Conventional Radiotherapy Timing and Wound Complication Avoidance After Surgery for Metastatic Spine Disease. A LatAm Modified Delphi Study

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■ BACKGROUND: **Combining surgery and radiotherapy is the gold standard in treating spinal metastasis when spinal stabilization or surgical decompression is required. Determining the optimal timing for radiotherapy post-surgery is crucial to balance treatment efficacy minimizing wound complications. The study aimed to identify consensus and nonconsensus areas among Latin American spinal surgeons regarding the use, timing, risks, and surgical approach to conventional external beam radiotherapy (cEBRT) following spinal surgery for metastases, specifically focusing on the risk of radiotherapy-related wound complications.**

■ METHODS: **A modified Delphi survey was conducted. The expert panel included active members of AOSpine Latin America with extensive experience in vertebral metastasis surgery. The surveys include 37 statements covering areas of interest. Inter-expert consensus was considered weak (70-79.9%), moderate (80-89.9%), and strong (≥90%).**

■ RESULTS: **At least 70% consensus was reached on 32 of the 37 statements (86.5%). This included strong consensus on 10 statements, moderate on 13, and weaker on nine. There was high consensus on sutures and lower consensus on risk factors for cEBRT delay. Experts reached strong agreement on the importance of poor nutrition as a risk factor for cEBRT-related wound complications. Perception of wound risk was greater with a posterior midline approach compared to other approaches, and the highest perceived complication risks were for junctional locations and sacral spine.**

■ CONCLUSIONS: **We report strong agreements among the experts on important issues such as waiting times and risk factors for cEBRT. The findings underscore the significance of considering factors such as, spinal levels, surgical approaches, and sutures when making clinical decisions.**

INTRODUCTION

Combining surgery and radiotherapy (RT) is considered the gold standard treatment for spinal metastasis when spinal stabilization or surgical decompression is required.[1,2] Surgeons and oncologists must carefully choose the best timing for surgery and RT to achieve maximum oncolytic effects while

Key words
- Metastatic spine Delphi study
- Radiotherapy timing
- Wound complication
- Wound dehiscence

Abbreviations and Acronyms
BMI: Body mass index
cEBRT: Conventional external beam radiotherapy
RT: Radiotherapy

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minimizing complications. However, administering radiation shortly after surgery can lead to complications that usually affect wound healing. Additionally, these patients are often malnourished, taking steroids, chemotherapy, and antiangiogenic factors, which can further weaken the tissues and hinder their healing ability.[3]

The timing of radiation therapy in relation to surgery has been a topic of considerable debate in the management of spine oncology over the past decades and there is limited evidence to guide decisions on the sequence and timing of surgery and radiation therapy concerning wound healing. Only a few systematic reviews have been conducted on the subject, concluding an interval of 1 to 2 weeks between RT-surgery or vice versa.[4-6]

Wound healing is the primary concern when deciding the interval between surgical treatment and RT.[7] If radiation treatment is indicated during the early stages of healing, it can cause damage to the treated area, depending on the total dose and frequency of radiation exposure.[3] Wound healing complications may also depend on the patient's characteristics, spine tumor location, and surgical technique.

The primary objective of this survey was to identify areas of consensus and nonconsensus among spinal surgeons across Latin America regarding the use, timing, risks, and surgical approach to conventional radiotherapy (conventional external beam radiotherapy [cEBRT]) following spinal surgery to stabilize metastatic spinal disease, specifically concerning to the risk of RT-related wound complications. We focused solely on cERBT due to the limited availability of SRS in our environment. A secondary objective was to determine the surgeon's relative rating of risk factors for wound-healing complications.

This information can assist spinal surgeons in selecting the appropriate surgical approach, refining their technique, identifying patient characteristics and spinal levels that may pose a higher risk of complications, and deciding the optimal timing for administering additional cEBRT following decompression and stabilization surgery for spinal metastasis.

METHODS

Study Design

A modified Delphi survey[8] was conducted using one face-to-face meeting (December 2023) and two subsequent web-based surveys (February to April 2024).

Recruiting the Expert Panel

All active members of AOSpine Latin America were invited to participate in the study. A detailed email was sent introducing the study objectives and format containing an initial survey to determine their experience level in spinal metastasis surgery. To be selected for the expert panel and participate in the in-person round 1 survey, participating surgeons met the following criteria: minimum 5 years practicing spine surgery, minimum 2 years performing minimally invasive spine surgery and/or open spine surgery for spinal metastasis, and an estimated minimum average of 10 surgeries performed for spinal metastasis per year over the past two years.

Survey Development

A systematic literature review was conducted using the PubMed/MEDLINE, Google Scholar, Cochrane, Clinical Key, Springer Link, Wiley Online Library, and EMBASE databases. This review aimed to examine the existing evidence on the timing of RT and its role in preventing wound complications following surgery for metastatic spine disease to identify the key topics to investigate.

With this information, the initial survey was developed by an advisory team that consisted of the principal investigator and coinvestigators aided by an international MD-PhD-level expert in survey design (K. P. W.), including Delphi survey design and orchestration. Delphi approach was selected because the anonymous voting characteristic of this survey approach should minimize the impact of peer-related acquiescence bias.

Core principles of the survey's design included a decision to have a preliminary, open-answered question round (round 0) among a smaller subset of experts to aid with sculpting the survey language and minimizing the risk of bias stemming from the wording of statements in itself. Following round 0, thirty-five statements were created covering the study areas of interest, then edited by the Delphi expert, both for clarity and to further reduce the risk of bias caused by the survey itself. A second core principle of survey development was to begin with a greater number of response options (e.g., level of risk rated from 1, very low to 5, very high) in the preliminary rounds with the flexibility of either eliminating response options never selected or grouping adjacent response options (e.g., risk high + very high) in subsequent rounds. In that way, we sought to provide voters with the means to temper their votes (e.g., selecting weaker vs. stronger agreement or disagreement). A decision was also made to have three rounds of voting from the entire panel (after round 0) to maximize the likelihood of reaching a consensus.

To further minimize bias from the statements themselves, the Delphi expert reworded statements to create as many nonjudgemental statements (neither favoring nor not favoring a particular approach) as possible, then balancing all remaining statements so roughly the same number of favorable and nonfavorable statements were included. The final survey consisted of 35 statements, divided into two modules: module 1, on radiation therapy waiting times and delays, and module 2, on surgical approaches and risks.

Survey Administration and Interim Analysis

Emails containing a link to the online survey were sent to all eligible experts who agreed to participate in the survey, under the understanding that their participation could involve three rounds. For each round, up to two weeks was granted for survey completion, after which the experts' access to the survey was terminated. Two reminder emails were sent over those two weeks to enhance survey participation. Data from each round were analyzed to identify all statements for which at least 70% interexpert agreement was reached (defined as consensus reached) and all statements for which the 70% threshold was not reached. Latter statements were included in the next round, accompanied by a percentage breakdown of all response options selected by the experts. Between the second and third rounds, unselected response options were eliminated, and an appropriate grouping of select response options (again, like very low and somewhat low

risk) was performed, primarily to permit experts to agree or disagree with the final statements. Also, between the second and third rounds, two statements were split into two separate statements to isolate individual response options for agreement versus disagreement. Hence, the experts ultimately voted on 37 statements.

Final Statistical Analysis of Results

In addition to calculating the percentage of interexpert agreement for each survey statement, the relative perceived risk of wound complications was rated by both the surgical access approach used (anterolateral, posterior midline, and posterior paramedian) and spinal level (craniocervical through sacral), and the different within-subject levels compared by two-tailed repeated-measures analysis of variance. Such ratings ranged from 1 (lowest risk) to 5 (highest risk). For this, $P \leq 0.05$ was set as the criterion for statistical significance. A decision also had been made a-priori to require at least 80% participation in voting on each statement to consider its vote valid. All analyses were performed using the statistical software package SPSS, version 28.

RESULTS

A total of 38 spinal surgeon members of AO-Spine Latin America agreed to participate in the survey, among whom all 38 participated in rounds 1 and 2 and 31 (81.6%) in round 3 (on all statements), thereby satisfying our 80% threshold for valid voting. The characteristics of the 38 experts are summarized in Table 1.

Tables 2 and 3 summarize voting on 'cERBT waiting times and delays' and 'surgical approaches and risks', respectively. Overall, at least 70% consensus was reached on 32 of the 37 statements (86.5%) over three rounds of voting. This included strong consensus (≥90%) on 10 statements, moderate consensus (80–89.9%) on 13 statements, and weaker consensus (70–79.9%) on nine statements. Among the 33 statements with agree/disagree as the final response option, agree was selected for 28 (consensus on 26) versus disagreement for five (consensus on two).

By topic, the highest average level of consensus (90.9%) was reached, spanning the seven statements on sutures (range: 81.6%–96.8%). In comparison, the lowest average levels of consensus were achieved, spanning the ten statements on risk factors for radiation therapy delay (75.3%), and three statements on the effects of delaying cERBT (76.8%).

Percentage agreement on various potential risk factors for cERBT-related wound complications is depicted in Figure 1, with strong agreement (97.4%) reached on the importance of poor nutrition, moderate agreement on the importance of a body mass index (BMI) ≥40 kg/m2 (class III obesity), and weaker agreement on the influences of diabetes mellitus and current tobacco use. Only a minority of experts considered the use of systemic corticosteroids, BMI 35–35.9 kg/m2 (class II obesity), past tobacco use, patient age, or BMI 30–34.9 kg/m2 (class I obesity) important risk factors for cERBT-related wound complications after spinal surgery for metastatic spinal disease.

On five-point rating scale from 1 (lowest risk) to 5 (highest risk), the perception of wound risk was statistically more significant with a posterior midline approach (3.67) than either the anterolateral (2.34) or posterior paramedian (2.79) approach (Figure 2), at $P < 0.001$. By spinal level, the highest levels of perceived cERBT-related wound complication risk were for the craniocervical and cervicothoracic spine (3.74 and 3.76, respectively) and for the lumbosacral and sacral spine (3.47 and 4.16, respectively), while the perceived risk rating averaged under 3 (2.96) from the thoracic through lumbosacral spine ($P < 0.001$).

Table 1. Practice Characteristics of the Expert Panel

	Number	Percentage
Country, N = 38		
Argentina	5	13.1
Brazil	15	39.5
Chile	3	7.9
Colombia	5	13.1
Mexico	8	21.1
Peru	1	2.6
Venezuela	1	2.6
Specialty		
Neurosurgeon	17	44.7
Orthopedic surgeon	21	55.3
Nature of practice		
Private hospital	28	73.6
Public hospital	18	47.4
University hospital	12	31.6
Years in spine surgery practice		
5–9 years	17	44.7
10 or more years	21	55.3
Years performing surgery for spinal metastases		
2–5	7	18.4
More than 5	31	81.6
Metastatic spine surgeries/year		
10–19	23	60.5
20–50	15	39.5

DISCUSSION

Currently, there are no clear guidelines on the best timing for postoperative radiation therapy following the surgical removal of spinal metastatic disease. The decision is often left to the discretion of the attending surgeon along with the oncologist, who must balance the need for enough time for postoperative wound healing with the requirement for radiation therapy to prevent tumor progression.[7,9]

Itshayek et al. performed a systematic review of RT timing, including 51 reports and 7090 patients; they concluded that waiting one week after surgery is a "safe window" for radiation.[4] However, this decision may vary between the oncologist and the

Table 2. Module 1 - Conventional External Beam Radiotherapy Waiting Times and Delays

Statements	Most Common Selection	% Consensus
Waiting times to radiotherapy		
cEBRT should almost never be initiated before 14 days after uncomplicated open short instrumentation (1 level above, 1 level below)	Agree	96.8%
cEBRT should almost never be initiated before 7 days after uncomplicated minimally invasive extended instrumentation (2 levels above, 2 levels below)	Agree	83.9%
cEBRT should almost never be initiated before 21 days after uncomplicated open extended instrumentation (2 levels above, 2 levels below)	Agree	80.6%
cEBRT should almost never be initiated before 14 days after uncomplicated minimally invasive extended instrumentation (2 levels above, 2 levels below)	Agree	80.6%
The minimum time to wait before starting cEBRT after uncomplicated minimally invasive short instrumentation (1 level above, 1 level below) should be less than 15 days	Agree	76.3%
Delaying radiation therapy		
Delaying the start of cEBRT after spinal metastatic surgery reduces the risk of wound dehiscence?	Agree	94.7%
Delaying the start of cEBRT after spinal metastatic surgery reduces the risk of wound infection?	Agree	71.1%
If wound dehiscence occurs during cEBRT after spinal metastatic surgery, radiation should be stopped	Agree	64.5%
Risk factors for radiation therapy delay		
Poor nutrition is a risk factor for delaying the initiation of cEBRT	Agree	97.4%
A body mass index from 30 to 34.9 kg/m^2 is a risk factor for delaying the initiation of cEBRT	Disagree	86.8%
A body mass index $\geq$40 kg/m^2 is a risk factor for delaying the initiation of cEBRT	Agree	84.2%
Diabetes mellitus is a risk factor for delaying the initiation of cEBRT	Agree	78.9%
Current tobacco use is a risk factor for delaying the initiation of cEBRT	Agree	76.3%
Patient age is a risk factor for delaying the initiation of cEBRT	Disagree	74.2%
If decompression is required, preserving midline structures (mainly the spinal process and the interspinous ligaments) might reduce the risk of wound-healing complications	Agree	71.1%
A body mass index from 35 to 39.9 kg/m^2 is a risk factor for delaying the initiation of cEBRT	Disagree	64.5%
Recent past tobacco use is a risk factor for delaying the initiation of cEBRT	Disagree	61.3%
Corticosteroid use is a risk factor for delaying the initiation of cEBRT	Disagree	58.1%

Gray-shaded statements did not reach 70% consensus.
cEBRT, conventional external beam radiotherapy.

spinal surgeon, who often wait longer as they have to deal with wound complications.

It is worth knowing what is considered too early, not what is too late to start RT. So, the issue of importance is: What is the minimum amount of waiting time needed? We found moderate to strong consensus that short or long minimally invasive instrumentation presents briefer waiting times to start cERBT than open instrumentation. For minimally invasive extended instrumentation, an 83% consensus indicated that clinicians should wait at least 14 days before starting cERBT to minimize the risk of wound complications. For a minimally invasive short procedure, there was 76% consensus that 14 or fewer days are an adequate wait. Minimally invasive approaches involve smaller skin incisions and less soft tissue trauma for percutaneous instrumentation and decompression if needed. Surgical wounds heal faster, allowing earlier initiation of RT.[10,11] According to our findings, if stabilization with screws is necessary and we have the option to perform it either conventionally or through a minimally invasive approach, choosing the latter could benefit the patient by reducing the waiting time before continuing with cERBT.

We found a strong consensus that delaying the start of cERBT after spinal metastatic surgery reduces the risk of wound dehiscence. However, we did not find agreement on whether radiation should be stopped in cases where wound dehiscence occurs during radiation treatment. Stopping RT should be avoided because it loses radiobiological effectiveness. Depending on the histological type and its replication kinetics, the arrest interferes with the results of treatment local control. Results from split-course therapy studies indicate that 14–16 day interruptions can significantly affect treatment outcomes.[12] A relative loss of local control ranging from 3%–25% (median 14%) occurs when treatment is prolonged by one week.[13,14]

Table 3. Module 2 - Surgical Approach and Risks

Statements	Most Common Selection	% Consensus
Surgical approach		
The level of risk for radiation therapy cEBRT wound-healing complications with the posterior midline approach is… (low, medium, high)	High	86.8%
Revision surgery approach is highly associated with cEBRT wound/healing complications	Agree	84.2%
The level of risk for cEBRT wound-healing complications with the anterior/lateral approach is… (low, medium, high)	Low	76.3%
The level of risk for cEBRT wound-healing complications with the posterior paramedian approach is… (low, medium, high)	Medium	73.7%
Spinal level		
The risk for developing cEBRT wound-healing complications after craniocervical surgery should be considered intermediate to high	Agree	93.5%
The risk for developing cEBRT wound-healing complications after cervical surgery should be considered low to intermediate	Agree	87.1%
The risk for developing cEBRT wound-healing complications after cervicothoracic surgery should be considered intermediate to high	Agree	96.8%
The risk for developing cEBRT wound-healing complications after thoracic surgery should be considered intermediate to high	Agree	64.5%
The risk for developing cEBRT wound-healing complications after thoracolumbar surgery should be considered intermediate to high	Agree	87.1%
The risk for developing cEBRT wound-healing complications after lumbar surgery should be considered intermediate to high	Agree	90.3%
The risk for developing cEBRT wound-healing complications after lumbosacral surgery should be considered intermediate to high	Agree	83.9%
The risk of cEBRT wound-healing complications for the sacral level should be considered high	Agree	71.1%
Sutures		
In patients about to receive cEBRT after uncomplicated spinal metastatic therapy, the preferred suture material is either nonabsorbable nylon OR nonabsorbable linen	Agree	96.8%
The recommended time-frame for removing stitches after a wound has healed after open spinal metastasis surgery in patients who are about to receive cEBRT should be 15 days or more	Agree	96.8%
In patients about to receive cEBRT after uncomplicated spinal metastatic therapy, the preferred suture material is non-absorbable nylon	Agree	93.5%
The recommended time-frame for removing stitches after a wound has healed after minimally-invasive spinal metastasis surgery in patients who are about to receive cEBRT should be 15 days or more	Agree	93.5%
Preferred skin stitches to use on patients about to receive cEBRT after uncomplicated spinal metastatic surgery include vertical mattress sutures	Agree	87.1%
In patients about to receive cEBRT after uncomplicated spinal metastatic therapy, the preferred suture material is absorbable/nonabsorbable	Non-absorbable	86.8%
Preferred skin stitches to use on patients about to receive cEBRT after uncomplicated spinal metastatic surgery include over and over interrupted sutures	Agree	81.6%

Gray-shaded statements did not reach 70% consensus.
cEBRT, conventional external beam radiotherapy.

Furthermore, wound dehiscence is a multifactorial complication of which radiation is just an aspect. It is difficult to provide a general recommendation, as the outcome depends on factors such as the location of the wound, the length and depth of the dehiscence, genetic factors affecting healing, patient hygiene, and the type of suture material used.

Our findings suggest that poor nutrition is one of the risk factors that should be considered when delaying the initiation of cERBT.

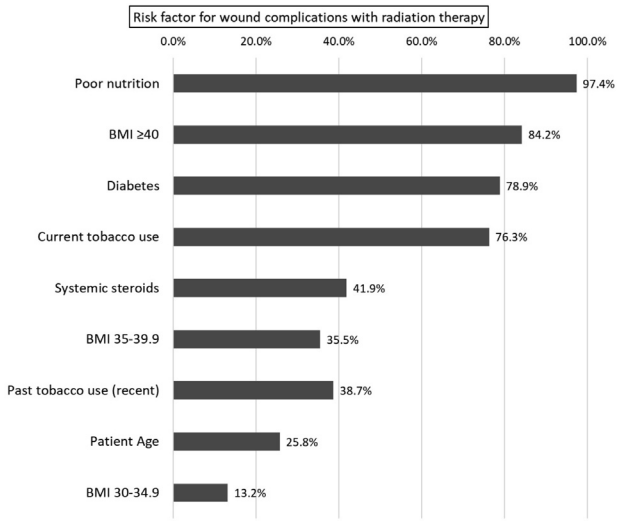

Figure 1. Risk factors for wound complications from conventional external beam radiotherapy (cEBRT).

Malnutrition may affect up to 75% of cancer patients and is linked to delayed wound healing, increased treatment side effects, higher complication rates, poor postoperative outcomes, and more extended hospital stays. It is recommended to assess the patient's nutritional status early on and monitor it throughout the treatment to enhance therapy tolerance, clinical outcomes, and overall quality of life.[15-17]

Sometimes, we can approach a metastatic lesion using different routes. Based on our findings, there is a moderate to weak consensus that posterior approaches pose a higher risk for cERBT wound-healing complications than posteromedial approaches. In contrast, anterior/lateral approaches are associated with the lowest

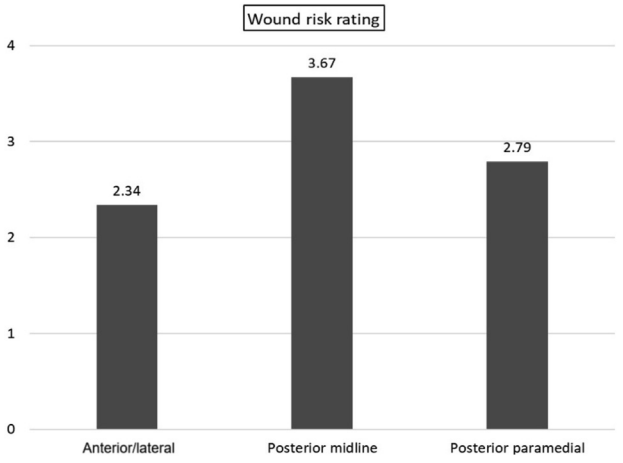

Figure 2. Perception of wound risk of wound complications from conventional external beam radiotherapy (cEBRT) by surgical approach.

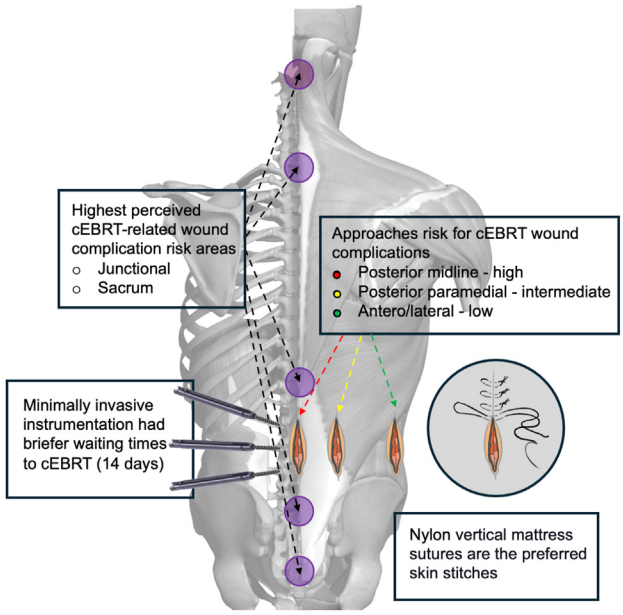

Figure 3. Recommendations for cERBT timing and avoiding wound complications from a more surgical standpoint.

risk (Figure 2). This is probably because midline approaches require the disinsertion of paraspinal muscles, while other approaches are transmuscular. In contrast, we only found a weak consensus that preserving midline structures might reduce the risk of wound-healing complications, considering possible differences between laminectomies and hemilaminectomies when decompression is required. The approaches performed for revision surgery were highly associated with cERBT wound/healing complications.

The spinal level is another factor to consider when assessing the risk of developing cERBT wound-healing complications. The highest perceived cERBT-related wound complication risk levels were the spine junctional areas and the sacrum. We consider this partly due to the requirement for more complex instrumentation systems that demand broader surgical approaches and, therefore, associated greater devitalization of the surrounding tissues. In addition to this are the local characteristics of the soft tissues, such as skin folds in craniocervical areas and tissue shortages at the sacral level. Considering these findings, we should monitor the healing of surgical wounds at the transitional and sacral levels more carefully.

We reached a strong consensus that for patients with cEBRT indication after uncomplicated spinal metastatic surgical treatment, the preferred suture material is nonabsorbable nylon. We also found moderate consensus that vertical mattress sutures are the preferred choice for skin stitches, followed by over-and-over interrupted sutures to a lesser extent.

Although monofilaments are less susceptible to infection, leaving the stitches in the surgical wound for too long can cause an inflammatory reaction that leads to superficial infections.[18]

For both open and minimally invasive surgery, there was a strong consensus that stitches should be removed no earlier than 15 days after the wound has healed following spinal metastasis surgery in patients who are about to receive cERBT.

Even though similar results have been reported in other studies,[4,9,19,20] the report of comparable findings in Latin America using the Delphi method is quite significant. We emphasize providing recommendations for cERBT timing and avoiding wound complications from a more surgical standpoint (**Figure 3**).

As with any study, there are limitations that should be considered when interpreting the findings. Firstly, the consensus and recommendations mentioned are based on expert opinions and available evidence at the time of the study. As medical knowledge evolves, these recommendations may need to be updated. Secondly, the consensus statements are generalized and may not account for individual patient variations or specific clinical scenarios. Patient-specific factors, such as overall health status, comorbidities, and tumor characteristics, may influence the optimal timing for postoperative radiation therapy. Furthermore, the study primarily focuses on the timing of cERBT following spinal metastatic surgery and its impact on wound healing. Other factors that could influence treatment decisions, such as patient preferences, cost, and resource availability, were not extensively addressed and may warrant further investigation.

Lastly, the study's findings and recommendations are based on the consensus of experts in the field. Different institutions and regions may have varying practices and resources, and local guidelines should be considered in clinical decision-making.

CONCLUSION

We provide valuable insights into the consensus and perceptions on various aspects of conventional RT timing and wound complication avoidance. We report strong agreements among the experts on important issues such as waiting times and risk factors for radiation therapy. The findings underscore the significance of considering factors such as, spinal location, surgical approaches, and sutures when making clinical decisions. The comprehensive data obtained from the survey can contribute to enhancing patient care and treatment protocols in spinal surgery.

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