Management of postoperative infections after spinal instrumentation

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The authors retrospectively reviewed 452 consecutively treated patients who underwent a spinal instrumentation procedure at a single institution to establish which patients and which surgical approaches might be associated with an increased risk of developing deep wound infections and to determine the efficacy with which the institution's current treatment strategy eradicates these infections. Wound infections occurred in 17 patients (10 men and seven women) with spinal instrumentation (incidence 3.8%). All infections occurred after posterior spinal instrumentation procedures (7.2%); there were no infections after anterior instrumentation procedures regardless of the level. Each patient was assigned an infection risk factor (RF) score depending on the number of RFs identified in an individual patient preoperatively. The mean RF score of patients who developed infections was 2.18, whereas the mean RF score for a procedure-matched, infection-free control group was 0.71. The mean number of days from surgery to clinical presentation was 27.6 days (range 4-120 days), and the mean increase in hospitalization time for the subset of patients who developed infections was 16.6 days. The most common organism isolated from wound cultures was Staphylococcus aureus (nine of 17 cases). Of the 17 patients, five had infections involving multiple organisms. All patients were infection free at a minimum of 8 months follow-up review. The current treatment regimen advocated at this institution consists of operative debridement of the infected wound, a course of intravenous followed by oral antibiotic medications, insertion of an antibiotic-containing irrigation-suction system for a mean of 5 days, and maintenance of the instrumentation system within the infected wound.

Key Words * spine * instrumentation * postoperative infection * deep wound infection * risk factor * irrigation-suction system

Over the last two decades, major advances in surgical instrumentation of the vertebral column have emerged for a number of spinal pathologies including fractures and degenerative and neoplastic diseases.[2,19,22,23,25] The inherent advantages of a number of instrumentation systems include immediate stabilization of the spine, which permits more rapid mobilization of the patient; correction of deformities; and maintenance and reconstruction of the spine after decompressive surgery. The potential hazards that result from the application of rigid internal fixation must also be appreciated by spinal surgeons; these include, among others, hardware failure and neurological injury. Infections may develop after any surgical procedure, and the management of this complication in the setting of spinal instrumentation is critical in providing appropriate postoperative care to these patients.
The incidence of wound infection after spinal surgery without instrumentation is relatively low. In an era in which antibiotic prophylaxis before spine surgery has become relatively routine, the incidence of infection after lumbar discectomy or laminectomy is approximately 1%.\[9,12\] The use of spinal instrumentation clearly increases the risk for postoperative infections of soft tissue, and recent estimates from retrospective reviews range from 2.1 to 8.5%.\[1,5,14,16,17\] A number of well-recognized risk factors for the development of postoperative wound infections are inextricably linked to the insertion of spinal instrumentation.\[4,11,17\] The recognition of such potential factors will permit their reduction and, consequently, may diminish the incidence of wound infections.

Given the wider application of spinal instrumentation in neurosurgery over the last 10 years, the management of related postoperative infections has become increasingly important. The major objectives of this study were to review retrospectively the clinical characteristics, operative management, and outcome of postoperative infections in patients with spinal instrumentation over a 2.5-year period at a single institution.

**CLINICAL MATERIAL AND METHODS**

This retrospective review was initiated by evaluating hospital and office medical records, a computerized database, and charts from 452 consecutively treated patients who underwent an operative spinal instrumentation procedure. The study spanned 2.5 years with a minimum of 8 months follow-up review (mean follow up 1.5 years). The patients pertinent to this stability were identified by the diagnostic codes for both spinal infection and instrumentation in the charts. The records from morbidity and mortality rounds, the infection control department, and individual surgeons' office files were also reviewed to minimize the chance of missing patients.

**Patient Population**

Inclusion criteria consisted of patients in whom any spinal instrumentation was placed by either of two neurosurgeons (V.K.H.S. and C.A.D.). Patients who underwent more than one instrumentation procedure either on the same or separate days were listed as separate procedures, and operative times and blood loss were individualized. Criteria for exclusion were: 1) patients who underwent spinal surgery including placement of bone graft without instrumentation (for example, cervical disc removal and iliac crest graft); 2) patients who had evidence of a spinal infection before their instrumentation procedure; and 3) patients who underwent an instrumentation procedure and then developed a bone-graft donor-site infection only.

Patient-related risk factors (RFs) that are important predictors for the development of postoperative infections include previous surgery, use of steroid medications, diabetes, malnutrition, intercurrent infection, skin disruption, paralysis, smoking, and rheumatoid arthritis.\[4,17,24\] To determine whether these RFs were equally important predictors of the development of infection in the setting of spinal instrumentation, we arbitrarily assigned a value of 1 for each of the RFs listed above and determined an RF score for each patient. The mean RF score of patients in whom instrumentation had been placed and who developed infections was compared to that of a control group (17 patients) who did not develop an infection and who were matched for type of instrumentation procedure.

The mean increase in hospitalization time was defined as the number of additional acute hospital days per patient required to treat the infection and its attendant complications. For the majority of patients who had been discharged and required readmission for treatment of the infection, this number simply
represented the number of days of the second admission. In the few patients who were never discharged, the additional days were calculated on the basis of their anticipated date of discharge had they not developed an infection.

**Operative Technique**

All patients received one dose of the second-generation cephalosporin Zinacef during induction of anesthesia and every 8 hours for the next 24 hours after their initial instrumentation procedure. The operative site was scrubbed with chlorhexidine gluconate for 4.5 minutes. In patients who developed wound infections, wound cultures were obtained at the time of the patient's readmission to the hospital or at the time of surgical debridement. Operative debridement of the wound consisted of reopening the entire length of the previous incision; draining pus from all potential spaces within the wound; and aggressively removing residual sutures, loose particles of bone graft, and purulent and necrotic tissues. We attempted to maintain the bulk of the grafted bone within the wound in an attempt to achieve bone fusion.

A closed irrigation-suction apparatus,[8,9] also known as the "feed-me/drain-me" system in our institution, was inserted as part of the treatment regimen in the majority of patients with wound infections. Catheters and drains were usually placed both deep and superficial with respect to the lumbodorsal fascia when a deep-seated infection was present. In some cases an additional catheter and drainage system was placed within the site of harvest of the iliac crest graft. Red rubber catheters (No. 12 French) with side holes created along their lengths were used for continuous irrigation by connecting them to an intravenous solution of normal saline.

Antibiotic medications were added to the intravenous bags immediately after a wound culture was obtained at the bedside. Antibiotic agents included nafcillin (1 g/L normal saline) or vancomycin (500 mg/L normal saline). The antibiotic agent was selected relative to the gram stain and culture results and delivered a high concentration of antibiotic therapy specific for the infecting organism(s) directly to the wound site. The rate of irrigation was typically maintained at 25 to 50 ml/hour. The drainage tubes were connected to medium-pressure hemovacs that exited through separate stab incisions (Fig. 1). The fascia was closed with several nonabsorbable interrupted No. 0 sutures. The skin was closed with several No. 0 retention sutures as well as with a watertight running 3-0 nylon stitch. Irrigation systems were placed for 5 to 7 days and then removed. The drainage tubes were kept in place an additional day to ensure that a minimum amount of irrigation fluid remained within the wound.
Fig. 1. Photograph showing one portion of the treatment of deep wound infection. The catheters are attached to an antibiotic-containing irrigation solution consisting of normal saline (one intravenous bag is seen here) as well as to a hemovac suction device (two suction containers are seen here) after wound closure.

**Statistical Analysis**

A paired t-test was used to determine whether the differences in mean RF score between the patients with infections and the procedure-matched control group were statistically significant.

**RESULTS**

Seventeen cases of infection occurred in the 452 consecutive cases in which instrumentation was placed, resulting in an overall incidence of 3.8%. There were 10 men and seven women in this group with a mean age of 57.3 years (range 34-83 years) (Table 1). The preoperative diagnosis of patients who subsequently developed infections consisted predominantly of degenerative spinal disorders (nine patients), but inflammatory spinal conditions (four patients) also figured prominently. The mean RF score (2.18) in patients who developed an infection was significantly greater ($t = 3.93$, $p < 0.001$) than that in the control group (0.71).
The mean duration of instrumentation procedures that became infected was 5.23 hours. In three of the 17 cases, the patient had undergone both an anterior and posterior surgical approach on the same day, and the listed times represent only the surgical time for the procedure that became infected. The mean estimated blood loss was 900 ml. The mean number of surgeons (including residents and fellows) was 3.06. In seven of the 17 cases, a drain was inserted into the wound before closure.

The types of implants (Table 1) were broadly categorized according to the largest component of the instrumentation used. Posterior thoracolumbar stabilization procedures using rods were divided according to whether hooks or pedicle screws were the predominant instrument used to gain attachment to the vertebrae. The number of vertebrae spanned by the instrumentation is also listed. Overall, hook-rod constructs spanned more levels than pedicle screw-rod constructs.

There was a marked variation in the incidence of wound infection, depending on the surgical approach (Table 2). The incidence of infection after anterior cervical instrumentation or anterior thoracolumbar instrumentation was 0%. In contrast, the procedure-specific incidence of infection after posterior instrumentation varied from 1.8 to 12.5% (Table 2). Thus, all infections associated with spinal instrumentation resulted from either posterior or posterolateral approaches to the spine, whereas no infections were associated with anterior approaches.
The mean number of days from surgery to clinical presentation was 27.6 (range 4-120 days) (Table 3). The most common clinical presentation was a partial wound dehiscence associated with the drainage of purulent fluid. Pain and redness around the wound were also common. Although some patients presented with a fever, temperature elevation was not a reliable feature in making the diagnosis of a postoperative wound infection. In fact, the mean readmission temperature was only 37.5°C. During the second admission, however, elevated temperatures were more common compared with admission temperatures (Table 3).
Wound infections were assessed by laboratory analysis of routine blood work, including a complete blood count. The mean white blood cell count on admission was 10.2 (X 10^6 cells/ml) with a range of 5 to 22.9 (X 10^6 cells/ml). The erythrocyte sedimentation rate was elevated in five of the 17 cases in which it was assayed with a mean of 57.4 mm/hour (normal 0–20 mm/hour) and a range of 45 to 84 mm/hour. The cultures were positive in all but one patient who had been on multiple high-dose intravenous antibiotic medications for an unrelated infection stemming from an obstruction of the small bowel. The most common single pathogen was *Staphylococcus aureus*, and multiple pathogens were identified on culture study in a number of cases (Table 4). Six of the 16 bacterial isolates were resistant to the prophylactic antibiotic agent Zinacef; these included methicillin- or oxacillin-resistant bacteria. Consequently, the most common combination of antibiotic medications initially selected consisted of intravenous vancomycin and oral rifampin.[6] The duration of administration of intravenous antibiotic medications was individualized according to the severity and extent of infection; it ranged from 1 to 6 weeks and was followed by a course of oral antibiotic medications.

**Table 3**

**Summary of Patient Presentations on Initial Diagnostic Workup**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Postop Day</th>
<th>Dx Day</th>
<th>Tadmit (C)</th>
<th>Tmax (C)</th>
<th>WBC/ESR†</th>
<th>Wound Culture</th>
<th>Add Hosp Days</th>
<th>Location of Infection</th>
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<tr>
<td>1</td>
<td>120</td>
<td>35.8</td>
<td>35.8</td>
<td>5.4</td>
<td>+</td>
<td>5</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>ND</td>
<td>37.7</td>
<td>21</td>
<td>+</td>
<td>9</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>37.8</td>
<td>38.0</td>
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<td>+</td>
<td>43</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>37.5</td>
<td>39.8</td>
<td>13.8</td>
<td>+</td>
<td>12</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>37.5</td>
<td>37.8</td>
<td>5</td>
<td>+</td>
<td>10</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>39.1</td>
<td>36.3</td>
<td>22.9</td>
<td>+</td>
<td>5</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>22</td>
<td>36.1</td>
<td>36.3</td>
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<td>ND</td>
<td>37.9</td>
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<tr>
<td>9</td>
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<td>ND</td>
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<td>8.9</td>
<td>+</td>
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<td>36.3</td>
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<td>ND</td>
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<td>S&amp;D</td>
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<tr>
<td>12</td>
<td>14</td>
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<td>7.660</td>
<td>+</td>
<td>32</td>
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<tr>
<td>13</td>
<td>26</td>
<td>37.3</td>
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<td>58.50</td>
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<td>9</td>
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<td>14</td>
<td>16</td>
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<td>8</td>
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<tr>
<td>15</td>
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<td>39.5</td>
<td>39.5</td>
<td>17.445</td>
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<tr>
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<td>37.5</td>
<td>37.5</td>
<td>10.7</td>
<td>+</td>
<td>8</td>
<td>S&amp;D</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>16</td>
<td>37.5</td>
<td>38.5</td>
<td>8.5</td>
<td>+</td>
<td>70</td>
<td>S&amp;D</td>
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<tr>
<td>mean</td>
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<td>37.5</td>
<td>37.9</td>
<td>10.2574</td>
<td>16+‡</td>
<td>16.6</td>
<td>14 S&amp;D§</td>
<td></td>
</tr>
</tbody>
</table>

* Add Hosp Days = additional days spent in hospital; D = deep; ESR = erythrocyte sedimentation rate; ND = never discharged; Postop Day Dx = postoperative day of diagnosis; S = superficial; Tadmit = temperature on admission; Tmax = maximum temperature during hospital stay; WBC = white blood cell count; + = positive; – = negative.
† The ESR was only assayed in five patients. Range of normal values: WBC, 4.5–11.0 (X 10^6 cells/ml); ESR, 0–20 mm/hr.
‡ Wound culture showed a positive infection in 16 cases.
§ In 14 cases infection was both superficial and deep.
In 14 of the 17 infections, the infection extended below the fascia and was considered a deep infection that contacted the hardware and the onlay bone grafts. All cases of infection underwent surgical debridement as described in Clinical Material and Methods. In 13 of the 17 cases, a feed-me/drain-me system was inserted and maintained a mean of 5 days. Two patients (11.8%) required repeated debridement and reinsertion of an irrigation-drainage system. In one case a musculocutaneous flap was required to cover the wound after the initial debridement. In only one case was the removal of the instrumentation required. In this case, the deep wound infection was diagnosed within a week of surgery; however, the patient adamantly refused early operative debridement and placement of an irrigation-suction device. After 7 months of superficial debridements in the referring surgeon's office with failure to contain the infection, the patient agreed to surgery. At surgery pus covered the instrumentation system, which had completely loosened and was removed easily. Fortunately, a solid bone fusion mass had formed and no further stabilization procedures were required.

The mean increase in hospitalization for the subset of patients who developed a postoperative wound infection after spinal instrumentation was 16.6 days. One patient was readmitted in septic shock as a consequence of dissemination of bacteria from his infected wound and required a lengthy stay in the intensive care unit. Most patients were discharged on intravenous antibiotic medications either to a rehabilitation facility or to home. The costs required for the administration of antibiotic agents at these locations were, therefore, not reflected in the additional hospital day numbers.

To summarize, the treatment regimen consisted of operative debridement of the infected wound (17 of 17 cases), insertion of a feed-me/drain-me system (13 of 17 cases), and maintenance of the instrumentation system (16 of 17 cases) within the infected wound followed by a course of intravenous and oral antibiotic medications (17 of 17 cases). There were no instances of neurological deterioration, spinal instability, or recurrent infection. All treated patients were asymptomatic with no clinical or radiographic signs of infection with a minimum of 8 months follow-up review.

### DISCUSSION

A low but definite risk of iatrogenic infection is present when surgery is required to manage a variety of spinal disorders. Potential infectious complications include superficial wound infections, deep wound infections, discitis, epidural abscess, meningitis, and osteomyelitis. The most common infection encountered after the insertion of hardware to the spinal column is a deep wound infection. The most appropriate method for managing wound infections in the presence of spinal instrumentation is debated. Given the increasing frequency in which spinal instrumentation is used to treat disorders of the spinal column in neurosurgery, this retrospective analysis evaluated the risk factors, presentation, and results associated with treating infections in the instrumented spine.
Risk Factors for Wound Infection

Risk factors for the development of wound infection after spinal instrumentation can be divided into factors primarily related to the patient and those more closely linked to the surgery itself. Our analysis revealed that the RF score was significantly higher in patients who developed infections compared to the procedure-matched control group. Overall, the individual number of infections within each surgical subgroup was small. The relatively high infection rate associated with occipitocervical stabilization procedures might reflect the high mean RF score (2.8) of these patients, many of whom had rheumatoid arthritis. Many risk factors are irreversible. However, surgeons may enhance the outcome by influencing at-risk patients to quit smoking or by providing nutritional supplementation to malnourished patients.

One of the most dramatic findings in the analysis is the important difference in the wound infection rates between anterior and posterior (including posterolateral) surgery. No infections were encountered with anterior surgical instrumentation, whereas a relatively high infection rate was associated with posterior instrumentation. Posterior spinal instrumentation requires extensive muscle dissection to expose the posterior elements of the spinal column. This exposure often extends well laterally to visualize the transverse processes and several levels above and below the pathology. The extended surgical exposures can devascularize paraspinal muscles and increase the potential for a deep-seated infection. Large retractors that generate high compressive forces on the paraspinal musculature can also render these muscles ischemic. Other potential RFs for infection that may be linked to spinal surgery with posterior instrumentation include lengthy surgical times, increased blood loss, and the creation of a large dead space that can fill with blood. Recent evidence indicates that the presence of instrumentation by itself may increase the risk of infection.[20]

Exposure of the anterior spinal column for the application of spinal instrumentation can be accomplished through relatively avascular tissue planes whether in the cervical, thoracic, or lumbar regions. Thus, the anterior approach avoids much of the extensive muscle dissection required for the application of posterior instrumentation and reduces the amount of devascularized and neurotic muscle that can serve as a nidus for infection. Although previous descriptions of anterior approaches for spinal pathology have emphasized the advantage of these techniques in accessing a variety of anteriorly located pathologies, the findings of this study indicate that another advantage of the anterior approaches includes a diminished risk of infection. Meticulous dissection of the ligamentous attachments of the paraspinal muscles, which minimizes tissue necrosis and reduces blood loss, should theoretically lower infection rates when a posterior approach is used. Similarly, intermittent release of paraspinal tissue muscle retractors will help reduce muscle ischemia and necrosis. The value of the insertion of surgical drains in reducing wound infections could not be assessed in this study; however, recent investigations have demonstrated that drains reduce wound seepage from the incision after spinal surgery (unpublished data).

Clinical Presentation

Previous studies[13,15] and reviews[9,11,16] on the management of spinal infections in the presence of instrumentation have primarily relied on data obtained from adolescents and young adults who received Harrington rods for the correction of a scoliotic deformity. The current study reflects a more diverse patient population with respect to age, admitting diagnosis, medical condition, and instrumentation procedure. This sample more accurately reflects the contemporary census of an active spinal surgeon.

Invariably, the patients presented with purulent drainage and partial wound dehiscence. Although infections may arise over a considerable range of time, most patients presented 2 or 3 weeks after
surgery. No cases of delayed infection[21] in which the patient presented more than 8 months after surgery were identified. Temperature and white blood cell count, which are traditionally elevated in the setting of an infection, were not reliable indicators of a spinal wound infection. The erythrocyte sedimentation rate was assayed in only five patients but was consistently elevated in all patients with wound infections. Wound cultures yielded an organism in all but one case.

Treatment With Irrigation-Suction Devices

The placement of an irrigation-suction system to treat postoperative infections has been described in the treatment of osteomyelitis of long bones,[18,26] craniotomy wound infections,[3] and infected spinal wounds,[7,8] including those associated with spinal instrumentation.[13,15] Some of the advantages of the closed irrigation-suction system include the avoidance of a secondary wound closure as well as the ability to maintain the spinal instrumentation, thus promoting spinal stability. The insertion of an irrigation-suction system in an infected wound will not compensate for a poorly debrided wound. The meticulous removal of infected tissues, necrotic muscle, and nonviable bone grafts is a mainstay in the treatment of wound infections. We usually maintained most of the bone autograft within the infected wound to maximize the chance of obtaining a solid bone fusion.

The presence of spinal instrumentation within an infected wound adds a degree of complexity to the treatment schema; some surgeons believe that the presence of foreign material such as a metal implant precludes successful treatment of a spinal infection.[1,21] Our data, however, indicate that one can successfully treat deep spinal infections using systemic antibiotic agents combined with an antibiotic-containing irrigation system without needing to remove the hardware if the treatment is promptly instituted. The major advantage of maintaining spinal instrumentation in place is the ability to obtain a solid fusion without the need for additional reconstructive surgery or orthosis. Multiple reoperations with insertion of antibiotic-impregnated beads,[10] reoperation with multiple debridements, and removal of the hardware[11,21] have all been advocated for infection associated with spinal instrumentation. Our treatment protocol has the advantage that for most patients only a single additional operation is required and the hardware is left intact. In the one case in which treatment was delayed because the patient desired to avoid further surgery, the hardware loosened and eventually required removal. Although two patients required a second surgical debridement and placement of another irrigation-suction system, all patients were eventually cured of their infection.

The potential advantage of using a broad spectrum antibiotic medication for prophylaxis must be weighed against the potential disadvantage of further selecting for resistant organisms. Insertion of a Groshong catheter facilitated early discharge for many patients who required extended periods of intravenous antibiotic medications. An indirect estimate of the economic impact of an infection after spinal instrumentation can be appreciated by the 16.6 day increase in hospitalization time. Given that most patients were discharged on intravenous antibiotic agents either to a rehabilitation facility or home, the true cost of treating these infections is much higher. Fortunately, no patient required further surgery for surgical stabilization, an outcome mostly attributable to the ability to maintain surgical instrumentation in place while treating the wound infection.

CONCLUSIONS

Wound infections represent a serious complication of spinal surgery with instrumentation. The risk of these infections after insertion of spinal instrumentation is much higher in patients undergoing posterior spinal fusion that in patients undergoing fusion using an anterior approach. All infections in this series
were successfully treated (and in all but one case without removal of the hardware) by using a combination of intravenous antibiotic medications and an irrigation-suction system that contained organism-sensitive antibiotic agents. Displacement of the vertebral column, neural compression, and paralysis are potentially devastating complications associated with the loss of spinal instability when spinal hardware is removed before adequate spinal fusion has occurred. Therefore, we advocate leaving the hardware in place whenever feasible as long as the fixation device is securely attached to the spine.

References


2. Cherny WB, Sonntag VKH, Douglas RA: Lateral mass posterior plating and facet fusion for cervical spine instability. BNI Quart 7:2-11, 1991


37:636-660, 1991


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