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Hemodynamic Neuromonitoring, a Proposed Spino-Cardiac Protective Reflex: Prospective Study in 200 Patients of Lumbar Surgery

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Abstract

Background: Parasympathomimetic reflexes are reported in literature in spine surgery. Our primary hypothesis is proposed that nociceptive stimuli can be elicited in various maneuvers of lumbar spinal surgery and the physiological manifestation depends on many patient variables and anesthesia. However, a sympathomimetic pathological response is indicative of potential neural damages, which may or may not be reversible. A spino-cardiac protective reflex (SPR), as a new entity for lumbar spinal surgery, is proposed.

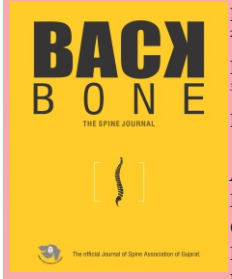
Study Design: This was a prospective single institution.

Materials and Methods: All the patients who were undergoing single motion segment transforaminal lumbar interbody fusion (TLIF) in our institute for lumbar disc herniation (LDH) or non-discogenic lumbar stenosis lumbar spinal stenosis (LCS) were included, who fitted into inclusion criteria till 200 subjects were recruited. Patients' pertinent vital data were collected at clinical first pre-operative visit and preoperatively on admission. The intraoperative parameters were recorded: Pre-induction, post-induction, post-positioning, before skin incision, after skin/subcutaneous exposure, pre-screw insertion, after screw insertion, after rod connection and distraction, during central decompression-laminotomy/laminectomy, during lateral recess decompression, discectomy, and segmental compression. A sudden change in reading of MAP(mean arterial pressure) by 20 and PR(pulse rate) by 20 was considered a significant change when compared with preceding step of surgery. If a rise was noted , a reason for increase is looked by visualization and exploration to look for any residual or new compressive nociceptive stimuli. Positive corrective measures reducing the vital readings back to normal were noted as culprit correction cases. The following criteria were needed to be present for this unique cause–effect relationship. Two domains for explanation including plausibility and reversibility were taken. Plausibility means the prompt appearance of the reflex must be explainable by an adequate stimulation of the nerve or any other nociceptive stimuli. Reversibility means the stimulus cessation abolished the reflex and hemodynamic parameters returned to immediate baseline. The MAP change from pre-operative fitness to 6 months follow-up of surgery was also noted and correlated with any need to change antihypertensive dosage.

Results: In the enrolled 200 patients, the change in mean MAP and PR changes in varying steps of TLIF were not significant. The plausibility and reversibility was noted in in 22 cases. Non-correlating rise in parameters were also noted in 35 cases. The antihypertensive dosage remained same in 101 patients as pre-operative, increased in 3 and decreased in 60 patients at 6 months follow-up. But, no statistical significant changes were found.

Conclusion: Spino-protective reflex exists like any reflex in body. Prospective study on huge database needs to be done to validate these observations. However, this study does make the surgeon think for finding clues to neurological damage or left out residual compressions which can be identified and rectified in real time in many cases. IONM is the standard of care and SPR should be compared with it to identify sensitivity and threshold of pathological response in future studies.

Keywords: Lumbar, Protective, Reflex, Spine, Sympathomimetic, Transforaminal lumbar interbody fusion.



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Introduction

Cardiovascular changes in neurosurgical patients, cardiac surgery, laparoscopic surgery, and periodontal surgery are reported with different mechanisms involved in these changes and are the result of various proposed/proved hypothesis including trigeminocardiac reflex (TCR), vasovagal reflex (VVR), cranial nerve stimulations, Cushing's triad, brainstem manipulations, neurogenic reflex, hypothalamic stimulation, venous air embolism, and also with its different subtypes [1, 2, 3, 4, 5]. Spinal shock, hypovolemic shock, autonomic dysreflexia, venous air embolism, parasympathetic hyperactivity, etc., all can be devastating if they occur during spinal surgeries. Few reports have been there in cervical and dorsal surgeries [1, 2]. There are limited data in lumbar spine surgery hemodynamic changes [6, 7, 8, 9, 10].

Chaudhary et al. reported a comprehensive review with detailed description of the possible mechanism underlying many hemodynamic changes in lumbar spine surgeries. They proposed a spino-cardiac reflex (SCR) responsible for a vagal type stimulation, probably due to dural manipulations during five different case scenarios picked up by a methodological literature review of lumbar surgery [2].

Intraoperative neuromonitoring (IONM) is an established method to check neural injuries and it has become popular in recent years [11, 12]. We for the 1st time propose a hypothesis that nociceptive stimuli can be elicited by various maneuvers of lumbar spinal surgery and the physiological manifestation depends on many patient variables and anesthesia. However, pathological response is indicative of neural damages, which may or may not be reversible. A spino-cardiac protective reflex (SPR), as a new entity for lumbar spinal surgery, is proposed. It is contrasting to TCR and SCR both of which are a variant of VVR and parasympathomimetic. Hemodynamic neuromonitoring would add on IONM and can be relied on exclusively in operative setups where IONM is not available. On this proposed hypothesis, operated transforaminal lumbar interbody fusion (TLIF) patients were assessed for variations in hemodynamics peroperatively, correlated with surgical maneuvers and patient demographics prospectively.

Materials and Methods

This is a single-center, prospective study. In this study, all the patients who were undergoing single motion segment TLIF in our institute for LDH or LCS were included till 200 patients got enrolled. This study is approved by the Institutional Ethical Committee and prospectively registered with CTRI (Clinical Trial Registry India) wide approval CTRI/2014/09/004951.

Patients are included in the study if they were skeletally mature adult between the ages of 30 and 70 years at the time of surgery and gave consent. Patients are excluded if any of the following criteria were noted: Has had previous lumbar spine surgery; patients with anemia (hemoglobin <9 mg/dL), heart disease, severe organ insufficiency, bleeding in excess of 500 mL, or experiencing unexpected intraoperative events; patients with diffused idiopathic skeletal hyperostosis; active infection; history of AIDS or HIV, hepatitis, active rheumatoid arthritis, non-controlled diabetes mellitus, immunologically suppressed, and any metabolic bone disease; previous known major allergy; morbid obesity, active malignancy, and substance abuse (e.g., recreational drugs, narcotics, or alcohol); and patients on beta-blocker group of anti-hypertensives.

Method of anesthesia

All the patients were operated under general anesthesia in prone position. The American Society of Anesthesiology Grade I to III was included. All patients were premeditated with injection fentanyl 1.0 mg/kg and injection glycopyrrolate 1 ml (0.2 ug) iv 5 min before induction. Patients where then induced with injection propofol 100 mg and injection atracurium 50 mg. Anesthesia was maintained with N20, oxygen, and isoflurane at standard rates range on dial. The dose was maintained to achieve a fall by maximum of 20% of baseline blood pressure. Injection atracurium (25 ug/h) infusion was given. Hypotension was labeled if systolic BP is <90 mm of Hg or diastolic <60 mm of Hg. Pulse rate (PR) <60 was labeled bradycardia and more than 100 as tachycardia. The patient was kept euvolemic. A monitor recording of 1 min interval automeasurement was set. In our cases always, additional pre-incision bolus dose of propofol was given as per institutional protocol.

Method of surgical execution

All the surgeries performed by the spine surgeon team. The pedicle screws with locally harvested (morselized posterior elements) bone grafts and interbody cage were used for TLIF. The patient was induced in supine position and shifted to operation table in prone position, bolsters were applied vertically, painting and draping done. Regular standard posterior midline 4–5 inches incision with exposure done up to facet. Level verified under image intensifier and then pedicle screw insertion done. Rods were connected and distraction done. Central decompression done by laminotomy/laminectomy and then lateral recess decompression done with the removal of the unilateral facet. Only Kerrison punches were used. No motorized tool was used. Foraminal decompression also done simultaneously when needed. Hemostasis achieved using bone wax, bipolar cautery, putting patties, and gel foam. Then, discectomy done from that side, end-plate preparation completed with curettes and other hand instruments. During this step, nerve roots and dura retracted with dural retractor when needed. Bone graft

and cage inserted in disc space. Positions confirmed under image intensifier, segmental compression done, and nerve roots were checked for their free mobility. Closure done in layers under drain. Postoperatively, routine analgesic antibiotic protocols were followed. All patients were mobilized as per tolerance and advised graded physiotherapy.

Patients' pertinent vital data were collected at clinical first pre-operative visit (This is the visits 1–2 weeks before surgery when the patient gets medical fitness by the physician) and preoperatively on admission. The intraoperative parameters were recorded: Pre-induction, post-induction, post-positioning, before skin incision, after skin/subcutaneous exposure, pre-screw insertion, after screw insertion, after rod connection and distraction, during central decompression-laminotomy/laminectomy, during lateral recess decompression, discectomy, and segmental compression.

Patients who fulfilled the inclusion criteria were reviewed for demography.

The radiological severity (on 1.5 Tesla MRI) of LDH and LSS was analyzed with qualitative grading system; morphological grades of stenosis according to Schizas et al. and grade of MSU classification for LDH were used, respectively. Description of Schizas grading of stenosis is as follows: Grade A (nil or minor), Grade B (moderate), Grade C (severe), and Grade D (extreme) [13]. Grading for LDH as Grades 1, 2, and 3 with type A, AB, and C lesions [14]. Dynamic lateral radiographs were used to note the presence of any instability.

Definition of hemodynamic changes and defining the hypothesis and outcome measures

Observation of severe painful stimuli especially new manipulation of root/cord in constrained space of stenosis or discogenic stenosis or a screw misplacement displacing the root was noted. A sudden change in reading of mean arterial pressure (MAP) by 20 and pulse rate (PR) by 20 was considered a significant change when compared with preceding step of surgery. A change of only one of MAP or pulse alone was not considered significant. This figure was arbitrarily taken as per past experiences of years of spine surgery practice by our team of surgeons and anesthetists. If a rise was noted, a reason for increase is looked for visualization and exploration to look for any residual or new compressive nociceptive stimuli. Positive corrective measures reducing the vital readings back to normal were noted as culprit correction case with the reasons there off, if found. All these were assessed after exposure level. Also, noted was any major change at all steps from fitness to post surgery. The MAP recording change after 6 months of surgery was also noted to assess if there is a reduced requirement of antihypertensive drugs after the overall betterment of the pain, disability, and health.

The following criteria were needed to be present for this unique cause–effect relationship. Two domains for explanation including plausibility and reversibility were taken. Plausibility means the appearance of the reflex answer must be explainable by an adequate stimulation of the nerve or any other painful stimuli. The reflex should have appeared promptly after the stimulus is applied. Reversibility means the stimulus cessation abolished the reflex and hemodynamic parameters return to immediate baseline.

Statistics

Patients' demographics and characteristic categorical variables were analyzed. Mean ± SD (minimum and maximum) for applicable variables were calculated. Each category was compared using appropriate statistical tools such as Pearson correlations, unpaired Student's t-test, and paired t-test. Statistical analysis was performed with SPSS software (version 20.0; SPSS, Chicago, Illinois). $P < 0.05$ was considered to be statistically significant.

Review of literature

We have searched terms including "Bradycardia," "Hypotension," "Asystole,", "hemodynamic changes/perturbations/disturbances," "lumbar spine surgery," "lumbar laminectomy/discectomy," "lumbar spine instrumentation," "cardiovascular changes/disturbances," "spine surgery," and "TLIF" in various search engines of PubMed, Google Scholar, Science Direct, and EMBASE from January 1, 1970, to June 30, 2020. For data extraction, all titles/abstract/detail articles were studied as needed. The selection of the included literature was performed according to the data contained in summary. English literature only was searched. This was not a review article so methodological search aspects may have missed.

Results

The study start date was December 23, 2014 and completion date was December 29, 2016. Two hundred and one consecutive cases enrolled were operated patients of TLIF fitting into the inclusion criteria. One patient was excluded after enrolment due to uncontrolled hypotension. There were 79 males and females 121 in the series with mean age of 52 ± 11 (30–78) years. MAP and PR at various steps of surgery changed but these changes were not significant. The change in mean MAP and PR with intubation, position, and post-incision were noted to be non significant. In 22 cases the positivity of a significant change in MAP and PR correlating with an evident manipulative/pathological cause was noted (plausibility), which could revert back to baseline (reversibility) after addressing the culprit (Table 1). The positivity of a significant change in MAP or PR non-

Table 1: Cases with plausibility and reversibility of Spino-Protective Reflex.

Case No. (n=200)	Reflex noted in different respective stage of TLIF surgery	Identified presumed causal reason and corrective step described. Following the corrective measure PR and BP returned to the baseline	Remark/clinical valuable tips in TLIF
2	Segmental compression	Sub-annular stenosis on same side behind the traversing root developed which was not there before segmental compression	Confirmatory checking of both side traversing roots for mobility and space around it circumferentially should be done
9	Screw insertion	Screw inferior breach noted on image intensifier and changed	Direct nerve injury is a nociceptive stimulus. Careful clinical insertion, radiological/fluoroscopy guidance/neuromonitoring/navigation would reduce the incidences
23	LR decompression	Significant tight lateral recess stenosis and stretched root which was non mobile. A calcified component of disc was present. Further surgery execution was done with smaller Kerrison and osteotome	Severe stenosis in lateral recess if present in degenerative stenosis with central disc prolapse, manipulation of root with Kerrison is inevitable. Burr and smaller instruments would help
27	Screw insertion	No screw violation was noted medially on image intensifier. However, a pedicle break and expansion were noted medially after decompression of lateral recess. Screw was not changed. Root was free and relaxed after decompression	Nerve root displacement by an expanding pedicle due to pedicle screw or violation can be significant in presence of existing severe stenosis
35	Through-out the surgery	Significant compression by a massive disc. The disc's extruded mass was bigger than that was seen on MRI. Patients MAP/PR remained high and did not reduce. Post-operative catheterization revealed a 1100 ml urine instantly. On enquiry patient had developed repeated frequency of urination previous night which was a cauda equine syndrome developing overnight	Cauda equina syndromesleading to retention can distend bladder and give uninhibited sympathetic stimulation leading to uncontrolled hypertension. Pre-operative catheterization can be a reasonable protocol to avoid so. More manipulations are expected in posterior approach massive ventral decompression as well
40	Screw insertion	Screw slippage superiorly outside pedicle pilot hole	Any sensitive structure irritation like a upper exiting root or the median bundle branch or a periosteal stripping is a nociceptive stimuli
48	Screw insertion	Screw medial breach noted on image intensifier and changed	Same as case 9
62	LR decompression	Severe stenosis grade Schizas Grade D with Disc protrusion MSU 2AB grade. Difficult entry into the lateral recess around fixed traversing stenosed root. Smallest Kerrison used	Same as case 23
64	Central decompression	Severe stenosis grade Schizas Grade D with Disc protrusion MSU 2AB grade. Difficult entry into the canal to do laminectomy. Calcified end-plate spur was also present ventrally	In severe stenosis entering into the canal with traditional Kerrison is manipulative and it is better to use motorized burr or bone scalpel to avoid secondary damages
69	Discectomy	Calcified disc excision needed more manipulation and bilateral disc incision and more medial retraction of the roots. Rods removed and more angulation achieved with the disc cutting and cage preparation tools	In case of ventral calcified discogenic stenosis, root retraction medially will stretch the elongated-stretched-fixed root and potentially further damage the neural tissue. Lateralization can be achieved by complete facetectomy and rod placement should be done lastly when doing a PLIF or TLIF especially in severe compression
73	Screw Insertion	Screw medial breach noted on image intensifier and changed	Same as case 9 and 48
74	LR decompression	Up-migrated disc prolapsed fragment. Manipulation to detether the fragment was needed	Hidden zone disc fragments if big may need indirect manipulation with hook in compromised space
76	LR decompression and Foraminal stenosis decompression	Stenosis in the foramen needed more Kerrison punch bites on same side	In narrow foramen in presence of ventral buckled annulus/pseudo bulge and disc space collapse the dorsal Kerrison punch may temporarily increase the compression on existing nerve root
77	LR decompression	Significant tight lateral recess stenosis in massive disc prolapse Grade 3AB	Before massive fragment retrieval, lateral recess decompression needs some manipulation which is inevitable. Osteotomes, burr, or bone scalpel may reduce manipulations
79	Discectomy	Sub-annular stenosis due to hardened annulo-cartilaginous fragment was present. It needed more repetitive manipulation to remove	Sub-annular piece of disc prolapses, especially the one with end-plate injury, may need more manipulation to separate from the remaining attachments
86	Segmental compression	Sub-annular stenosis opposite side behind the traversing root. This was not present initially and developed after segmental compression. Opposite side discectomy was done to correct (Fig. 1)	Confirmatory checking of both side traversing roots for mobility and space around it circumferentially should be done when decompression is done and it should be repeated again after segmental compression is done.
87	Segmental compression	Small piece of bone graft below exiting nerve root noted. It was then removed	Bone graft spillage should be checked. Usage of funnel can help. Always it should be customary to check after completion of all steps of surgery
96	Segmental compression	Sub-annular stenosis was noted on opposite side behind the traversing root. Opposite side discectomy was done	Same as case 86
127	Screw insertion	Screw slipped inferolateral outside pedicle pilot hole	Any sensitive structure irritation like exiting root or a periosteal stripping is a nociceptive stimulus
160	Segmental compression	In this L5 S1 TLIF, sub-annular stenosis ventrally was present after the segmental compression. This ventral stenosis along with the inferior margin of the superior vertebra (L5) squeezed the dura which was appreciable on exploration. The down migrated piece of this case was removed but there existed an annular piece at the discal level which was a significant big piece of hard annulo-cartilaginous fragment with a residual attachment. Removal of the piece and trimming of the laminotomy inferior margin of L5 could free the neural tissue	Overdoing the compression and calcified spur of annulo cartilaginous hard part at the discal level can produce new compression after segmental compression
172	Segmental compression	Foraminal stenosis on opposite side behind the exiting root. Decompression done	Segmental compression can narrow opposite foramen in presence of ventral buckled annulus/pseudo bulge, in disc space collapse. Probing should be done of the same and opposite foramen and clearance confirmed

PR: Pulse rate, BP: Blood pressure, TLIF: Transforaminal lumbar interbody fusion, LR: Lateral recess, MAP: Mean arterial pressure

correlating with an evident manipulative/pathological-demographic cause was also noted in 35 cases. These returned to normal without any corrective measure in 24 cases and did not go back to immediate baseline in 11 cases. However, no manipulative or damaging preceding events were noted in these 35 cases. The antihypertensive dosage remained same in 101 patients as pre-operative, increased in 3 and decreased in 60 patients at 6 months follow-up. But, these all changes were statistically insignificant.

Discussion

Spinal decompression surgery is be considered for radicular pain or claudication or mechanical backache when non-surgical treatments have been unsuccessful and clinical and imaging findings indicate association of symptoms with LDH or LSS [15].

The body responds to pain through numerous and interconnected physiological processes through the sympathetic nervous system, neuroendocrine system and immune system, and by emotions. These responses include mainly positive chronotropic changes, increased respiration, increased blood glucose and cortisol levels, reduced gastric motility, increased muscle tension, and overall activation of sympathetic tone [16]. Physiologically homeostasis is achieved by these responses but when nociceptive stimuli cross certain threshold then homeostasis is disturbed, and it gives severe pathological response. These reflex instantaneous responses are known to occur normally as well as in surgical procedures under general anesthesia [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 16].

Hemodynamic changes/perturbations during spine surgeries are reported in literature [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. These changes include major bleeding, spinal shock, autonomic dysreflexia (AD), parasympathetic nerve root activation and venous air embolism, and traumatic spinal cord injury [1, 2]. In higher level, spine injuries decreased sympathetic outflow accompanied by constant parasympathetic flow leading to bradycardia and hypotension. This autonomic dysfunction with loss of reflex and subsequent reappearance of reflex is called spinal shock [17]. In some cases, after spinal cord injury at T6 level or higher level sympathetic activity becomes overactive instead of typical decrease which leads to paroxysmal episodes of sympathetic activity and hypertensive crisis. This phenomenon is called AD. AD is triggered by both noxious and non-noxious stimuli [18, 19, 20, 21].

Chowdhury and Schaller recently proposed SCR hypothesis for justifying decreased hemodynamic changes in lumbar spine surgery [2]. This is likely a vasovagal reflex and not justified normal in view of the fact that lumbar outflow is sympathetic and not parasympathetic. Although, a pain or other factor induced direct parasympathetic hyperactivity may be an explanation. Second, their reporting is on the basis of their own previous work and based on case reports identified from literature reports of lumbar surgery based on a methodological search.

The ventral spinal dura contains a dense, longitudinally oriented, nerve plexus, which receives its contributions from: (I) The sinuvertebral nerves, (II) the nerve plexus of the posterior longitudinal ligament, and (III) the nerve plexus of radicular branches of segmental arteries. Dorsal dural nerves are much smaller in number, do not form evident plexus, and do not reach the medial region of the dorsal dura. The dorsal nerves are derived from the ventral dural plexus at the level of the "inter sleeval" parts of the dura mater [22]. Dural nerves are considered to be sympathetic, but there is debate for it [23, 24, 25]. As the sinuvertebral nerves exclusively originate in rami communicants [26], a sympathetic nature of at least a part of the dural nerves is evident. These fibers, perhaps together with viscero-afferent nerve fibers which pass along the described sympathetic pathways, may explain why electrical epidural stimulation has a beneficial effect on vascular insufficiencies as reported by Meglio et al. [27].

Important principles of general anesthesia are reversible loss of consciousness with a lack of movement, a lack of awareness, unresponsiveness to painful stimuli, and a lack of recall of the surgical intervention and monitoring [28]. To ensure adequate depth of anesthesia for preventing awareness without inadvertently overloading the patients with potent drugs require monitoring of depth of anesthesia. There are various subjective and objective methods available for measuring depth, which include monitoring of hemodynamic responses, lacrimation, sweating, isolated forearm technique, heart rate variability, lower esophageal contractility, electromyogram, bispectral monitoring (BIS), median frequency, and various evoked potentials such as auditory evoked potential, visual evoked potential, and somatosensory evoked potential (SSEP) [29].

Monitoring of potential or manifesting neural injuries is done by IONM. To identify and correct damage to neural tissues in neurosurgical patients, use of various IONM techniques is popular [11, 12]. It can identify cord or root injuries in a predictive way and offers real-time management for corrections/rectifications of damaging interventions. In their studies of IONM, Wiedemayer et al. demonstrated patients' groups as follows: 105 (16%) true positives, 26 (3.9%) false positives, 27 (4.1%) false negatives, and 500 (76%) true negatives [30]. Although advantageous and the recommended standard worldwide, with IONM in single-level procedures, neurological complications were decreased only among lumbar laminectomies. No difference was observed in anterior cervical discectomy and fusions, lumbar fusions, or lumbar discectomies. There was a significant increase in total

payments associated with the index procedure and hospitalization as well [31].

According to Prys-Roberts, common feature of general anesthesia is suppression of conscious perception of noxious stimuli. Analgesia, autonomic stability, and muscle relaxation are desirable but not actual components of anesthesia. They divided the noxious stimuli into somatic and autonomic components, which were further divided into sensory, motor and respiratory, hemodynamic, pseudomotor, and hormonal [32].

In 2008, Poon et al. in their study of hemodynamic changes in spine surgery in prone position demonstrated that decreased stroke volume and cardiac index are the main causes of hypotension [33]. Savitha et al. described in a comparative study group that intubation and change of position need deeper plane of anesthesia compared to skin incision [34]. No positive significant responses were noted in our cases at incision. This could be because always before incision a bolus dose of propofol was given in all cases as per institute protocol.

The large diversities of hemodynamic responses to various nociceptive stimuli in the studies might have been caused by mixed data obtained from various surgeries. Also, there are different effects of various anesthetic agents on physiology of body . Furthermore, variation in results is due to use of various monitoring technique from surgical depth index, BIS, analgesia nociception index, Cardean index, surgical plethysmographic index, spectral entropy, skin conductance, pupillometry, heart rate and blood pressure monitoring, and normalized reflex threshold [35].

Universal predictive response could not be found statistically significant in the massive data collected as per steps of surgery in our series. However, the 22 cases showed that alteration in PR and BP can occur pathologically when nociceptive stimuli are there. This alteration should draw the attention of the surgeon and help reverse reversible maneuver that can objectively lead to new symptoms and/or not relieve old preoperative symptoms. The case remark and clinical implications with their presumed inference are also quoted (Table 1). This may explain also the reason for contralateral new radiculopathy which is reported in open or new minimally invasive spine surgery (MISS) [36, 37]. For posterior approach surgeries in central disc and calcified disc, retraction manipulation of the dural sac tends to be greater and proposed solutions to these problems are of the transdural approach and the bilateral approaches [38, 39, 40]. Posterior spinal surgery itself as the cause of approximately 15% of total numbers of cauda equina syndromes brings to notice the true under reporting of iatrogenic injuries in literature [41].

Our results prove that SPR is a protective spinal reflex which mediates through sympathetic system (Fig. 1). This was in controlled settings of enrolled cases. It may happen even more

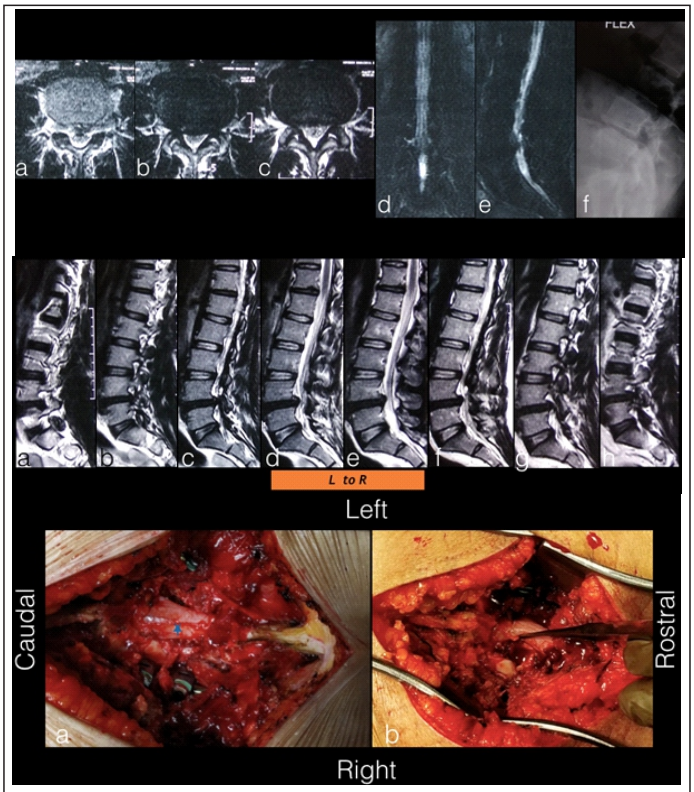

Figure 1: Magnetic resonance imaging and radiograph of the patient showing as listhesis L4-5 with lumbar spinal stenosis and lumbar disc herniation. After transforaminal lumbar interbody fusion surgery cage insertion from the left side done and segmental compression done. A raised pulse rate and mean arterial pressure occurred. A significant opposite side (Rt side) bulge (asterisk) was noticed. It was a redundant annulus with a small disc fragment below it which was substantially lifting the traversing root on Rt side. Opposite side discectomy-annulectomy was needed for decompression and to bring vitals back to baseline

in complex cases, MISS, and simple discectomies due to more manipulations in limited approach spaces. Furthermore, the MAP reduced in many patients and leads to reduction of antihypertensive usage (n = 61) at follow-up. This additionally suggests that it may be the nociceptive stimulus and anxiety that may be increasing the BP and drug need of pre-operative spine surgery patients.

Our study has many limitations as well. It's not a randomized or multicentric study. However, it is a prospective analysis. Studies with matched controls are necessary before we can determine the full clinical value of the proposed reflex but that is not practically ethically possible. The depth of anesthesia was monitored by clinical parameters and the dosage of drugs used was arbitrarily used based on the experience, hemodynamic response, and body weight-based regimen to maintain a plane adequate for the surgery. Furthermore, propofol was used regularly. However, now, the standard of care is going toward target control infusions and the use of propofol is limited due to negative hemodynamic effect and antiplatelet actions [42, 43]. Beta-blocker was the only drug which was considered an exclusion for selection though there may be many drugs which may be interfering with the proposed reflex. A rise of MAP and PR of 20 was the only criteria chosen to find a change in hemodynamic objectively on the positive side or negative side.

There is no reference for it, and it was chosen arbitrarily. Although literature mentions a change of more than 20% change from baseline as a significant response . There are usually four major domains for explanation including plausibility, reversibility, repetition, and prevention to establish cause–effect relationship. These criteria have been used as previously to demonstrate a cause–effect relationship in TCR and SCR [1, 2, 4, 5, 9]. Two domains, plausibility and reversibility, were only included in our study protocol. Repetition is reapplication of the stimulus leading to result in similar hemodynamic changes as previous. Prevention includes: (a) A lighter stimulus of the same type does not lead to the same severe reflex. (b) Nerve block abolished the reflex. (c) Application of anticholinergic drugs blocks the occurrence of the reflex [9]. In conducting our research, the repetition and prevention domains were not attempted as it seems unethical. Surgical steps are also not intricately same between surgeons of the team. This also may contribute to variability. The medicolegal aspect of lighter anesthesia plane can also be questioned as a response to nociceptive stimuli can be argued against its ethics. Although it is desired, analgesia, autonomic stability, and muscle relaxation are not always the complete components of anesthesia [43].

Negative cardiovascular changes have been recently also reported following lumbosacral spine surgery [44, 45]. Application of a local esthetic agent to neural tissue, maintaining hemodynamic, and avoiding the stimulus was the corrective measures taken by few recent reports [44, 45]. A temporal relationship of bradyarrhythmia and cardiac arrest after stimulation in neuromonitoring and polypharmacy has also been reported. Corrective measures and completion of surgery or abortion and return to operating room for completion after a stable interval were followed by them successfully [46, 47].

In conclusion, spino-protective reflex exists like any reflex in body. Prospective study on huge database needs to be done to validate these observations. However, this study does make the surgeon think for finding clues to happening neurological damage or left out residual compressions which can be identified and rectified in real time in many cases. IONM is the standard of care and SPR should be compared with it to identify sensitivity and threshold of pathological response in future studies.

Conclusion

Spino-protective reflex exists. It can be applied in practice for rectification of potential damages or missed neural compression or new 'add on' stenosis in real time in many cases

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Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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