Peer Review File

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Reviewer A

This is a prospective cohort study evaluating 20 patients treated with preoperative planning and PSSRs by a single surgeon over 3.5 years.

The authors should be commended on looking further than radiographic parameters and adding PROMs to the study. Further, junctional failure is a universal issue that continues to plague spine deformity surgery.

Comment 1.1: The authors acknowledge being "outside" the learning curve, but further data regarding this would be valuable. Is there an established learning curve? Did the surgeon change their surgical technique based on/during the initial treatment of patients with PSSRs? While the suggestion of being "outside" the learning curve is important, further commentary is necessary to quantify/qualify this statement.

Reply 1.1: Thank you. The original meaning of this statement was to suggest the surgeon was very experienced and not still learning the intricacies of ASD surgery. We have added to the sentence with a reference. We think this sufficient commentary.

Changes in text: Lines 495-497 (Discussion)

This study represents the experience of a single surgeon past their learning curve *of conventional ASD surgery with over 100 cases experience and a well-developed, systematic, and safe approach to the operation (47).* Several limitations are present in this non-randomized, observational single centre case series.

Comment 1.2: The authors note that the SRS-Schwab criteria were not utilized specifically for planning, but do not specify how patients were planned? They also comment on age-adjusted parameters, but were these used? Were patients planned to any specific goals? Also, with the utilization of interbody cages, there has been significant increased interest in the literature regarding L4-S1 lordosis, distribution of lordosis, and the effects of these parameters on outcomes. Was this focused on in planning, and was this achieved with outcomes?

Reply 1.2: Thank you for this expert opinion. We deleted the reference to the Schwab criteria as we used the surgical specific machine learning software (UNiD™ Adaptive Spine Intelligence™, Medtronic, MN). We do recognise the significant interest in L4-S1 lordosis and the effect on outcomes as outlined from line 168-173.

Changes in text: Lines 153-157

The PSSR were manufactured to a planned sagittal and coronal deformity correction made between the patient, surgeon, and surgical specific machine learning software (UNiD Adaptive Spine Intelligence, Medtronic, MN). The patient was consented appropriately for risks, benefits, and length of procedure. The spinal sagittal shape was characterised by pre-operative EOS scans which was analysed by specific software.

Comment 1.3: Also, the authors note DEXA scans for all patients, but that were tactics for those cases in which bone density was low, intra-operative bone quality was considered inadequate, ect?

Reply 1.3: Thank you for this advice. DEXA scans were not undertaken by all patients, only if considered clinically relevant. Hence, we have added the following statement. Lines 130-133 explain our considerations for patients with decreased bone mineral density.

Changes in text: Lines 177-182 (Methods)

Preoperative radiological investigations included dynamic X-Rays, computed tomography (CT), magnetic resonance imaging (MRI), bone density scan (DEXA), and nuclear medicine bone scans. *If investigations were not considered clinically relevant, they were not undertaken. Patients at risk of reduced bone density were screened with DEXA scans as per Royal Australasian College of General Practitioners (RACGP) guidelines.*

Comment 1.4: No tethers were used, but was cement augmentation ever utilized?

Reply 1.4: No cement augmentation was used.

Changes in text: Lines 174 (Methods)

No junctional tethers / ligament *or cement* augmentation was used proximally.

Comment 1.5: The above highlights the understanding PJK/F and DJK/F are multi-factorial, and likely we do not fully understand the issues, however, did the authors stratify based on UIV? The comment is made that surgical regret in UIV was noted for at least one case. Were there any indicators that UIV had an effect on the rates of kyphosis/failure.

Reply 1.5: Thank you for this professional recommendation. We believe the strength of the study limits the ability to do further analyses as it increases the probability of statistical errors. We also use the Lafage et al. (2019) PJK risk scoring system. One of the criteria of which is the position of the UIV. We believe this is sufficient for the strength of our cohort (limited by its sample size). We have added a section to address this also. We acknowledge at line 258 there was an error in surgical planning.

Changes in text: Lines 462-465 (Discussion)

Ideally, we would analyse the impact of these factors on PJK in our own cohort. However, our small sample size limits the ability to do so without additional errors. Hence, we used Lafage et al. (2019) PJK risk scoring system which includes 5 of the aforementioned risk factors but not all of them.

Comment 1.6: Further, PJF was reported purely as return to the OR, but it has been radiographically defined as UIV +2 angular change >20 degrees. If this is applied, how many patients had PJF (asymptomatic)?

Reply 1.6: Thank you for your expert review. We believe our definition (adding Vercoulen et al (2022) as a reference) is sufficient to explain why we used PJF as return to the OR not based only on radiological findings. We also report PKA (UIV+2). We believe this is adequate for readers to interpret the results, especially in context of the PKA, PJK, and PJF.

Changes in text: Line 195-196

We defined PJF and DJF as a patient requiring revision surgery *(19).*

Comment 1.7: While it is understood this was a prospective cohort study, what was the primary surgeons PJK/F and DJK/F rate prior to implementation of the technique? This seems important, as the goal is not only to identify improvement over the rates in the literature, but surgeon improvement based on new technology may have value as well. Ultimately this may be too difficult to quantify due to changes in surgical/patient management, but if it can be obtained would add to the value of the paper. It appears the authors were able to note that surgical time did not change, and hint at the fact that surgical treatment may have changed due to increased osteotomies to fit the patient to the rod, so perhaps the cohorts would be too varied.

Reply 1.7: This is an expert recommendation. We unfortunately do not have access to this data. Perhaps future comparisons of PSSR vs conventional rod cohorts could answer this question.

Changes in text: *None*.

Reviewer B

Comment 2.0: This is a short but very interesting series of PSRods for adult surgery.

My comments:

Reply 2.0: Thank you for this professional review and suggestions. We have identified your expert changes to the text below.

Comment 2.1: In the title, abstract, and text, I suggest adult spine deformity instead of thoracolumbar kyphoscoliosis

Changes in text: Lines 1-3

Patient-specific spinal rods in *adult spinal deformity* surgery reduces proximal junctional failure: a review of patient outcomes and surgical technique in a prospective observational cohort

Comment 2.2: I would write “prospective observational cohort” instead of “prospective observational study”.

Changes in text: Lines 1-3

Patient-specific spinal rods in adult spinal deformity surgery reduces proximal junctional failure: a review of patient outcomes and surgical technique in a prospective observational *cohort*

Comment 2.3: Add max and min follow-up in the abstract and results.

Changes in text: Lines 46-47

Results: Mean age of 71.9 (±6.9) years and BMI of 27.8 (±4.8) kg/m2. *Mean follow-up 25.2 ± 8.6 (7-40) months*. No modification to PSSR shape.

Lines 226-227

Twenty patients underwent PSSR within the study period, had a mean age at operation of 71.9 (±6.9, standard deviation) years, 15 (75%) were female, with an overall mean BMI of 27.8 (±4.8) kg/m2 (Figure 1). *Follow-up time ranged from 7 to 40 months (mean 25.2 ± 8.6)*. Six patients were ex-smokers. Five patients had osteoporosis (T score □ -2.5) and four had osteopenia. Patient demographics are displayed in Table 1.

Comment 2.4: Results section of the abstract: please avoid writing results that have not been announced in the methods: cages, modification to rods...

Reply 2.4: Thank you. We have deleted the modification to rods. We have added a sentence to the methods about cages.

Changes in text: Line 39-43 (Abstract)

Sagittal spinopelvic parameters (SVA, PT, and PI-LL) measured by serial EOS scans were performed preoperatively then compared to planned correction and postoperative measures reported by independent radiologists. *Interoperative cages (narrow / wide) were placed for interbody support*.

Line 46-47 (Abstract)

Results: Mean age of 71.9 (±6.9) years and BMI of 27.8 (±4.8) kg/m2. *Deleted "No modification to PSSR shape."* Mean follow-up 25.2 ± 8.6 (7-40) months.

Comment 2.5: Conclusion section of the abstract: please add comparison between your rate of PJK, PJF, and DJF and current literature. A single % without comparison in unclear for a common reader.

Reply 2.5: Thank you for your suggestion. We have added the literature value for PJF. We don't believe we need the literature values for DJF and PJK in *conclusion* because we do not 'compare' to a value here. We hope this is sufficient.

Changes in text: Line 57-58

PJF was reduced, *compared to the literature (35%)*, with no rod breakages, but PJK was observed over time.

Comment 2.6: Add adults pine deformity to keywords; I would write patient specific rods instead of Patient-specific spinal rods

Changes in text: Lines 62-63

Keywords: Patient-specific *deleted 'spinal'* rods, *adult spinal deformity*, sagittal parameters, junctional complications, patient reported outcomes

Comment 2.7: Intro, line 90, please add a reference to "This manual bending can cause under- or over-correction of the deformity or rod breakage."

Changes in text: Lines 91-92

This manual bending can cause under- or over-correction of the deformity or rod breakage *(3).*

Comment 2.8: Intro, line 97-99, I am not sure you can transpose this sentence from 3D printed implants to PSR.

Reply 2.8: Thank you for this professional revision. After reviewing the literature we agree with this statement, hence, we have removed it.

Changes in text: Lines 99-101

Deleted "The benefits of PSSR…" Notably, there are reduced operation times because PSSR do not require contouring during surgery which results in fewer rod microfractures, decreased fatigue-life *and fewer mechanical complications* (5, 6, 7).

Comment 2.9: Methods, line 132, please specify that Patients who were diagnosed with low bone mineral density were included

Changes in text: Lines 130-133

Patients who were diagnosed with low bone mineral density were referred to consultant endocrinologist to optimize bone health before surgery; *these patients were included for surgery*.

Comment 2.10: Methods, line 152: what is the role of the patient? Please specify.

Reply: Thank you. We have modified the paragraph.

Changes in text: Lines 155-156

The patient was consented appropriately for risks, benefits, and length of procedure.

Comment 2.11: Methods, line 159: what screws did you use? Solera medtronic? Please specify.

Changes in text: Lines 161-163

All posterior pedicle screws (PASS LP pedicle screw fixation system, Medtronic, MN) were placed by open technique aided by computer guided navigation.

Comment 2.12: Methods and results: did all patient undergo at least one interbody fusion? Please specify

Changes in text: Line 160-162

A PSSR template was used for all intraoperative patient positioning. The number of *interbody fusion levels* were dependent upon the patient-specific surgical plan provided. *Not all patients had an interbody cage placed*.

Comment 2.13: In results, you mention footprint cages but did not announce them in methods. Please add a sentence in methods.

Changes in text: Line 170-172

Anterior column interbody cages (ALIF/LLIF/PLIF) were considered wide footprint and TLIF were considered narrow footprint cages.

Comment 2.13: Line 250-255, if the journal allows it, could you provide x-ray as supplemental material?

Changes in text: Lines 688-690

Appendix:

Figure 3 Case of operative proximal junctional failure. a Coronal EOS scan b Sagittal EOS scan

Comment 2.14: line 262-264: did all these patients undergo to-pelvis fusion?

Changes in text: Lines 266-269

Four patients suffered DJF needing revision surgery *(3/4 were fused to pelvis)*. Of these, 3 patients had no L5/S1 interbody cages inserted and 1 patient had a single TLIF cage at L5/S1. No patients suffered DJF with wide footprint cages at L5/S1 *(14/16 were fused to pelvis)*.

Comment 2.15: Discussion, line 299, this is a near significant difference. Since you did not calculate the number of subjects before, you should not conclude this is "not significant" but that this difference is doubtful of debatable or needs further investigations etc. The P-value is the probability of obtaining "by chance" a result (eg, mean difference) equal to (or more extreme than) what we actually observed when the null hypothesis is true. Therefore, P-values can indicate how incompatible the data are with a null hypothesis. (Why a P-Value is Not Enough.

Solla F, Tran A, Bertoncelli D, Musoff C, Bertoncelli CM.

Clin Spine Surg. 2018 Nov;31(9):385-388. doi: 10.1097/BSD.0000000000000695.)

Reply 2.15: Thank you for this expert comment and reference. We agree that p-values were not intended to be purely binary, and have added the comment below.

Changes in text: Line 303-305

However, we did not find a difference in PT between preoperative versus surgical plan, *although the result narrowly failed to approach statistical significance* ($p = 0.058$).

Comment 2.16: Lines 437-445 are currenly "background', not "discussion". COuld you add a comparison between these statements and your data? Otherwise, please move to introduction.

Reply 2.16: Thank you. We have added a statement at the end of the paragraph to clarify why we could not specifically compare this information to our own cohort. We hope this is sufficient.

Changes in text: Line 462-465

Ideally, we would analyse the impact of these factors on PJK in our own cohort. However, our small sample size limits the ability to do so without additional errors. Hence, we used Lafage et al. (2019) PJK risk scoring system which includes 5 of the aforementioned risk factors but not all of them.

Comment 2.17: Line 454, could you add a comment about this?

Reply 2.17: Thank you. We are unsure on which part of this section you would like us to comment on. However, after reviewing we felt the comment below clarified your suggestion.

> Lafage et al. (2019) developed a simple risk scoring system for PJK at 2 years follow-up (43). The authors used 5 factors corresponding to a 6-scale risk score (Table 6). The factors were defined as: [1] age > 55 years, [2] fusion including S1 / ilium, [3] UIV in upper thoracic spine (T1-T6), [4] UIV in lower thoracic spine (T7-T12), and [5] $>10^{\circ}$ of lordotic correction. A score of 5 corresponded to an increased odds of 11.0 and a score of 4 corresponded to 5.3 increased odds of developing PJK. We report a mean PJK risk score of 3.7 ± 1.0 and found no significance between the PJK risk score and development of PJK ($p=0.258$).

Changes in text: Lines 474-477

Our non-significant results suggest that our cohort does not align with the PJK risk score previously validated by Lafage et al (2019) (43). But we think it pertinent to investigate these results in the future and consider analysing the effects of each separate factor especially the position of the UIV.

Comment 2.18: Line 48, please write "mean follow-up of 24 months"

Reply 2.18: We have edited the paper according to your comment (**2.3**). We feel this is sufficient.

Changes in text: *As above*.

Reviewer C

The authors present clinical, radiographic, and PROMs outcomes for twenty patients who received patient-specific spinal rods (PSSRs) for adult spinal deformity. The language is clear and readable. There were several notable findings in the analysis, but these do not appear to be specific to PSSRs.

I will return frequently to the author's stated objective, which I believe was discussed but with some questionable interpretations:

"The aim of this study was to report patient satisfaction and clinical and radiological outcomes using PSSR, comparing pre-operative planning to post-operative correction and maintenance of the sagittal parameters to mid-term follow-up. Specifically, we investigated rates of junctional complications both proximally (kyphosis/failure) and distally (failure)."

Comment 3.1: While there is value in reporting that the PSSR delivered the desired radiographic results on postoperative radiographs, the discussion on DJF is not specific to PSSRs. The authors note cage footprint influenced DJF, but it is unclear whether the PSSR did as well. A similar pattern is seen for PJK. More clarity here/evaluation of feasible PSSR roles in these outcomes is necessary.

Reply 3.1: Thank you for your professional comment. We agree that the discussion is not specific to PSSR, hence, we have added comments to provide clarity on the references used in the discussion.

Changes in text: Lines 380-384

Likewise, Park et al (2021) found ALIF superior to TLIF at the lumbosacral junction (28). Charles et al (2019) suggested anterior fusion combined with posterior instrumentation was protective against non-union and DJF (29). *Whilst this literature does not report DJF rates with PSSR we believe* that restoration of lordosis and the additional stability from a wider footprint cage at the junction protects against DJF (30).

Lines 458-460

Significant risk factors for development of PJK *in ASD surgery (without PSSR use)* have been identified and divided into 3 categories (radiological, surgical and patient-related) (40, 41, 42).

Comment 3.2: In addition, the statement "PSSR was an effective tool for improving PROMs and treatment of ASD in this series" is misleading. Without a control group OR controlling for final alignment parameters in the statistical analysis, this is an overstatement of the PSSR's power.

Reply 3.2: Thank you for this review. We agree and have made the necessary changes.

Changes in text: Line 56

Conclusions: *In this series PSSR improved PROMs and treated ASD*.

Line 504

In this series PSSR improved PROMs and treated ASD to a mean of 25 months.

Comment 3.3: There is promise in the operative variable outcomes discussion but with some lack of cohesiveness. The authors state that OR times did not decrease with PSSRs, anecdotally finding that PCOs were more laborious. This is a detail of interest as it illuminates a barrier to implementation that assumably other surgeons might encounter. This should be connected to EBL, which would not likely be impacted by PSSRs unless (1) operative time changed or (2) osteotomy quality/frequency changed. Similar point for wound infections and neurological deficits. It is unclear whether the authors believed PSSRs would impact these metrics and – if so/not – why? While it is appropriate to report these outcomes out of necessity/completeness sake for a case series, there should be more attempts to connect their findings with the paper's objective.

Reply 3.3: Thank you for this expert advice. With the following changes in text we aimed to add more clarity to the paper, connecting our findings with the objective. We believe these changes fairly address your concerns.

Changes in text: Lines 367-369

The literature reporting on PSSR focuses on sagittal alignment goals and the utility of PCOs, however, often lacks discussion on the intricacies of surgical technique (3, 8, 9, 10, 11, 12).

Lines 369-371

McDonnell et al. (2021) stated that anterior-posterior (versus posterior-only) surgery, fusion to the sacrum, and younger age (< 60 years) was protective of DJF *with conventional rod use*.

Lines 358-361

The authors note the paucity of PROMs and patient satisfaction data in the literature surrounding the use of PSSR in management of ASD. To our knowledge, we are the first paper to report on PROMs and patient satisfaction in the postoperative follow-up of patients who have undergone ASD surgery with PSSR.

Lines 395-398

In ASD surgery PCOs have been validated to reduced PJF rates *with conventional rods and achieve better alignment of sagittal parameters with PSSR (10, 12, 33)*, which is consistent in our study with all patients having PCOs.

Lines 402-4011

Operation time was consistent across our cohort with a mean of 590±165 minutes and a median estimated blood loss of 800 (IQR: 1000) mls. *Using PSSR* our operative time did not decrease*, and the EBL was reduced*. The total operation time of our cohort was more but EBL less than results reported in a recent systematic review of a mean operation time of 370 (±161) minutes and mean EBL of 1,828 (957) mls (15). *Similarly, using PSSR Sadrameli et al. (2020) reported an operation time of 411 (±93) min with EBL of 861 (±354) mls (11)*. *It is important to highlight the increased operation time with an accepted EBL, whilst different to the current literature, it notes a possible barrier in implementation of PSSR.* The surgeons believe the time saving from eliminating the need for rod bending was counteracted by the need for increased time whilst performing PCOs to fit the PSSR.

Lines 415-416

Our results remain unclear to whether the implementation of PSSR would influence these complication rates.

As such, the current article reads more like an ASD outcomes case series than a PSSR-specific review. Of note, there are several papers (many cited) reviewing projected versus obtained alignment with PSSRs, but a dearth of literature evaluating PROMs + costs + long-term following. As such, should the authors focus the outcomes + paper discussion on variables pertinent and novel in the PSSR literature, then the manuscript would be worthy of publication.

Reviewer D

The authors find a reduction in the frequency of Proximal Junctional Failure in spinal deformity surgery with the use of Patient-Specific Spinal Rods.

Sagittal balance is an essential element in surgery for extensive arthrodesis performed in spinal deformities, as evidenced by the high number of sagittal balance disorders after spinal deformity surgery.

Each patient has their own balance which must be understood and measured before surgery. It is no longer acceptable to entrust the surgeon's intuition alone with bending rods in the sagittal plane.

It is the great interest of PSSR which oblige to think before the operation and to precisely calculate lumbar lordosis and thoracic kyphosis that one must give to his patient to ensure a good sagittal balance and thus reduce the complications related to an insufficient balance.

This article goes in this direction and as such must be published.

No comment on methods and results.

Well organized discussion.

Many questions remain and we must continue in this direction.

Congratulations to the authors for this prospective and serious work.

Reply: Thank you for your review and expert opinion. We included paragraph 3 of your comments in the paper.

Lines 284-293

Years lived with disability due to low back pain is higher in women, consistent with the majority (75%) of our cohort being female (1). Recent literature has indicated that the use of templates with surgical specific software modelling and PSSR decreases overbending of rods and leads to improved patient outcomes (5, 22). We recognise that surgical specific software modelling is a useful adjunct and guide in surgical management of ASD. Each patient has their own spinal balance which must be understood and measured before surgery. It is no longer acceptable to entrust the surgeon's intuition alone with bending rods in the sagittal plane. However, it is not an absolute and the surgeon must follow established deformity principles and techniques that they are experienced and competent in performing.