplasty compared with placebo (17,18). Thus the literature regarding cement augmentation in the management of VCFs does not provide completely consistent guidance regarding the appropriate use of the procedure, and has a history of significant reporting bias by certain authors (19). The importance of developing a pathway for optimal care of VCFs is a well-recognized, clear priority for a growing aging population who are at high risk for suffering osteoporotic-related compression fractures VCFs (20,21).

Cement augmentation for VCFs represents an opportunity to use registry outcomes to assess and understand population health issues around VCFs. The VCF registry tracks comparable outcomes of various cement augmentation treatments to support the development of an evidence-based approach to appropriate care. Health care stakeholders, including patients, physicians, payers, purchasers, policy makers, and pharmaceutical and medical device manufacturers, are increasingly turning to prospective observational research (registries) to track safety, quality and efficacy of treatments, medical devices, and surgical procedures. Registry data can answer many population health questions and can compare the effectiveness of various treatments for a specific condition (i.e., VCFs).

Global interest in comparative effectiveness research is a response to evolving payer requirements for supporting evidence prior to providing coverage for authorized treatments. Increasingly, drug regulatory authorities, Health Technology Assessment Committees, and pricing and reimbursement authorities are using registry studies as the preferred methodology for evidence development. Registries embrace the normal heterogeneity of patients, conditions, and treatments. Registries track real-world practices and outcomes. Cost-effectiveness research produced by registries informs patients, physicians, and decision-makers of what works and what does not work for a specific condition or treatment.

Noridian Healthcare Solutions, the Medicare vendor in Jurisdictions E and F, and the authorized registry data vendor Talosix collaborated to design and implement the VCF Registry in response to the Noridian Healthcare Solutions Local Coverage Determination (LCD) released in April of 2014, which specified requirements for VCF treatment authorization. The strengths of the registry have been mentioned and are expounded later in the text. This collaborative prospective observational VCF Registry provides the payer data to support "coverage with evidence development" and to support continued access to cement augmentation treatments for this vulnerable population. The purpose of this article was to report the outcomes of patients included in the Talosix VCF Registry, and to support an evidence-based approach to appropriate care of osteoporotic compression fractures.

Methods

Database

The VCF Registry is a prospective observational study, which evolved from a collaboration between Noridian Healthcare Solutions, Talosix, and clinicians caring for patients with VCFs. The LCD released in April 2014 required treating clinicians to comply with payer data requests around authorization and reimbursement for cement augmentation treatments of VCFs. The VCF Registry was developed in 2014 with the primary purpose to provide a structured, easy-to-use format for medical providers to accurately submit information required by the LCD implemented by Noridian Health Services. Clinical evidence submissions around authorization and outcomes of cement augmentation treatments were required by the VCF LCD. Compliance with clinical evidence submission qualified the patient

for treatment authorization review by Noridian. The LCD was designed to allow a decision for authorization for care under a "coverage with evidence development" determination. Authorization and coverage of cement augmentation treatments for painful, acute VCFs only occurred for qualified VCFs (22). The LCD outlined clinical and process of care parameters that had to be recorded and submitted, as well as patient-reported outcomes (PROs) at 1, 3, and 6 months postsurgery.

The VCF Registry is a national ongoing registry with no specified end time or designated sample size. Any clinician and/or clinical site that performs vertebral augmentation is able to participate in the registry. Participants range from small private practices to large hospital systems. The open-ended nature of the VCF Registry, with respect to sample, inclusion, and exclusion criteria, was chosen deliberately to provide data that most accurately reflects the outcomes of typical patients presenting with painful VCFs.

Because the primary objectives of the registry are to collect data to support reimbursement and/or return aggregate data to VCF treatment providers for their internal quality improvement initiatives, it was determined that the VCF Registry is subject to the HIPAA Privacy Rule but not the 45 CFR Part 46 (The Common Rule) and is not engaged in research as a primary activity.{AU: Please spell out CFR at first use as an abbreviation} The Business Associate and Data Use Agreement allows for deidentified datasets to be made available to third parties, and secondary analysis of a deidentified dataset does not constitute as human subjects research (23). Per CFR 45 46.102, human subjects are explicitly defined as identifiable private information. This study was determined to be exempt from human studies by the University of Washington institutional review board. However, all third party users are responsible for seeking appropriate determination of human subject research through their respective institutional review boards.

All clinical site participants are provided with an enrollment packet that contains a registry overview, a Business Associate Agreement, a Data Services Agreement, and a site registration form. An online training session with designated clinical site personnel is completed with Talosix. This session provides training regarding the use of the Talosix web-based, HIPAA-compliant registry platform through which patients are enrolled and data are recorded. On completion of the training session, Talosix creates secure user accounts for each clinical site user, with unique login credentials. In addition to training regarding the data collection process, clinical sites are provided with a narrative that can be used to explain the registry to patients and, specifically, the PROs component of the registry.

The PRO surveys are conducted by Talosix via telephone calls to the patients at 1, 3, and 6 months postsurgery. A minimum of 4 contact attempts are made at each time point as per the requirements of the Noridian Healthcare Solutions LCD. The collaborative data requirements of Noridian's LCD included baseline patient characteristics, diagnosis, process of care elements, and outcomes surveillance. The PROs collected included pain and function. Pain was assessed by the Numeric Rating Scale (NRS-11; 0 = no pain, 10 = most severe pain) and the function was assessed using the Roland Morris Disability Questionnaire (RMDQ; 0–24, 0 = no disability, 24 = maximal disability). Treatment alternatives were at the discretion of the clinician and the procedures were tracked for adverse events and outcomes.

Study Design and Analysis

Data for this study were obtained from 10 sites nationwide that enrolled patients between July 12, 2014 and November 30, 2017. The last follow-up date was June 30, 2018. Patients were included in the registry database if they completed baseline and had at least one follow-up PRO assessment within 6 months after surgery. The primary outcome variables were pain and disability improvement from baseline at 6 months. We also reported a minimal clinically important difference (MCID), which was defined as a change of ≥2 points from baseline on the NRS-11 for pain, and ≥5 points from baseline on the RMDQ for function (24). Secondary outcome variables were cement leakage, new neurologic deficit, adverse events, hospital readmission, and death.

Patient characteristics were summarized using means and standard deviations (SDs) for continuous variables, and frequency distributions for categorical variables. Median and mean PROs were reported at baseline and each follow-up time point along with their corresponding interquartile ranges. All analyses were performed using Stata version 14 (StataCorp LP, College Station, TX).

Results

Demographics

One thousand ninety-six patients with osteoporotic vertebral fractures were included in the database. Only 732 of these had baseline PROs and one or more completed follow-up surveys. Follow-up surveys were

available at 1, 3, and 6 months in 69%, 66%, and 45% of patients who had baseline data, respectively (Tables 1 and 2). Women accounted for 72% of patients. The mean age was 78.1 (SD 10.5), and age ranged from 39 to 101 years.

The most common treated levels centered at the

Table 1. *Patient characteristics*.

Characteristics		n (%)
n		732
Age, mean (SD)		78.1 (10.5)
Female		529 (72.3%)
Dialysis	No	363 (49.6%)
	Yes	3 (0.4%)
	Missing	366 (50.0%)
Steroids use	No	275 (37.6%)
	Yes	91 (12.4%)
	Missing	366 (50.0%)
Smoking history	Current smoker	45 (6.1%)
	Former smoker	143 (19.5%)
	Never smoked	166 (22.7%)
	Unknown	378 (51.6%)
Osteoporosis	No	86 (11.7%)
	Yes	451 (61.6%)
	Missing	195 (26.6%)
Osteoporosis medications (among those with osteoporosis)	Bisphosphonates	51 (11.3%)
	Anabolic agent: parathyroid hormone	6 (1.3%)
	Calcium w/ vitamin D	166 (36.8%)
	Calcium w/o vitamin D	17 (3.8%)
	Vitamin D only	55 (12.2%)
	Other	12 (2.7%)
	None	206 (45.7%)
Routine back pain	No	242 (33.1%)
	Yes	489 (66.8%)
	Missing	1 (0.1%)
Failure of conservative medical management for back pain	No	114 (15.6%)
	Yes	616 (84.2%)
	Missing	2 (0.3%)
Received nonoperative treatment	No	23 (3.1%)
	Yes	530 (72.4%)
	Missing	179 (24.5%)
Other degenerative spine disease	No	195 (26.6%)
	Yes	338 (46.2%)
	Missing	199 (27.2%)
Procedure technique	Balloon kyphoplasty	419 (76.9%)
	Cavity creation	342 (62.8%)
	Other technique	12 (2.2%)
	Vertebroplasty	75 (13.8%)
	Missing	187 (25.5%)

Table 2. *Primary outcomes.*

	Baseline	1 month	3 months	6 months
Number of patients	732	505	481	332
NRS-11, median (IQR)	9.0 (8.0, 10.0)	2.0 (0.0, 5.0)	1.0 (0.0, 4.0)	0.0 (0.0, 4.0)
RMDS, median (IQR)	21.0 (18.0, 22.0)	12.0 (6.0, 16.0)	9.0 (3.0, 14.0)	7.0 (3.0, 12.0)
Percent achieving MCID improvement in NRS-11 from baseline		438 (86.7%)	430 (89.4%)	293 (88.3%)
Percent achieving MCID improvement in RMDS from baseline		364 (72.1%)	394 (81.9%)	282 (84.9%)

IQR, interquartile range.

thoracolumbar junction (T11-L2). Treated levels spanned from T1 to L5 and there were few treated VCFs above T7. Prior to cement augmentation, nonoperative treatment was attempted in 96% of patients. Prior to vertebral fracture, 451 (84%) patients who responded to the osteoporosis question had a diagnosis of osteoporosis. Of these patients, 51 (11%) were prescribed bisphosphonates and 6 (1%) teriparatide. Calcium supplementation with vitamin D was used in 166 (37%) patients and without vitamin D in 17 (4%). Vitamin D without calcium supplementation was used in 55 (12%) patients.

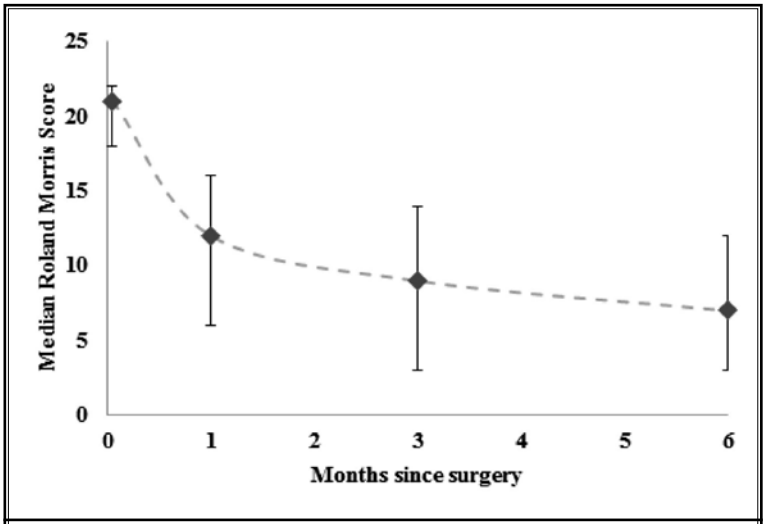

Fig. 1. *Primary outcome of function as measured by the median RMDQ at baseline and at 1, 3, and 6 months following treatment. Error bars represent interquartile range.*

Primary Outcomes

The median Roland Morris Disability Questionaire (RMDQ) at baseline was 21. Postoperatively, the median disability score was 12, 9, and 7 at 1, 3, and 6 months, respectively. The improvement from baseline was statistically significant ($P < 0.001$) at all time points (mean change: 8.5 at 1 month, 10.8 at 3 months, 11.4 at 6 months) (Table 2; Fig. 1). Proportions of patients achieving an MCID improvement in the RMDQ were 72%, 82%, and 85% at 1, 3, and 6 months, respectively.

The median pain NRS-11 was 9 at baseline. Postoperatively, the median pain score was 2, 1, and 0 at 1, 3, and 6 months, respectively. The improvements from baseline were statistically significant ($P < 0.001$) at all time points (mean change: 5.8 points at 1 month, 6.4 at 3 months, and 6.5 at 6 months) (Table 2; Fig. 2). Proportions of patients achieving at least an MCID improvement in the NRS-11 were 87%, 89%, and 88% at 1, 3, and 6 months, respectively.

Secondary Outcomes

Adverse events during index hospitalization related to the procedure (Table 3) were rare and occurred in 2 of 365 patients. No patients experienced new neurologic deficits after the procedure. Cement leakage was reported in 24% of patients. Four of 732 (0.5%) patients died at index hospitalization but were unrelated to the cement augmentation procedure. Hospital readmissions after cement augmentation occurred in 26 of 505 (5%) patients within 1 month, in 38 of 418 (8%) patients within 3 months, and in 53 of 332 (16%) patients within 6 months. Hospital readmissions were calculated cumulatively so that each follow-up time point considers prior readmissions.

Discussion

The treatment of patients with painful VCFs with cement augmentation has been performed for over 35 years and, in addition to clinical experience, there have been high-quality RCTs and meta-

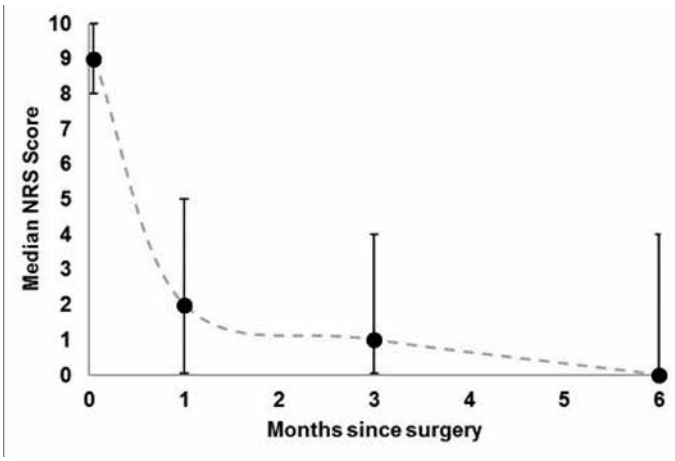

Fig. 2. *Primary outcome of pain as measured by the NRS-11 at baseline and at 1, 3, and 6 months following treatment. Error bars represent interquartile range.*

analyses supporting both vertebroplasty and kyphoplasty (4-14). Mortality has also been shown to lessen in patients with VCF who are treated by cement augmentation (15). Despite the copious amount of supporting data, conflicting results from 2 sham RCTs have created confusion as to indications and value of these treatments (17,18). The pain and function improvements documented in this study are impressive and sustained. This is the largest study that documents the real world beneficial results of cement augmentation for VCFs. Safety of cement augmentation was also adequately demonstrated.

In addition to the level I and II evidence and the meta-analyses on vertebral augmentation, there has also been a recent publication providing the only as-treated on-label vertebral augmentation evidence that reports a significant reduction of pain and improved function and quality of life for Medicare patients (14). In this postmarket study, there was also a significant improvement in the patient's ability to provide self-care and a significant reduction in pain medication usage. This trial reported statistically significant improvements for all primary endpoints and all measured secondary endpoints at every measured time point throughout the entire study (14).

Notwithstanding this high level of evidence, there remains a paucity of well-designed and well-implemented prospective observational trials (registries) that are well maintained and involve representative patient populations. There are some registries that have been used to show basic safety and efficacy data (16), as well as to illustrate some modifiable factors that can improve vertebral augmentation outcomes (25) but data from larger longitudinal analyses from well-designed registries are not well represented in the literature.

The magnitude of pain relief found in this registry data compares very favorably to recent RCTs and meta-analyses. The NRS-11 score reduction (Table 2) is profound and represents a real-world result from patients treated in uncontrolled and heterogeneous ways. The results of this study are similar to results of RCTs, such as the FREE trial and the Vertos II trial, which showed 3.5 and 5.7 point reductions in pain respectively (8,26). The registry pain reduction scores also compare very favorably to recent meta-analyses from Gu et al (4) and Papanastassiou et al (5), which showed mean pain reduction scores of 5.1 and 4.55, respectively.

The mean reduction of disability scores (Table 2) was equally impressive. In the FREE trial and in Vertoss II the mean reductions in RMDQ were 8.0 and 9.6, respectively. The mean reductions in disability in the Gu et al (4) and Papanastassiou et al (5) meta-analyses when converted to percentage reductions were 17.7% and 36.3% compared with 48% reduction in disability for all patients within the registry.

Data and results from RCTs and meta-analyses have long been regarded as the primary basis of assessing treatment effect. Although this is appropriate, it also should be considered that these are specific treatments rendered by specific providers in a specific way and guided by a specific protocol with various inclusion and exclusion criteria. The same treatment provided across the eligible patient population is dissimilar and nonspecific to the treatment provided in RCTs. Therefore other methods of assimilating evidence must weigh into the body of information necessary to assess a particular treatment or types of treatments.

The registry data results not only compare favorably with the results from prominent RCTs and high-quality meta-analyses, these exceed the magnitude of improvements in pain, function, and disability of previously reported results. These also exceed observational data previously reported from the Swiss registry by Hübschle et al (26) who reported a 4.0-point reduction in pain that remained present up to 1 year.

Table 3. *Adverse events and hospital readmissions after vertebral augmentation.*

Adverse events, readmissions	Total N	Number of events (%)
During index hospitalization:		
Cement leak detected	546	133 (24.4%)
New neurologic deficit related to procedure	554	0 (0%)
Adverse events related to the procedure	365	2 (0.5%)
Death	732	4 (0.5%)
Readmission		
Within 1 month	505	26 (5.1%)
Within 3 months	481	38 (7.9%)
Within 6 months	332	53 (16.0%)

1. Contains uniform standardized definitions, metrics, PROs, and real-world data.
2. Demonstrates consistent data collection.
3. Accommodates the heterogeneity of the population and variations in treatments.
4. Delivers robust analytics for comparative effectiveness research.
5. Is considered a trusted source by the primary participants in health care for what works and does not work for the treatment of VCFs.

The vast majority of the body of literature for cement augmentation reports significant improvements in pain, function, and quality of life when comparing cement augmentation with nonsurgical management (NSM) (4,5,7), but these improvements have not been compared with the real-world results of prospective observational trials nearly as often. The results from this registry reported significant improvements in pain and function that are at least as good or better than the results of the best quality RCTs, and these results may be a better representation of the type of outcomes that patients receive when they are treated in the various types of practices around the country. The registry data demonstrates significant improvement in every domain of health status measured and supports a pathway of early treatment of VCFs with cement augmentation.

Strengths and Weaknesses

The nature of the registry data are that these studies contain nonrandomized, nonplacebo controlled data and should not be perceived as such (Table 4). The real-world setting and the large number of patients within the dataset should increase the external validity of the findings. This registry data may also be used in assessing other outcomes as well. The indications for cement augmentation was well defined and controlled by insurance approval processes. Patients had imaging demonstrating acute or subacute fractures and concordant physical examination pain, and over 95% had some attempted nonoperative care. Limitations are similar to other registry investigations, including the risk of confounding and bias. Follow-up was inadequate after 3 months. Further we did not evaluate any radiographic studies to independently assess results. Adverse events were self-reported, and therefore likely to be underreported although insurance data were available to identify significant complications.

Several observations regarding population health were identified. After VCF, all of these patients would be considered to have osteoporosis by current guidelines, American Association of Clinical Endocrinologists (AACE). However, only 84% of patients had a prior diagnosis of osteoporosis, although the majority of those patients were being treated with pharmaceutical agents. We believe that improved screening and primary treatment of osteoporosis are needed to prevent VCF, and thus the need for cement augmentation. Patients sustaining VCFs utilize health services as indicated by the hospital readmission rate of 5% within the first month. We do not know if these were related to the spine or other fractures. We believe that secondary fracture prevention programs, such as Own the Bone (American Academy of Orthopaedic Surgery), can reduce risk of secondary fractures, and thus further hospitalizations.

The use of a registry to assess PROs is unique. In the future, further efforts to improve follow-up and define adverse events are needed. As more patients are added, subgroup analyses evaluating risk factors for poor outcomes, recurrent fractures, and complications can be performed.

The VCF Registry delivered economic efficiencies

Table 4. *Talosix VCF Registry strengths and advantages.*

1. Contains uniform standardized definitions, metrics, PRO's, real world data
2. Demonstrates consistent data collection
3. Accommodates the heterogeneity of the population and variations in treatments
4. Delivers robust analytics for CER
5. Is considered a trusted source by the primary participants in healthcare for what works and does not work for the treatment of VCF's

for the clinical practices, reliable compliance with payer evidence needs, and real-time reporting of PROs for the clinicians via a dashboard statistic. Registry enrollment provided clinicians the assurance that they would avoid claw back of payments for those deemed to be non-compliant with the evidence requirements.

Conclusions

The VCF Registry delivered validated outcomes data in support of a "coverage with evidence development" decision. This registry data platform accommodated the heterogeneity of VCF disease and allowed the heterogeneity in treatments to be accurately measured. The VCF Registry contained standardized definitions, outcomes metrics, and time points for surveillance. Consistent data collection permitted robust analytics for comparative effectiveness research. Cement augmentation for VCFs resulted in highly significant improvements in pain and function scores for this vulnerable population. Further, registry enrollment was shown to demonstrate "real-world" outcomes and deliver impactful insights for all personnel involved in the treatment process.

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