Peer Review File

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REVIEWER A

Excellent detailed and well written paper reviewing the data from a large data set.

Comment 1: It seems that SSCs associated with the index surgery that were not yet discharged would be included in the non SSC group. Do you have data on cases with SSCs that were treated in the primary admission? If data is available on these cases, do they have the same profile as the SSC group?

Reply 1: We appreciate this question for clarification. All index surgeries had been discharged by the time of the study. A total of 1169 (0.7%) cases encountered an SSC during the index hospitalization but were not followed by an SSC-related readmission. These cases were categorized under the label "No SSC" in the original submitted manuscript These cases demonstrated a lower overall patient risk, as indicated by their Charlson Index Score (2.7 vs. 3.1), a lower percentage of complex procedures (defined as the number of ICD-10 procedures ≥ 10) (6.5% vs. 7.3%), a reduced percentage of surgeries lasting longer than 5 hours (15.2% vs. 42.4%), and a slightly lower representation in teaching hospitals (59.1% vs. 60.1%) when compared to the SSC group.

Changes in the text: To mitigate potential misinterpretation of the comparison groups, we have modified the group labels to "No SSC-AR" and "SSC-AR" in Table 1, and have incorporated the same terminology into the corresponding text of the Results (P11) and Discussion (P18). "AR" stands for associated readmission.

Comment 2: As such the 'non SSC' group is really a 'non readmission for SSC' group

Reply 2: Correct, and good point. We have updated the designation to the "No SSC-AR" group, where AR stands for "associated readmission." Your comment has enhanced the clarity of our labeling.

Changes in the text: Per Reply 1, we have made corresponding modifications to the group labels in Table 1 and throughout the text.

Comment 3: Recent papers have suggested that lumbosacral fusions, where the incisions are very distal, are more prone to deep SSIs, often with non-staph infections. Was location of surgery a factor that was considered in this review?

Reply 3: We concur with your observation regarding the significance of surgical incision location with respect to associated SSIs. In our originally submitted/reviewed manuscript, we did include a quantitative assessment of the surgical location as a risk factor in our full prediction model. To address your concern, we have added to the underlying rationale of this quantitative assessment along with additional citations. The spinal region risk score was not selected to be included in the reduced model because it was not as influential as the other surgery related risk factors, such as operative duration, urgent/emergency cases, and revision/primary procedures, in predicting SSC readmissions.

Changes in the text: We have expanded our explanation of the spinal region score

and included pertinent references to support our methodology. Additionally, we have corrected an earlier mistake in the coding description in the Methods section as follows:
"Each surgery's spinal region risk score was calculated as the sum of the points assigned to three different spinal regions (cervical= 1, lumbosacral = 2, and thoracic = 3). This scoring methodology is derived from existing literature, which provides compelling evidence that the anatomical location of spine surgery is associated with the risk of SSI, following this hierarchical order: thoracic procedures > lumbosacral/lumbar procedures > cervical procedures (54, 55)." (P9)

Comment 4: Complications such as CSF leaks can be associated with SSIs. Could this be identified in your database?
Reply 4: Thank you for this suggestion and the opportunity to clarify our approach. We had indeed investigated the incidence of post-surgical CSF leaks for our data analysis. In our study population, we identified 356 cases (0.2%) with post-surgery readmissions linked to CSF leaks. Among these CSF leak cases, approximately 20% occurred concurrently with SSIs. Because no definitive association can be made between CSF leak and SSI based on empirical data,[1,2] we chose to restrict the selection criteria to the CSF leaks occurring concomitantly with SSIs, excluding readmissions unrelated to surgical wounds. Additionally, we excluded spine surgeries involving planned durotomies (n=112), as these could potentially elevate the risk of CSF leaks. We believe this approach best aligns with the focus of our study.
1. Li D, Guo W, Qu H, et al. Experience with wound complications after surgery for sacral tumors. *Eur Spine J*. 2013;22:2069–2076.
2. Sciubba DM, Nelson C, Gok B, et al. Evaluation of factors associated with postoperative infection following sacral tumor resection. *J Neurosurg Spine*. 2008;9:593–599.
Changes in the text: To address concerns regarding post-surgical CSF leaks, we further clarified the exclusion criteria for the study population as follows: "*Surgeries involving planned durotomies, patients under the age of eighteen, or utilization of negative pressure therapy over the closed incision were excluded from the analysis*." (P8)

Comment 5: Do you feel your data will lead to certain patients being denied surgery by insurance companies?
Reply 5: This is a valid concern. A US regulation that prohibits health insurance companies from denying coverage or charging significantly higher rates due to pre-existing health conditions, such as asthma, diabetes, or cancer (2014 Affordable Care Act), has considerably reduced the occurrence of higher risk patients being denied appropriate surgery in the US. However, results of risk stratification studies from large databases, such as this one, may be used to inform decision making by insurance companies and hospital administrations worldwide, particularly with respect to establishing prices.
Changes in the text: To address potential concerns raised, we added more text (as shown below) with pertinent references in the Discussion to underscore the

importance of this assessment tool in informing proactive peri- and post-surgical infection prevention strategies, thereby minimizing adverse patient outcomes. It is important to emphasize, as per your feedback, that the primary purpose of this tool is to enhance patient safety and ensure positive surgical outcomes, prioritizing these over insurance-related considerations.
"*Such risk score cutoff levels, characterized by a high density of unplanned readmissions, can serve as clinical indicators for employing more aggressive measures, such as implementing advanced incisional management strategies,(56, 57) to reduce the occurrence of SSCs and ultimately bolster patient safety and surgical outcomes.*" (Pp14-15)

REVIEWER B
Comment 1. Authors present a robust prediction model for readmissions related to surgical site complications. It is expanded on their previous SSI prediction model. Using a large sample size, they were able to demonstrate specific significant variables that demonstrate high risk factors relating to readmission.
The manuscript is well written and adds a practical clinical tool for spine surgeons to counsel patients.
The methodology seems sound and appropriate.
Reply 1: Thank you for your encouraging summary of the strengths of our work.

REVIEWER C
Thanks for this important Topic. I need more details to be included in this Study to make it more helpful:
Comment 1: Known Infection Pre- primary operation, When Yes, Which Pathogen and Antibiotic therapy. Or Infection of primary operation excluded?
Reply 1: Thank you for your insightful input. In the United States, elective primary spine surgeries are typically contraindicated for individuals with active infections anywhere in the body. Also, for this study, we assessed infections for the index surgery upon admission using ICD-10 diagnosis codes, given that a substantial portion of our study population lacked laboratory data. We identified a minimal occurrence rate (0.2%) of index surgeries associated with systemic inflammatory response syndrome (SIRS). Our predictive model incorporated 'Emergency/Urgent Surgery' as a predictor to account for risk factors linked to the urgent or emergent need for spine surgery, such as pre-existing infections and contaminated/dirty wounds.
Changes in the text: Please see *Changes in the Text* for Reply 8.

Comment 2: With revision surgery: is it infectious, when Yes, Which Pathogen and Antibiotic therapy.
Reply 2: Unfortunately, due to the absence of laboratory data for the majority of our selected patients, we were unable to determine whether a revision surgery was infectious or not. However, we did observe that the revision surgery cohort exhibited a higher SIRS rate (1.6%) compared to primary surgeries (0.2%). We utilized the 'Primary/Revision Surgery' predictor to assess the increased risk of SSC

associated with the potentially higher infectious nature of revision surgeries, although we were unable to further refine predictions to distinguish infectious from non-infectious revision surgeries.
Changes in the text: We appreciate your feedback for Comments 7 & 8. We have included the limitation of model refinement due to the lack of laboratory data in our limitations paragraph: "*Owing to the lack of laboratory data for the majority of the study population, we were unable to identify preoperative infections or infectious surgeries to enhance the refinement of our model*." (P18)

Comment 3: Localization und approach of Operation: Cervical, Thoracic, lumbar?. Position of. Pat. (prone, back, on the side).
Reply 3: We concur that surgical localization, approach, and type are pivotal in predicting postoperative complications for spine surgery patients. As such, we had incorporated two quantitative variables into our full prediction model to capture a multitude of aspects within a unified and computationally feasible framework: 1) The Spine Surgery Invasiveness Index, and 2) The Spinal Region Risk Score. Your feedback has prompted us to describe the significance of these factors more prominently within our methodology. Importantly, however, when we processed the model selection using statistical techniques, these factors were not included in the reduced model because they were found to be less influential than other surgery-related risk factors, such as operative duration, urgent/emergency cases, and revision/primary procedures.
Changes in the text: To underscore the importance of the aforementioned surgery-related risk factors, we have expanded upon the rationale and provided supporting references to elucidate the individual and collective influence of surgical localization, approach, and type in predicting SSCs. These changes have been incorporated into the Methods section:
"The spine surgical invasiveness index (33, 34), a composite metric evaluating the invasiveness of the surgical approach (anterior/posterior), surgical modality (decompression/fusion/instrumentation), and vertebral levels (Thoracic/Lumbar/Sacral) concurrently, was computed as a proximate estimate based on procedure codes listed for each patient within the scope of this study."
....
Each surgery's spinal region risk score was calculated as the sum of the points assigned to three different spinal regions (cervical= 1, lumbosacral = 2, and thoracic = 3). This scoring methodology was derived from existing literature, which provides compelling evidence that the anatomical location of spine surgery is associated with the risk of SSI, following this hierarchical order: thoracic procedures > lumbosacral/lumbar procedures > cervical procedures." (Pp9-10)

Comment 4: Types of Primary Operations: Nucleotomie, TLIF, PLIF, fusion, Copectomie...etc.
Reply 4: In the study population, primary operations predominantly consisted of fusion procedures (98.7%), with a minor representation of stabilization (1.0%) and decompression (0.3%). Although this limited diversity of surgical procedure types mirrors published prevalence of spinal fusion as the most common procedure in the

domain of open spine surgeries (https://www.medicinenet.com/what_is_the_most_common_spine_surgery/article.htm), we acknowledged in this manuscript that this relative homogeneity in our surgical cohort may limit our ability to detect significant impacts on SSCs stemming from different surgical techniques. In response to your feedback, we have elaborated on the composition of primary operations in this revised manuscript. Specifically, we have included more descriptive details regarding the primary fusion cohort, which accounts for nearly 80% of our study population. This additional information will assist readers in better aligning their surgical cases with ours for benchmarking purposes.

Changes in the text: To clarify the utility of our tool and facilitate a more precise evaluation of its applicability to various patient populations, we have incorporated detailed information about the surgical approaches within the primary fusion cohort in the revised manuscript:

"Twenty percent of patients underwent revision surgeries, and 79.8% primary surgeries, which were composed of 78.7% primary fusion, 8.8% revision fusion, 0.8% primary non-fusion, and 11.7% revision non-fusion surgeries. The primary fusion surgeries consisted of posterolateral (28.0%), anterior (26.9%), posterior interbody and lateral (23.1%), posterior interbody (13.7%), and anterior and posterior combined (8.3%) approaches."

Comment 5. Please include these criteria in this study and do analysis between each other as well as the criteria you mentioned in your study. I think you will get more specific and sensitive result.

Reply 5: Thank you for your constructive review. We have integrated discussion and clarification text in the revised manuscript to address each of your comments, and sincerely hope that these revisions will improve the relevance and readability of our work for a broader audience.