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ARTICLE INFO

PURPOSE: To compare the accuracy of diagnostic CT-imaging and SPECT/CT imaging (using the CT for anatomical referencing only) for the purpose of assessing loosening of pedicle screws following lumbar fusion surgery using revision surgery and clinical follow-up as gold standard.

METHODS: This was a retrospective observational study on 36 patients with lumbar arthrodesis who were referred to our department for SPECT with diagnostic CT imaging because of post-operative recurrent or persistent low back pain. The sensitivity and specificity for loosening of the prosthetic material was calculated using clinical follow-up (> 1 year) or perioperative findings as gold standard.

RESULTS: Mean time from primary surgery to SPECT/CT was 49.8 months (range: 7-270 months). Mean follow-up time for the 30 patients that did not undergo revision surgery was 28 months (range: 12-48 months). The prevalence of loosening of the lumbar fusion material was 16.7 %. Diagnostic accuracy was 94.4% for SPECT (using the CT for anatomical referencing only) and 97.3% for diagnostic CT-imaging. ROC-curve analysis for both techniques yielded an AUC-value of respectively 0.9 for SPECT and 0.92 for CT, which proved not significantly different from each other (p= 0.87). When using positive imaging findings for loosening on either one of the two imaging modalities as indicative of loosening (combined SPECT/diagnostic CT imaging), sensitivity increased from 83% for either imaging modality alone to 100% while specificity remained high at 97%

CONCLUSIONS: Combined SPECT/diagnostic CT-imaging increased sensitivity for pedicle screw loosening from 83% for either imaging-modality alone to 100%, while maintaining a high specificity of 97%. Given the overall relatively low prevalence of loosening of pedicle screws as evidenced by this and other studies in this patient population presenting with post-operative lumbar pain, the reported potential of combined SPECT and diagnostic CT imaging for the purpose of identifying pain generators other than pedicle screw loosening warrants further prospective exploration.

Keywords: pedicle screw loosening-SPECT-diagnostic CT

ABSTRACT

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INTRODUCTION:
Pedicle screw fixation is widely used in spine surgery as part of lumbar inter-body fusion as it reduces the range of motion of the stabilized spine, increases the fusion rate and is generally considered to be safe with a relatively low complication rate associated with the device (1,2). Disease processes that have been treated with pedicle screw fixation as part of lumbar inter-body fusion include discogenic back pain, recurrent disc herniation, spondylolisthesis, spinal instability, scoliosis, sagittal plane instability syndrome and spondylosis (3,4).

Pedicle screw loosening is a common complication following spinal arthrodesis, potentially leading to pseudarthrosis and possible surgical re-intervention (5,6,7). Reported rates of pedicle screw loosening in literature have varied from 0.6-27% (1,5-7). Given patient-outcome following surgical re-intervention is poorer than with primary surgery, accurate non-invasive identification of those patients most likely to benefit from re-intervention is critical. Currently, non-invasive diagnosis of pedicle screw loosening is largely CT based, using a lucency rim around the screws that exceeds 2 mm or that has increased in size as a sign of loosening (8,9). However, it has been suggested that because of the presence of non-specific post-operative changes and the presence of metallic artefacts, CT-imaging of pedicle screw loosening may be suboptimal (10,11). As compared to CT imaging, bone scintigraphy with SPECT (single photon emission computed tomography) is not affected by metallic devices. Furthermore the specificity of SPECT-imaging has significantly improved with the advent of hybrid imaging, due to more accurate anatomical information. Thus our group previously performed a retrospective analysis of SPECT/CT imaging findings performed for the purpose of evaluating loosening of fusion hardware in a series of 48 patients, finding a diagnostic accuracy of 92% for SPECT/CT imaging. However in this series, CT examinations performed were non-diagnostic, low-dose CTs, and thus the study did not allow a direct comparison of diagnostic CT and SPECT-findings. In this retrospective study, we report on the direct comparison of diagnostic CT-imaging and SPECT imaging findings in a series of 36 patients that underwent SPECT/Diagnostic CT imaging for the purpose of assessing hardware loosening following lumbar fusion with pedicle screws.

PATIENTS AND METHODS

PATIENTS
This retrospective study was approved by the Ethics Committee of our hospital, AZ Groeninge. Given patient data were anonymised, no written informed consent was required. A total of 52 patients presenting with low back pain after lumbar arthrodesis that were specifically referred for evaluation of the fusion material underwent a bone SPECT/CT scan with a standard-dose CT protocol in our centre between September 2014 and September 2019. Out of these, patients that had undergone revision surgery as well as patients that had been in follow-up following their SPECT/CT examination for at least one year were included in the study. Patients were evaluated clinically and by radiography following their initial surgery until the surgeon decided to refer them for bone SPECT/diagnostic CT imaging due to persistent or recurrent pain suspicious for pedicle screw loosening.

METHODS
Bone SPECT/CT (diagnostic) images were acquired three hours after intravenous injection of 740 MBq technetium-99m hydroxymethylene diphosphonate on a GE Optima NM/CT 640 (GE Healthcare, Milwaukee, WI, USA) gamma camera (two detectors equipped with low-energy/high-resolution collimators, 128x128 matrix, 180° rotation with 60 projections of 20s). Diagnostic bone CT scans were acquired per specifications by the CT-vendor. Bone scintigrapies were evaluated by two experienced nuclear medicine physicians (MA and CVDW). Acquired images were carefully evaluated for misalignment between SPECT and CT data and, if necessary, realigned using commercially available software. CT- data were used for anatomic localisation only by the nuclear medicine physicians. Lesions indicative of loosening on SPECT were defined as markedly elevated activity (compared to background) at typical anatomical sites of hardware loosening: the
tip of the screws, along the screw shaft or at the entry points of the screws. Differences in interpretation were resolved by consensus.

Diagnostic CT-scan were evaluated by two experienced radiologists (VF and VDS). Loosening was identified as a lucency rim of 2 mm or greater around the screw on CT. Differences in interpretation were resolved by consensus. The results of the bone scan and the CT were separately compared to the gold standard of surgical evaluation of the stability of the fusion material when applicable. If no surgical evaluation was performed, results were compared to the clinical follow-up, equal to or exceeding one year in duration in all patients. The diagnosis of loosening on bone scan or CT was considered as true positive when the surgeon confirmed the presence of loose screws perioperative or if clinical and other examinations were completely consistent with the positive SPECT or CT findings. They were considered false positive if the fusion hardware was still firmly attached or if symptoms subsided with non-surgical therapy. Patients with negative imaging and tight screws perioperative or with a stabilization or decrease of their symptoms during a minimal clinical 12 months follow-up period, were considered as true negatives. Finally, if imaging findings were judged negative and subsequent surgery was still required demonstrating loosening of the pedicle screws, findings were determined to be false negative.

Aside from positive or negative evaluation of loosening of the fusion material, other findings in the lumbar spine were noted; we evaluated if any of the other abnormal findings on SPECT or CT could possibly explain the complaints.

**RESULTS**

There were 16 men and 20 women with a median age of 55.5 years (range: 32-85 years). Mean time from primary surgery to SPECT/CT was 49.8 months (range: 7-270 months). Six patients underwent revision surgery whereas in 30 patients diagnosis was established through long-term clinical follow-up. Mean follow-up time in the latter patient group was 28 months (range: 12-48 months)).

According to the gold standard used, the prevalence of loosening of the lumbar fusion material in our patient population was 6 out of 36 patients, or 16.7%. All cases of loosening were confirmed through surgical intervention. Loosening was correctly identified by bone scintigraphy (using the CT-images for anatomical referencing) and diagnostic CT in 5 out of 6 patients. The patient that was missed on CT was different from the one whose loosening was missed by bone scintigraphy (see Figures 1 and 2). The 30 remaining patients did not suffer from pedicle screw loosening according to the gold standard used. Out of these, one patient was judged positive on bone scintigraphy (SPECT). Inversely, all of the 30 remaining patients were judged as negative by CT-imaging alone.
Figure 1. SPECT/CT findings in a patient showing a lucency around the screws in L1 (A and B (red circle)) indicative of loosening, whereas no significant tracer uptake was seen around the screws on SPECT images (C) and fused (D) images.
Figure 2. Whole body (A), SPECT (B) and SPECT/CT (C) findings indicative of loosening of the pedicle screws in S1 on SPECT as evidenced by increased tracer uptake along the screw shafts (red circles), whereas no bone resorption (lucency rim) around the screws was seen on the standard-dose CT scan (D).
Figure 3. ROC-curve analysis demonstrating a comparable AUC-value for diagnostic CT imaging and SPECT/CT using the CT data for anatomical localisation only.

Thus, the sensitivity of SPECT for identification of lumbar pedicle screw loosening was 83% and the specificity was 97%. The positive and negative predictive values (PPV and NPV) were 96.8% and 94.5%. Positive and negative likelihood ratios were 25.15 and 0.18, respectively. Overall diagnostic accuracy was 94.5%. The sensitivity of CT for the identification of lumbar loosening was 83% and the specificity was 100%. The positive and negative predictive values (PPV and NPV) were 100% and 96.2%. Positive and negative likelihood ratios were infinite and 0.17, respectively. Overall diagnostic accuracy was 97.3%. ROC-curve analysis for both techniques yielded an AUC-value of respectively 0.9 for SPECT and 0.92 for CT, which proved not significantly different from each other (p= 0.87) (see Figure 3). Using positive imaging findings for loosening on either one of the two imaging modalities as indicative of loosening (combined SPECT/diagnostic CT imaging), sensitivity was 100% and specificity 97%, NPV was 1.0 and PPV 0.86.

Positive and negative likelihood ratios were respectively 30 and 0. Diagnostic accuracy was 97.2%.

In the true negative group, both CT and SPECT showed no additional abnormalities that might explain their complaints in 5 patients. In an additional 5 patients, CT identified disc-arthritis or facet-joint arthrosis which proved not active on SPECT. In another 8 patients, CT findings proved negative whereas SPECT identified increased activity in facet-joints below or above the level of the arthrodesis. Finally, in the remaining 12 patients, CT identified extensive disc-arthritis and facet-joint arthrosis, of which a limited number of sites proved positive on SPECT.

DISCUSSION

The aim of this study was to compare the diagnostic accuracy of high-dose CT imaging and SPECT-bone scintigraphy/CT (using CT for anatomical referencing only) for the detection of pedicle screw loosening in patients who previously underwent lumbar fusion.
The use of radiography and CT-imaging in routine clinical practice for identifying screw loosening in patients that have undergone lumbar spine fusion is based on a limited number of publications showing that a radiolucent zone surrounding a pedicle screw is a potential sign of screw loosening. In a series of 21 patients by Sanden et al. in whom fixation material was removed from 11 to 16 months after implantation and in whom extraction torques of the screws were recorded, the mean maximum pull-out resistance for screws and the mean bone-to-screw contact was significantly lower in patients presenting with radiolucent zones on plain radiography, when compared to those without on conventional radiography (16+/− 10 Ncm versus 403+/− 220 Ncm; p < 0.0001) suggesting that a radiolucent zone is a good indicator of loosening of a pedicle screw (8). Using an unscrew torque cut-off of 40 Ncm, radiolucent zones could be separated from non-radiolucent zones with 100% accuracy. Furthermore, these authors additionally reported on an experimental study in a sheep model in which the mean maximum pull-out resistance for screws with radiolucent zones were significantly lower and did not overlap with those with no radioluency (p = 0.0006). Othori et al. and Abul-Kasim et al. subsequently showed that diagnostic CT imaging is more sensitive than radiography for detecting screw loosening (11,12). Comparing teriparatide and bisphosphonate treatment to reduce pedicle screw loosening following lumbar spinal fusion surgery in postmenopausal women with osteoporosis, Othori et al. found that at 12 months follow-up, the incidence of loosening of pedicle screws as assessed by conventional radiography versus CT was 7% versus 13% in the teriparatid group (20 patients), 13% versus 26% in the resildronate group (20 patients) and 15% and 25% in the normal control group (22 patients). In the series by Abul-Kasim, out of 81 patients suffering from adolescent idiopathic scoliosis that had undergone corrective surgery with pedicle screw constructs, at 2 years follow-up, pedicle screw loosening was observed in 11 patients on conventional radiography versus in 26 patients on diagnostic CT. Of interest, the latter two studies did not include an external standard to which radiography and CT-imaging was compared as is the case in the series presented, rather the incidence of peri-screw osteolysis on both imaging modalities was compared relative to each other. In the series presented, using a combination of at least 1-year clinical follow-up and surgical revision as gold standard, corresponding to current routine clinical practice, diagnostic CT imaging was capable of identifying screw loosening with a sensitivity of 83% and a specificity of 100%. These results compare favourably, to the only reported study including an external gold standard to which CT-imaging was compared, respectively intra-operative unscrew torque measurement by Spirig et al. (13). In their series, using a screw torque < 60 Ncm as cut-off, the reported sensitivity and specificity of peri-screw radiolucency findings on CT for screw loosening using was 64.8% and 96.7% versus 54.2% and 83.5% for plain radiography, suggesting CT as well as radiography are suboptimal imaging techniques for identification of screw loosening when compared to their gold-standard used. However, the cut-off of 60 Ncm used in their study was based on a questionable assumption of two normal distributions and is in sharp contrast with the cut-off of 40 Ncm reported by Sanden et al. allowing 100% separation of radiolucent from non-radiolucent peri-screw zones (14-18).

Damgaard et al. and Hudyana et al. have previously assessed the clinical value of SPECT combined with low dose, non-diagnostic CT imaging for the purpose of identifying screw loosening following lumbar fusion using an external gold standard (19,20). Damgaard et al. using surgical evaluation as gold standard, found bone SPECT/low dose CT to be true-positive in eight patients and false positive in one patient. Hudyana et al., using surgical evaluation and clinical follow-up as gold standard in a series of 48 patients found an overall sensitivity and specificity for the detection of loosening of 100% and 89.7% respectively, results comparable to those obtained in this series for SPECT, respectively 83% and 97% when using the diagnostic CT examination purely for anatomical referencing. In the series presented, false positive increased peri-screw tracer uptake was identified in only one patient, versus in 4 patients in the series by Hudyana et al. CT-findings in the latter patient proved negative. Markedly increased tracer-
uptake at the operative site following lumbar fusion surgery can be found up to 1 year post-op. However, all patients included in this study were referred for bone SPECT/CT imaging at least 12 months following primary surgery. Furthermore, a possible misalignment between the SPECT-images and CT-images could be ruled out in this patient.

When comparing the results obtained by SPECT and diagnostic CT-imaging for the purpose of identifying pedicle screw loosening, a comparable very high diagnostic accuracy was found, suggesting performing either one imaging modality would suffice. However, both imaging modalities alone would have missed 1 out of the 6 patients that were ultimately proven to suffer from pedicle screw loosening, whereas using positive imaging findings for loosening on either one of the two imaging modalities as indicative of loosening (combined SPECT/diagnostic CT imaging) resulted in a diagnostic sensitivity of 100% and an unaltered very high specificity of 97%. Furthermore, the prevalence of pedicle screw loosening in this study was 16.7%, indicating that other underlying causes than loosening were responsible for the post-operative lumbar pain in the majority of patients. The potential role of combined SPECT/CT imaging as a tool to identify the primary pain generator in patients suffering from degenerative spinal diseases has been previously addressed by Tender et al. (21). In their series, out of a total of 315 patients that had undergone diagnostic SPECT/CT imaging, 48 patients subsequently underwent either cervical or lumbar fusion of segments identified on SPECT/CT. Visual analogue pain scores at 6 months post-operatively were shown to significantly improve when compared to base-line values in these patients. Likewise, Brusko et al. reported similar results in a series of 23 patients (22). In their series, complete symptom resolution at 6-month follow-up was reported in 11 patients whereas at 1 year postoperatively, a significant relief of symptoms following surgery was found in 19 patients. In our series, CT identified disc-arthritis or facet-joint arthrosis that proved negative on SPECT in 5 patients and thus likely of no clinical relevance. Inversely, in another 8 patients, CT findings proved negative whereas SPECT identified increased activity in facet-joints below or above the level of the arthrodesis, potentially responsible for the complaints of the patients. Prospective studies on the complementary role of SPECT and CT imaging for the purpose of identify pain generators in this patient population are warranted.

CONCLUSION
Diagnostic CT-imaging and combined SPECT/CT with the CT data being used for anatomical localisation only (low-dose CT), have a comparable high accuracy for identification of pedicle screw loosening. However, using positive imaging findings for loosening on either one of the two imaging modalities as indicative of loosening (combined SPECT/diagnostic CT imaging) resulted in an increase of sensitivity from 83% for either imaging modality alone to 100% without a significant loss in specificity, respectively 97%. Given the overall relatively low prevalence of loosening of pedicle screws as evidenced by this and other studies in this patient population presenting with post-operative lumbar pain, the reported potential of combined SPECT and diagnostic CT imaging for the purpose of identifying pain generators other than pedicle screw loosening warrants further prospective exploration.

DECLARATIONS
The authors declare that they have no conflict of interest nor did they receive funding related to this study.

Procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. As patient data were anonymised, informed consent was not required by our Ethics Committee.

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