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ORIGINAL ARTICLE

A novel less invasive endoscopic-assisted procedure for complete reduction of low-and high-grade isthmic spondylolisthesis performed by anterior and posterior combined approach

Roberto Bassani[1] · Carlotta Morselli[1] · Agostino Cirullo[1] · Andrea Pezzi[2] · Giuseppe Maria Peretti[1,3]

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Abstract

Purpose The optimal surgical management of low- and high-grade isthmic spondylolisthesis (LGS and HGS -IS) is debated as well as whether reduction is needed especially for high-grade spondylolisthesis.

Both anterior and posterior techniques can be associated with mechanical disadvantages as hardware failure with loss of reduction and L5 injury. We purpose a novel endoscopic-assisted technique (Sled technique, ST) to achieve a complete reduction in two surgical steps: first anteriorly through a retroperitoneal approach to obtain the greatest part of correction and then posteriorly to complete reduction in the same operation.

Methods ST efficacy and complications rate were evaluated through a retrospective functional and radiological analysis.

Results Thirty-one patients, 12 male (38.7%) and 19 female (61.3%), average age: 45.4 years with single level IS underwent olisthesis reduction by ST. Twenty-three IS involved L5 (74.2%), 7 L4 (22.5%) and 1 L3 (3.3%). No intraoperative complications were recorded. One patient required repositioning of a pedicle screw.

A significant improvement of functional and radiological parameters (L4-S1 and L5-S1 lordosis) outcomes was recorded ($p < 0.001$).

Conclusion ST provides a complete reduction in the slippage in LGS and HGS. The huge anterior release as well as the partial reduction in the slippage by the endoscopic-assisted anterior procedure, because of the cage is acting as a “guide rail”, facilitate the final posterior reduction, always complete in our series, minimizing mechanical stresses and neurological risks. ClinicalTrials.gov Identifier: NCT03644407.

Keywords Anterior lumbar interbody fusion · Isthmic spondylolisthesis · Reduction · Endoscopy · Radiculopathy

Introduction

Isthmic spondylolisthesis (IS) is a condition deriving from a pars interarticularis interruption usually at the L5 vertebra. Common symptoms are low-back and leg pain caused by L5 radiculopathy [1, 2]. In such cases, the radicular compression is due to both fibrous tissue formation and to the compression exerted by the pars as L5 slips on S1[3].

The optimal surgical management of low and high-grade IS (LGS, HGS) is debated, without a clear consensus regarding whether reduction is needed or not [4–6]. The correction of segmental kyphosis and reduction find an indication according to different parameters such as grade of slippage, pelvic retroversion, local kyphosis, and severity of disk degeneration [7–11]. Recent evidence in spinal care shows that sagittal balance is an independent predictor of clinical outcomes. Moreover, the reduction of slippage and the correction of spinopelvic parameters might potentially improve the overall spinal biomechanics and clinical outcomes [12].

Among the studies published in the literature, there are only few case series describing the rate of reduction in spondylolisthesis as a function of the surgical approach [13].

✉ Carlotta Morselli
cmorselli822@gmail.com

1 Spine Surgery II, IRCCS Ospedale Galeazzi Sant’Ambrogio, Via Cristina Belgioioso, 173, 20157 Milan, Italy

2 Residency Program in Orthopedics and Traumatology, University of Milan, Milan, Italy

3 Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

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Although there is a general agreement that surgery for HGS is associated with more complications than LGS, the relevant literature primarily consists of a limited number of case reports and small cases series that are predominantly restricted to children or adolescents [14]. Studies comparing the outcomes of partial versus complete reduction, or the rate of reduction based on different approaches are still lacking. The extent of reduction and its clinical safety, as well as the rate of neurological complications are controversial. Nonetheless, a successful clinical outcome of the procedure is associated with slip reduction without an increased risk of neurological complication [15].

The overall complications rate (mechanical, clinical and neurological) as a function of surgical approaches is also poorly reported, even though the rates may vary depending on the approach itself [13, 15, 16]. The incidence of L5 root injuries after posterior L5-S1 IS reduction is reported between 9 and 30% whereas the vulnerability of the L5 nerve root during anterior lumbar interbody fusion at L5-S1 ranged from 1.5 to 5.6% [17, 18].

We propose, for those IS which require reduction, a novel technique (Sled technique, ST) to achieve complete slippage reduction in two surgical steps during the same operation. The first step is performed through an endoscopic-assisted anterior retroperitoneal approach to obtain the greatest part of the reduction (approximately 75%) implanting a lordotic anterior cage filled with bone substitute (anterior interbody fusion, ALIF). An open midline posterior approach is then performed to implant pedicles screws and rods. This second procedure is necessary to ultimate roots decompression and to complete the reduction (remaining 25%) making the slipped vertebral body sliding back on the cage acting as a "sled". This is a novel application of an already verified surgical technique that we have applied to achieve complete reduction in LGS-HGS IS, restoring spinopelvic parameters and improving outcomes.

Materials and methods

A retrospective analysis from the review of the 2° Spine Surgery Unit of IRCCS Galeazzi Hospital database (IOG Spine-Reg) was performed between 2017 and 2021. Patients ≥ 18 years old with single-level lumbar IS, with axial low back pain with or without severe leg pain or neurological impairment and considered candidates for surgery, were included in the study.

The mean follow-up time was 35,6 months. Pre and postoperative clinical, functional, and radiological data were collected. The IOG Spine-Reg was used to track clinical follow-up. Functional outcomes data were assessed by visual analog scale (VAS) for back pain and leg pain and Oswestry Disability Index (ODI) scoring systems. Radiological follow-up was obtained on 2nd day post op, after 3 months, and then every 12 months for the following 2 years. Radiological data were obtained by direct measurement of biplanar Full Spine X-rays on EOS™ imaging platforms and collected in the Institutional Radiological Registry. Each image was imported in Sectra Workstation IDS7 and elaborated with Ortho Toolbox to measures spino-pelvic parameters [7, 16].

Pre and postoperative CT scans were performed in all cases as well as preoperative MRI. Each preoperative and postoperative images were assessed and compared.

Our surgical planning is usually performed on standing standard whole spine X-rays to get pelvic parameters, grade of slip and to classify the type of IS according to the Spinal Deformity Study Group (SDSG) classification, as well as to Meyerding grade. The goal of our surgery in these cases was to correct the segmental kyphosis deformity, restoring the pelvic retroversion according to the pelvic tilt and the severity index (PI, PT, SI) [7, 11, 12, 19].

Data about intra-operative and post-operative complications were collected.

Clinical and Radiological de-identified registries were used to track patients follow-up care and clinical outcomes without a direct patient involvement. All patients gave their written informed consent to publish the gathered data. Each score was collected in the Institutional Spine registry: Galeazzi Spine Surgery Registry "SPINEREG".

Sled technique description (Fig. 1)

The ST was the choice for all the included patients. Front and back-sided surgery was performed on the same day in all cases.

Each surgery was executed by an orthopedic surgeon or neurosurgeon trained in anterior approaches without any access surgeon involved. [20–22]. Figs 1 and 2.

Anterior approach: with the patient in a supine slight Trendelenburg position, an endoscopic-assisted miniopen anterior retroperitoneal approach was performed in all L5-S1 cases with a standard transverse modified Pfannenstiel incision of 5 cm [20, 21]. A 270° peri navel key-hole skin incision was performed to approach L4-L5 and L3-L4 [20, 21, 23]. To preserve the muscular integrity and function of the abdominal wall the anterior sheath of the left rectus abdominis muscle is cut longitudinally from the left side, about 2 mm lateral to the Linea alba; the left rectus muscle is then retracted upward and laterally with careful blunt finger dissection of the extraperitoneal space. During blunt dissection the rectus muscle is retracted upward avoiding damage to the inferior epigastric vessels. The peritoneal sac is thus exposed and bluntly pushed aside. The most lateral tract of the arcuate line (Douglas Line) is cut or bluntly dissected to reach the retroperitoneal space. The psoas muscle and genitofemuralis nerve are visualized; the ureter and the left

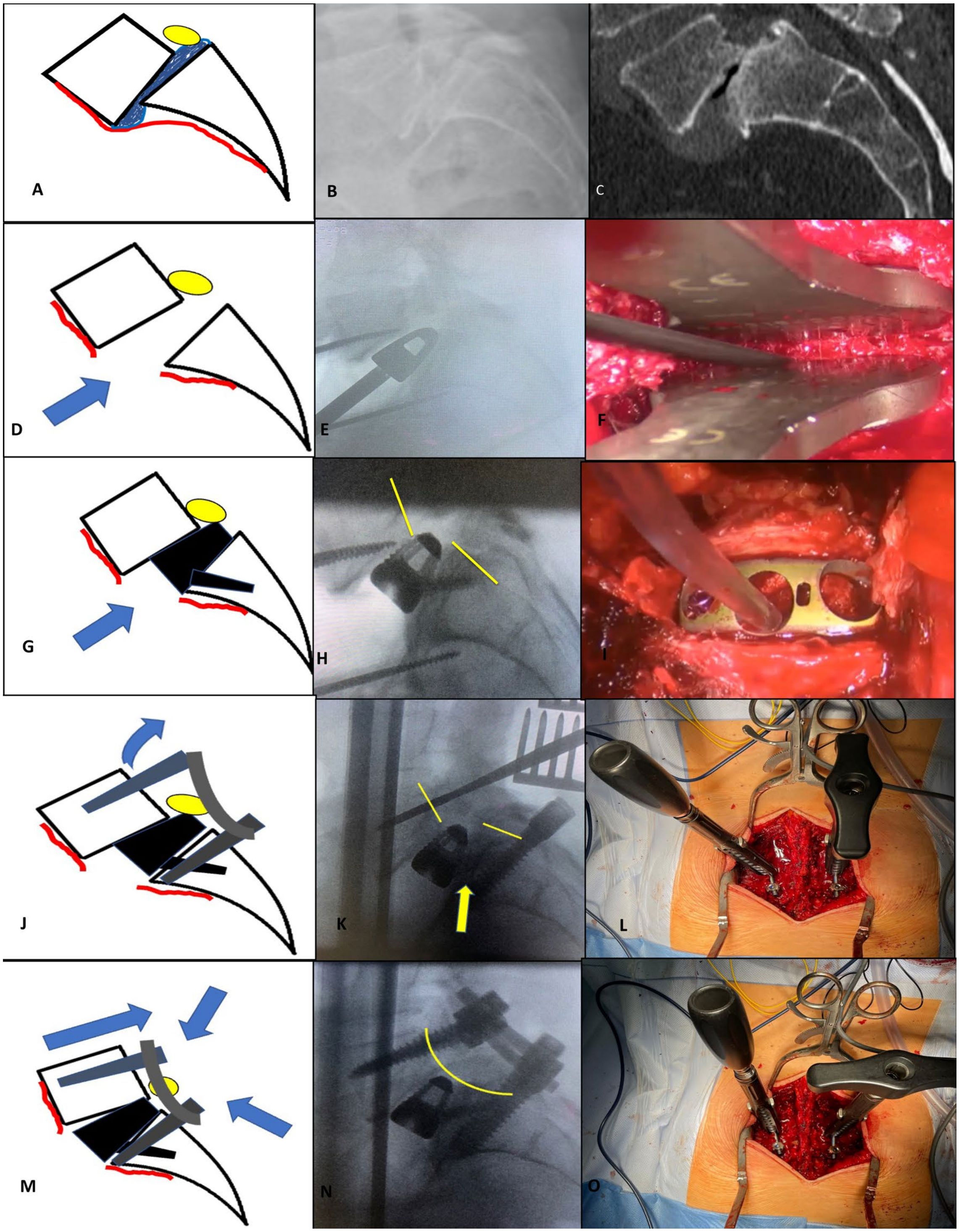

Fig. 1 Schematic, radiological and intraoperative presentation of ST. **A** Schematic illustration of L5 IS showing as the true disk space overlapped by the slipped vertebra. **B**, **C** Preoperative lateral X-ray and CT scan showing L5 IS. **D** Schematic illustration: through a retroperitoneal approach the index level is identified, and the anterior longitudinal ligament (LLA) is open. A complete release of the disk space is performed (discectomy, endplates preparation). **E** Once the discectomy is completed a powerful interbody distraction with spreader instrument is performed and increased size templates are implanted to find the proper fit. **F** In this phase a rigid endoscope (30 degrees – 10 mm cold light endoscope coupled to a High Definition -HD screen) allows (due to high sacral slope) a better view and magnification. **G**, **H**, **I** The insertion of a wide lordotic cage fixed on the body of S1, that allows a partial reduction (2/3) of the olisthesis preparing "a slide rail" for a complete posterior reduction. **J**, **K**, **L** Pedicle poliaxial screw insertion and roods fixation. **M**, **N**, **O** The progressive roods compression allows to use the cage fixed on the lower vertebra as a "guide rail" for the recall of the slipped one (slide technique), minimizing the traction forces

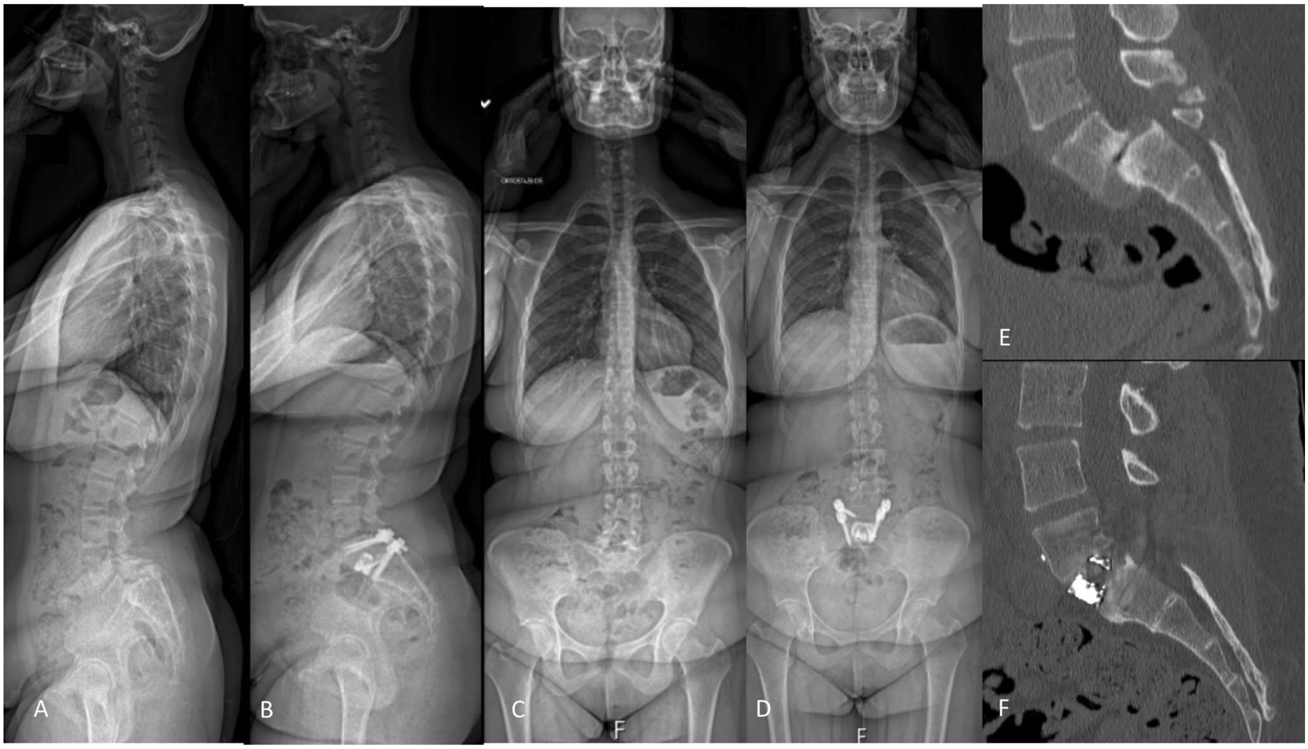

Fig. 2 Preoperative (**A**, **C**) and postoperative **B-D** full spine standing X-rays (EOS) showing the complete reduction of L5 IS **E**, **F** Sagittal pre and postoperative CT scan showing evidence of L5 IS and thus the fusion at the last follow-up

common iliac artery and vein should then be identified to expose L5-S1 disk (located generally in between the bifurcation) or L4-L5 disk (dissecting laterally to the left common iliac vessels). In L5 IS, the slippage of the vertebral body as well as an high sacral slope can limit the direct visualization of the surgical target [20, 21]. Especially in IS graded ≥ 2 according to Meyerding [7], the disk space may be overlapped by the body of L5, determining a more complex and challenging disk exposure. Usually, fibrous tissue between the anterior bony surface and iliac veins is abundantly represented. Thus, a blunt and sharp dissection and careful manipulation at this stage are crucial to avoid vascular injuries. A complete mobilization of the left iliac vein at its most distal portion from the bifurcation is recommended to avoid tearing of the vessels during the cage insertion and distraction maneuvers. Once the disk (anterior anulus) is exposed and the vessels mobilized and gently retracted the middle sacral vessel are then ligated. Four retracting blades are then connected to an autostable ring and each blade fixed with dedicated pins to the bony surface (usually in L5, as well as in S1 if possible) to protect soft tissues and vessels during discectomy, disk space distraction and cage implant. Fig. 1.

After the resection of the anterior longitudinal ligament (ALL) the "true" disk space (often covered by the slipped vertebra) should be approached carefully with angulated Cobb elevator avoiding endplates violation to perform a complete discectomy. During this procedure a rigid endoscope (30 degrees – 10 mm cold light endoscope coupled to a High Definition -HD screen) allows a better view and magnification, which would not otherwise be possible due to the high sacral slope and to the overlapped L5 vertebral body [20, 21, 23]. Application of endoscopic tools in anterior lumbar surgery offers a good magnification and illumination of the surgical field, minimizing the incision and tissue damage and further increasing the surgical precision. Moreover, the use of 30° endoscope allows to perform an adequate and complete discectomy and endplate preparation as well as removal the posterior anulus to achieve a real direct decompression under visual control of the dural sac and the nerve roots. Thus, reducing surgical time and the risk of complications. [20, 21, 23].

Once discectomy is completed a powerful interbody distraction with an interbody spreader is performed. This maneuver allows to expose and decompress the posterior anulus and, in some cases, also to identify and directly decompress the L5 roots. Templates of increasing size are thus implanted until the proper fit is achieved. The powerful distraction of the vertebral bodies obtained by the insertion of a wide lordotic cage fixed to the body of S1 with two screws allows a partial reduction in the slippage preparing a "sliding rail" to achieve complete posterior reduction with "little effort" in the second surgical step. Fig. 1.

Posterior approach: it was performed in all cases with a standard open midline incision with a subperiosteal, paraspinal muscular dissection. In all cases a complete bilateral laminectomy with neural decompression was performed. Pedicle polyaxial screws positioning was implanted with free hand technique.

The vertebral anatomical landmarks that guide screws insertion are found in a more favorable site for hardware placement to the previous anterior partial reduction and distraction producing a slight vertebral elevation.

In our series slippage reduction was always completed using the cage, fixed on the lower vertebra acting as a "guide rail" to pull back the slipped vertebral body, minimizing the traction forces on it using standard screws and rods without special instruments. Fig. 2.

Statistical analysis

Analysis was performed using R software v4.1.1 (R Core Team, Vienna, Austria). Categorical data are reported as absolute or relative frequency; continuous data are reported as mean ± standard deviation. Shapiro–Wilk test was used to evaluate normal distribution of continuous variables. Differences between values obtained before and after surgeries were tested by Student paired *t* test (or Wilcoxon matched pair test in case of non-normal distribution). Differences in categorical variables were tested using Fisher's exact test or Chi-square test. Correlation between variables was tested using Pearson's or Spearman's methods, according to data distribution. *P* values < 0.05 were considered statistically significant.

Results

Regarding the present series, we summarized descriptive data, clinical and functional outcomes in Tables 1, 2 and 3, considering both the entirety of the cohort and the group of subjects treated with L5-S1 fusion.

The comparative analysis of clinical and functional outcomes and relative changes from pre-operative to postoperative follow-up showed that the difference in ODI, VAS (back-leg) between preoperative, 3 and 12 months follow-up was significant in all patients ($p < 0.001$). In L5 IS a significant difference between the pre-operative, 3, and 12 months follow-up values of VAS back ($p < 0.001$) and VAS leg (p 0.004) was observed. Two patients reported residual mild low-back pain at the last follow-up (6.5%).

Postoperative spinopelvic parameters were compared for all patients (Fig. 2). L4-S1 and L5-S1 segmental lordosis significantly increased in all patients ($p < 0.001$). The mean L4-S1 lordosis increase was 12.5°. Considering the entire population,

Table 1 Descriptive analysis of the present patient series considering the entire sample and only those with L5-S1 fusion

Variables	Entire sample	L5-S1 group
N	31	23 (74.2%)
Age	45.4 ± 11.7 (median 46)	44.0 ± 12.0
Sex	F 19 (61.3%)/M 12 (38.7%)	F 13/M 10
BMI	24.6 ± 4.0	25.3 ± 4.2
Surgical time	315.4 ± 68.6	317.4 ± 75.5
ASA score	1: 14 2: 16 3: 1	1: 11 2: 11 3: 1
Meyerding grade [7, 8]	1: 20 2: 8 3: 3	1: 15 2: 5 3: 3
SDSG classification [12]	NA	1: 0 2: 6 3: 14 4: 2 5: 1
Blood transfusions	0: 16 1: 1 2: 2 3: 2 (NA: 10)	0: 14 1: 2: 1 3: (NA: 8)
Intraoperative complications	1 (screw malpositioning in L5-S1 group)	1 (screw malpositioning)
Postoperative complications	7 clinical (5 anemia, 1 ECG T wave inversion, 1 radiculopathy)	3 (1 anemia, 1 ECG T wave inversion, 1 radiculopathy)

ASA (American Society of Anesthesiologists); *SDSG* (Spinal Deformity Study Group (SDSG)

Table 2 Analysis of clinical and functional outcomes and relative changes from pre-to postoperative timing considering all patients (entire sample) and only those with L5-S1

Variables	Entire sample			L5-S1 group		
	Pre	Post	*p*-value	Pre	Post	*p*-value
Low back pain	31/31	2/31	< 0.001	23/23	1/23	< 0.001
Radiculopathy	20/31	3/31	< 0.001	16/23	2/23	< 0.001
Motor weakness	2/31	0/31	0.492	1/23	0/23	0.999
Sensory deficits	0/31	1/31	0.999	0/23	1/23	0.999
ODI	36.4 (SD 15.7, Range 16–73)	20.0 (SD 15.9, Range 0–62)	< 0.001	36.4 ± 15.7	21.9 ± 17.7	0.012
VAS back	6.9 (SD 2.6, Range 0–10)	3.6 (SD 2.4, Range 0–10)	0.002	6.9 ± 2.6	3.4 ± 2.6	< 0.001
VAS leg	6. 4 (SD 2.8, Range 0–10)	2.7 (SD 3.0, Range 0–10)	< 0.001	6.4 ± 2.8	3.1 ± 3.1	0.004
Hb	14.2 ± 1.4	11.4 ± 1.7	< 0.001	14.6 ± 1.4	11.8 ± 1.7	< 0.001

ODI (Oswestry disability index); *VAS* (Visual analogue scale); *Hb* (Hemoglobin)

Table 3 Analysis of radiological outcomes and relative changes from pre-to postoperative timing considering all patients (entire sample) and only those with L5-S1

Variables	Entire sample			L5-S1 group		
	Pre	Post	*p*-value	Pre	Post	*p*-value
PI	66.9 (median value 68°, SD 11.9)	67.4 (median value 69°, SD 11.5)	0.367	67.3 (median value 68, SD 11.7)	67.5 (median value 69, SD 11.3)	0.742
PT	22 (median value 21, SD 8.3)	20.6 (median value 20, SD 6.5)	0.278	22.2 (median value 21, SD 6.4)	20.1 (median value 20, SD 6.0)	0.142
SS	44.6 (median value 45, SD 9.3)	46.9 (median value 45, SD 9.4)	0.045	44.7 (median value 45, SD 10.1)	47.7 (median value 48, SD 9.4)	0.232
L5S1	19.2 (median value 20, SD 9.5)	33.7 (median value 37, SD 12.5)	< 0.001	20.1 (median value 20, SD 9.3)	38.1 (median value 38, SD 10.5)	< 0.001
L4S1	36.2 (median value 38, SD 10.4)	48.7 (median value 48, SD 9.5)	< 0.001	38.5 (median value 39, SD 8.2)	50.4 (median value 49, SD 8.7)	< 0.001
LL	63.3 (median value 65, SD 12.6)	62.6 (median value 65, SD 9.6)	0.530	62 (median value 62, SD 13.9)	62 (median value 65, SD 9.2)	0.681
SVA	12.1 (median value 8, SD 28.3)	21.5 (median value 20, SD 25.8)	0.009	15.7 (median value 11, SD 28.3)	24.7 (median value 20, SD 25.6)	0.014
SI	NA	NA	–	35.2 ± 10.9	37 ± 12.4	0.999
DLA	NA	NA	–	106.8 ± 11.8	123.5 ± 11.0	< 0.001

PI (pelvic incidence); *PT* (pelvic tilt); *SS* (sacral slope); *LL* (whole lumbar lordosis); *SVA* (sagittal vertical axis); *SI* (severity index); *DLA* (Dubousset lumbosacral angle)

the mean L5-S1 lordosis increase was 14.5°; (18° if we consider only L5 IS). Significant correlations were found between changes from pre to postoperative values of L5-S1 and L4-S1 lordosis (moderate positive correlation, $r = 0.650$, $p = 0.023$), L4-S1 and PT (weak and negative correlation, $r = -0.250$, $p = 0.002$), L4-S1 and LL (weak positive correlation, $r = 0.290$, $p = 0.005$).

Discussion

ST was performed in 31 patients with IS. Twenty-three (74.2%) of these were L5 IS. The aim of this study was to evaluate the ST efficacy to achieve complete reduction in terms of restoration of ideal spinopelvic values, complications rate and clinical outcomes. We supposed that achieving a complete slippage reduction in two surgical steps (first anterior and then posterior) could be associated with a low rate of mechanical stress on the vertebral pedicles as well as reduces neurological complications on L5 roots. Indeed, the stretching and subsequent strain of up to 75% of the nerve may occur during the second half of the posterior reduction [24]. We assumed that the first anterior stage of a powerful partial reduction allows to limit the fusion area at the index level. Posterior IS reduction techniques (posterior or transforaminal interbody fusion PLIF-TLIF) require optimal screws placement for tightness: there is a complex interplay between the screws (long, bicortical, convergent and large in diameter) on which apply distraction to insert the cage and the rods that are positioned to obtain subsequent reduction and compression.

Despite the efficacy of the posterior approach, the risk of screws loosening and pull-out with following loss of reduction and residual local kyphosis are consistent, as well as the stretching or ischemic injury of the nerve roots, especially in the HGS [25]. Since the presence of soft tissues (intervertebral disk and ligaments) can hinder reduction maneuvers, a wide decompression is crucial to achieve optimal reduction only from the back. Furthermore, especially when a suboptimal release is performed, the traction on pedicles during vertebral pull-back can increase the risk of hardware pullout.

In the technique that we have described, the anterior disk space release and the high and lordotic cage positioning act as a “sled” facilitating the following posterior surgical step. This maneuver reduces the powerful traction forces on L5 screws and thus the risk of pullout.

The anterior approach allows a complete release of the disk space and a more favorable reduction maneuver. This is made possible by distracting the intervertebral space, allowing for a wider distribution of forces over the endplates.

The use of the endoscope during the whole anterior release procedure allows to optimize the vision of the entire space. In patients with high sacral slope, the use of a 30 degrees endoscope connected to an HD monitor at higher magnification and the use of special angled instruments easily allow a good “indirect” vision of the posterior part of the disk and make easier the eventual osteotomy of the sacral dome when necessary. Thus, the anterior release can be completed more comfortably.

Once enough distraction and reduction are obtained, a large and lordotic cage is implanted [20, 21]. According to some biomechanical studies the anterior lever reduction requires less effort with respect to the posterior lever reduction [26]. Due to the significant traction forces, a stand-alone anterior reduction and fusion are not able to maintain the correction and to achieve fusion in IS [27]. For these reasons, our proposal is a combined surgical procedure performed in two consecutive steps in the same operation. The role of a combined approach (first posterior and then anterior) in HGS was introduced by Bradford et al. [28]: this technique consisted in external skeletal traction and osteotomy of the sacral promontory when indicated. The anterior surgical step, performed after the posterior decompression (Gill’s procedure) provided the insertion of a L5-S1 supporting bone graft, avoiding over-distraction and limit L5 root injury. In their series of 10 patients, L5 root injury was due to preoperative traction or bone graft insertion/mobilization (30%) [28]. Recently, Tu et al. described preliminary results of anterior cantilever reduction procedure and ALIF followed by posterior mono-segment instrumented fixation [29]. In our experience, dividing the reduction procedure in two step allows a less effort demanding retrieval of the vertebral wedge reducing the risk of implant failure. During the posterior pedicle exposure, the vertebral anatomical landmarks, that guide screws insertion, are found in a more favorable site for hardware placement with respect to a posterior only procedure thanks to the previous anterior partial reduction and distraction that produce a slight, yet advantageous vertebral elevation. Moreover, by employing a high, large and lordotic cage neural foramen became wider thus favoring a more gradual and gentler stretching of the roots.

No intraoperative complications were recorded in our series except for one pedicle screw malposition (3.2%) requiring repositioning with subsequent immediate pain relief. Complete reduction in the slippage has been observed in all patients at the post-operative CT scan and maintained throughout all follow-up (FIG 2). No loss of reduction, hardware mobilization or adjacent disk diseases were observed. One patient showed mild sensitive dysfunction (3.2%) at the last follow-up, while no new motor deficits were recorded (0%). A significant improvement of functional and radiological outcomes was recorded ($p < 0.001$) with a significant progressive improvement in functional score ($p < 0.001$). The reasons for root injury are not understood, although an ischemic mechanism is likely to be involved (reduced arterial flow; venous stasis) [18]. We cannot establish exactly why no root injuries were recorded in our series. We speculate that the first step of the huge anterior release, distraction and partial reduction allows to complete the delayed reduction posteriorly ensuring a more gradual correction of the slippage. With this strategy, probably we give the roots an adequate amount of time to adapt to the new position reducing ischemic risk. On the other hand, we observed a residual postoperative pain in our pool of patients. Despite each postoperative score being significantly reduced ($p < 0.05$) with respect to the pre-operative data, we can suppose that this result might be a consequence of the roots stretching because of the increased height of interbody space and of the correction of the segmental kyphosis during both anterior and posterior steps [30]. Nonetheless, we observed a steady progression in pain reduction throughout follow-up.

Conclusions

ST provides a complete reduction of the slippage in LGS and HGS. The huge anterior release as well as the partial reduction in the slippage by the endoscopic-assisted anterior procedure, because of the cage is acting as a "guide rail," facilitate the final posterior reduction, always complete in our series, minimizing mechanical stresses and neurological risks.

Author contributions 'Not applicable' for that section.

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Data availability No data have been fabricated or manipulated (including images) to support our conclusions. No data, text, or theories by others are presented as if they were the author's own ("plagiarism").

Code availability 'Not applicable' for that section.

Declarations

Conflicts of interest This research did not receive any specific grant from founding, agencies in the public, commercial, or not-for-profit sectors. Any acknowledgments for grants technical support or corporate support were necessary.

Ethical approval Ethic Committee approval was not requested for this study. Clinical and Radiological de-identified registries were used to track patients care and outcome without a direct patient involvement even if all patients gave their written informed consent to publish their data for the Institutional Spine registry: (Galeazzi Spine Surgery Registry "SPINEREG").

Consent for publication Informed consent was obtained from each patient included in the study. Copyright to reproduce materials was not necessary.

Consent to participate Informed consent was obtained from all patients included in the study. Copyright to reproduce materials was not necessary.

Informed consent Consent to submit has been received explicitly from all co-authors, as well as from the responsible authorities-tacitly or explicitly-at the institute/organization where the work has been carried out.

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