Dipeptidyl peptidase 4 inactivates the proinflammatory peptide substance P that is released by sensory nerve fibers of the nasal mucosa during neurogenic inflammation. In pigs, the administration of recombinant DPP4 considerably attenuated the proinflammatory effect of histamine and capsaicin that causes the release of substance P, as well as the effect of substance P itself. Therefore, DPP4 should be considered as a modulator of the proinflammatory action of substance P.

The review by Amori et al also found a higher incidence of headaches in patients treated with gliptins but did not note whether these patients were the same as those who developed nasopharyngitis. Headache is a major symptom in chronic sinusitis in association with mucosal congestion and decreased sinus drainage. Furthermore, substance P is hypothesized to have a key role in certain forms of headache. These data suggest that DPP4 may play a significant role in the development of inflammatory processes in the upper airway mucosa. Consequently, it would be important to evaluate potential disadvantages of DPP4 inhibitor use in patients with diabetes who have chronic sinusitis and headache.

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Financial Disclosures: Dr Grouzmann reports receiving honoraria for consulting from Novartis and Phenomix. No other disclosures were reported.


In Reply: The findings previously reported by Dr Grouzmann and colleagues regarding DPP4 activity in nasal tissues and the effect of DPP4 on substance P in patients with chronic rhinosinusitis provide a potential explanation and support for our clinical findings of increased risk of nasopharyngitis and headache in patients with type 2 diabetes treated with DPP4 inhibitors. In our review, we included only publicly available data from the published literature, which did not specify whether there was overlap among patients reporting nasopharyngitis and headache. Therefore, we cannot determine whether, in patients treated with DPP4 inhibitors, headache is a component of nasopharyngitis or if it constitutes a distinct clinical entity. We agree that it would be reasonable for clinicians to be cautious when using DPP4 inhibitors in patients with chronic rhinosinusitis or headache.

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Financial Disclosures: None reported.

RESEARCH LETTER

Thoracic and Lumbar Vertebroplasties Performed in US Medicare Enrollees, 2001-2005

To the Editor: Percutaneous vertebroplasty involves the vertebral injection of polymethylmethacrylate cement. Although some indication that this procedure is safe and effective for treating osteoporotic compression fractures exists, the US Medicare program promulgated no national coverage policies for this procedure after reviewing the available nonrandomized evidence. Nevertheless, local Medicare contractors in multiple jurisdictions have covered vertebroplasty for various indications since at least 2001. We examined vertebroplasty-use patterns in Medicare patients for 2001-2005.

Methods. Using vertebroplasty-related Current Procedural Terminology, 4th Edition (CPT-4), codes 22520 (primary thoracic vertebroplasty) and 22521 (primary lumbar vertebroplasty), we performed cross-sectional analyses of aggregate 2001-2005 fee-for-service data from the Medicare all-age Part B Extract Summary System, which excludes denied claims and claims for Medicare managed care enrollees. Annual primary vertebroplasty rates (which exclude additional vertebral levels also treated) were therefore expressed per 100 000 Part B fee-for-service enrollees.

Part B Extract Summary System data are cross-stratified by the billing physician’s reported specialty and by the listed place of service. We grouped physician specialties into 5 categories: diagnostic or interventional radiology, orthopedic surgery, neurosurgery, anesthesiology or pain management, and other (including neurologists, physiatrists, internists, emergency department physicians, physi-
cians identified only as members of multispecialty groups, and nonphysicians). We grouped places of service into 4 categories: inpatient hospital settings, outpatient hospital settings, physicians' offices, and ambulatory surgery centers.

Because we analyzed data on 100% of known cases, inferential statistics were not required. This study received institutional review board approval.

Results. Vertebroplasty rates nearly doubled from 2001 to 2005, increasing by 32.3% from 2001 to 2002 alone (Table). However, 2005 rates were only 5.0% higher than those from 2004.

Most procedures were performed by diagnostic or interventional radiologists (Table). The proportion performed by anesthesiologists or pain management specialists increased from 4% to 5% during 2001-2004 to 7.1% in 2005; the proportions performed by other specialties remained stable or declined.

Although outpatient hospital settings were the most common treatment sites, the proportions of procedures performed in physician offices and ambulatory surgery centers increased markedly in 2004-2005 (Table) with varying mixtures of specialist intervention. For example, among office-based procedures from 2005, 37.2% were performed by radiologists, while anesthesiologists or pain management specialists performed 35.9%, and orthopedists performed 19.7%. Among ambulatory surgery center procedures from 2005, anesthesiologists or pain management specialists performed 50.5%, while radiologists performed 37.2% and orthopedists performed 18.8%.

Comment. Most of the observed growth—rates nearly doubled from 2002 to 2005—preceded the US Food and Drug Administration's approval of polymethylmethacrylate cement use for vertebroplasty in December 2004. Growth may better reflect factors including shifts in clinical opinion, patient demand, Medicare coverage policies, and the availability of vertebroplasty relative to that of other treatment approaches. The overall increase in outpatient vertebroplasty may mirror earlier trends seen in the growth of outpatient lumbar spine surgery.

Limitations of our data included a lack of clinical and demographic detail and the potential for coding errors. However, with the exception of transient shortfalls, Medicare claims data may be generally concordant with other population-based clinical procedure data. For example, cataract-procedure volume concordance with record-based data from the Rochester Epidemiology Project was nearly 96% when excluding a circumscribed data shortfall period. Our inability to capture denied claims, those for patients with Medicare managed care or Part A coverage alone and for vertebroplasties billed as “unspecified procedures,” makes our vertebroplasty volume data conservative. However, if such cases decreased over time, then we may have overestimated the actual growth of vertebroplasty use. Our data may not apply to Medicare managed care or non-Medicare populations with differing clinical presentations. Finally, available CPT-4 codes did not capture volumes of competing alternative procedures (eg, kyphoplasty).

Nevertheless, the increase in the volume of vertebroplasty procedures seen in our study is noteworthy given the expected contribution of the Medicare population to vertebroplasty volumes. This increase, especially regarding procedures performed in nonhospital settings, has uncertain clinical and resource use implications and argues for close tracking of future vertebroplasty practice patterns and outcomes.

Table. Primary Vertebroplasty Procedures From 2001-2005 Among Medicare Part B Fee-for-Service Enrollees, 2001-2005

<table>
<thead>
<tr>
<th>Specialty</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 14 142)</td>
<td>(n = 19 341)</td>
<td>(n = 24 556)</td>
<td>(n = 27 549)</td>
<td>(n = 29 090)</td>
</tr>
<tr>
<td>Rate per 100,000 Part B fee-for-service enrollees</td>
<td>45.0</td>
<td>59.5</td>
<td>74.9</td>
<td>82.8</td>
<td>86.8</td>
</tr>
<tr>
<td>Specialty</td>
<td>2001</td>
<td>2002</td>
<td>2003</td>
<td>2004</td>
<td>2005</td>
</tr>
<tr>
<td>Diagnostic or interventional radiology</td>
<td>9863 (69.7)</td>
<td>14 124 (73.0)</td>
<td>18 422 (75.0)</td>
<td>21 387 (77.6)</td>
<td>22 215 (76.4)</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>1789 (12.7)</td>
<td>2346 (12.1)</td>
<td>2834 (11.5)</td>
<td>2529 (9.2)</td>
<td>2485 (8.5)</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>1035 (7.3)</td>
<td>1386 (7.2)</td>
<td>1615 (6.6)</td>
<td>1653 (6.0)</td>
<td>1805 (6.2)</td>
</tr>
<tr>
<td>Anesthesiology or pain management</td>
<td>742 (5.2)</td>
<td>920 (4.8)</td>
<td>1080 (4.4)</td>
<td>1383 (5.0)</td>
<td>2058 (7.1)</td>
</tr>
<tr>
<td>Otherb</td>
<td>713 (5.0)</td>
<td>566 (2.9)</td>
<td>605 (2.5)</td>
<td>597 (2.2)</td>
<td>527 (1.8)</td>
</tr>
<tr>
<td>Treatment site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient hospital settings</td>
<td>5932 (41.9)</td>
<td>8466 (43.8)</td>
<td>10 724 (43.7)</td>
<td>11 508 (41.8)</td>
<td>11 597 (39.9)</td>
</tr>
<tr>
<td>Outpatient hospital settings</td>
<td>7899 (56.6)</td>
<td>10 667 (55.1)</td>
<td>13 558 (55.2)</td>
<td>14 979 (54.4)</td>
<td>15 098 (51.9)</td>
</tr>
<tr>
<td>Physicians’ offices</td>
<td>173 (1.2)</td>
<td>151 (0.8)</td>
<td>194 (0.8)</td>
<td>757 (2.7)</td>
<td>1884 (6.5)</td>
</tr>
<tr>
<td>Ambulatory surgery centers</td>
<td>48 (0.3)</td>
<td>67 (0.3)</td>
<td>80 (0.3)</td>
<td>305 (1.1)</td>
<td>511 (1.8)</td>
</tr>
</tbody>
</table>

aData are presented as No. (%) except as noted. Percentages may not total 100% due to rounding.

bIncludes neurologists, physiatrists, internists, emergency department physicians, physicians listed only as members of multispecialty groups, and nonphysicians.

Includes the less than 1% of all cases that were coded as being performed in emergency departments, skilled nursing facilities, urgent care facilities, comprehensive inpatient or outpatient rehabilitation facilities, or other unlisted facilities or at home.
Author Contributions: Dr Gray had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gray, Jarvik.

Acquisition of data: Gray, Onwudiwe.

Analysis and interpretation of data: Gray, Hollingworth, Onwudiwe, Deyo, Jarvik.

Drafting of the manuscript: Gray, Hollingworth.

Critical revision of the manuscript for important intellectual content: Gray, Hollingworth, Onwudiwe, Deyo, Jarvik.

Obtained funding: Deyo.

Administrative, technical, or material support: Onwudiwe, Deyo, Jarvik.

Study supervision: Gray.

Financial Disclosures: None reported.
Poisson regression models by practice site. Di Comite and Rossi also suggest that we investigate the effects of anti–TNF-α medications on the incidence of diabetes in our patients with rheumatoid arthritis. We found no difference in these rates based on anti–TNF-α exposure. A total of 526 patients with rheumatoid arthritis reported use of at least 1 anti–TNF-α agent, for a total of 1776 person-years of exposure to an anti–TNF-α drug. Using a Cox time-varying regression model with adjustment for age, sex, race, year of study entry, duration of rheumatoid arthritis, body mass index, Health Assessment Questionnaire disability index, use of methotrexate and hydroxychloroquine, use of prednisone (yes/no), and study site, the hazard ratio for developing diabetes in patients with rheumatoid arthritis treated with anti–TNF-α medications (etanercept, infliximab, or adalimumab) was 1.05 (95% confidence interval, 0.50-2.21; P = .89). This may be due to the limited person-years of observation for patients taking anti–TNF-α medications during this study. Alternatively, it may indicate no difference in diabetes incidence associated with the use of these drugs.

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Financial Disclosures: Dr Wasko reported being a consultant to Centocor in cardiovascular outcomes in ongoing rheumatoid arthritis clinical trials; having been a consultant to Roche in the relationship between inflammatory cytokines and cardiovascular disease; having been a coinvestigator in a Merck-sponsored study of thromboembolic markers in rheumatoid arthritis and osteoarthritis; receiving contractual reimbursement as site principal investigator for an Aventis-sponsored clinical trial of leflunomide in rheumatoid arthritis, ending in November 2002; serving on the speakers bureau for Bristol-Myers Squibb; and receiving contractual reimbursement as site principal investigator for rheumatoid arthritis clinical trials sponsored by Centocor, Roche, Human Genome Sciences, and Novartis. No other authors reported financial disclosures.


CORRECTION

Incorrect Date: In the Research Letter entitled “Thoracic and Lumbar Vertebroplasties Performed in US Medicare Enrollees, 2001-2005” in the October 17, 2007, issue of JAMA (2007;298[15]:1760-1762) an incorrect year range was published in the “Comment” section. The year range in the sentence that read “Most of the observed growth—rates nearly doubled from 2002 to 2005—preceded the US Food and Drug Administration’s approval of polymethylmethacrylate cement use for vertebroplasty in December 2004” should have been “2001 to 2005.”