Separation surgery for metastatic epidural spinal cord compression: comparison of a minimally invasive versus open approach

*Murray Echt, MD,^{1,2} Ariel Stock, MD, PhD,^{1,2} Rafael De la Garza Ramos, MD,^{1,2}
Evan Der, PhD,¹ Mousa Hamad, MD,^{1,2} Ryan Holland, MD,^{1,2} Phillip Cezayirli, MD,^{1,2}
Rani Nasser, MD,³ Vijay Yanamadala, MD, MBA,^{1,2} and Reza Yassari, MD, MS^{1,2}

¹Spine Research Group and ²Department of Neurological Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York; and ³Department of Neurological Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio

OBJECTIVE The aim of this study was to compare outcomes of separation surgery for metastatic epidural spinal cord compression (MESCC) in patients undergoing minimally invasive surgery (MIS) versus open surgery.

METHODS A retrospective study of patients undergoing MIS or standard open separation surgery for MESCC between 2009 and 2019 was performed. Both groups received circumferential decompression via laminectomy and a transpedicular approach for partial corpectomy to debulk ventral epidural disease, as well as instrumented stabilization. Outcomes were compared between the two groups.

RESULTS There were 17 patients in the MIS group and 24 in the open surgery group. The average age of the MIS group was significantly older than the open surgery group (65.5 vs 56.6 years, $p < 0.05$). The preoperative Karnofsky Performance Scale score of the open group was significantly lower than that of the MIS group, with averages of 63.0% versus 75.9%, respectively ($p = 0.02$). This was also evidenced by the higher proportion of emergency procedures performed in the open group (9 of 24 patients vs 0 of 17 patients, $p = 0.004$). The average Spine Instability Neoplastic Score, number of levels fused, and operative parameters, including length of stay, were similar. The average estimated blood loss difference for the open surgery versus the MIS group (783 mL vs 430 mL, $p < 0.05$) was significant, although the average amount of packed red blood cells transfused was not significantly different (325 mL vs 216 mL, $p = 0.39$). Time until start of radiation therapy was slightly less in the MIS than the open surgery group (32.8 ± 15.6 days vs 43.1 ± 20.3 days, $p = 0.069$). Among patients who underwent open surgery with long-term follow-up, 20% were found to have local recurrence compared with 12.5% of patients treated with the MIS technique. No patients in either group developed hardware failure requiring revision surgery.

CONCLUSIONS MIS for MESCC is a safe and effective approach for decompression and stabilization compared with standard open separation surgery, and it significantly reduced blood loss during surgery. Although there was a trend toward a faster time to starting radiation treatment in the MIS group, both groups received similar postoperative radiotherapy doses, with similar rates of local recurrence and hardware failure. An increased ability to perform MIS in emergency settings as well as larger, prospective studies are needed to determine the potential benefits of MIS over standard open separation surgery.

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KEYWORDS metastatic spinal cord compression; separation surgery; minimally invasive spine surgery; radiotherapy

ADVANCES in systemic therapies for oncological diseases have brought greater attention to a multimodal approach utilizing surgical and radiation treatments for metastatic spinal tumors. Metastatic spinal disease may lead to instability, neurological deficits, and/

or pain due to metastatic epidural spinal cord compression (MESCC). The national incidence of spinal metastases requiring surgery is increasing, along with an overall increase of patient comorbidities and in-hospital complication rates.¹ Surgery provides immediate spinal stabili-

ABBREVIATIONS KPS = Karnofsky Performance Scale; MESCC = metastatic epidural spinal cord compression; MIS = minimally invasive surgery; RT = radiation therapy; SINS = Spine Instability Neoplastic Score; SRS = stereotactic radiosurgery.

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* M.E. and A.S. share first authorship of this work.

zation and decompression of the neural elements, while radiation therapy (RT) provides local control. The main treatment goal in these patients remains palliative with regard to symptoms, emphasizing preservation or restoration of spinal stability and neurological function.² As such, treatments are focusing on utilizing less aggressive, minimally invasive techniques.

Standard external-beam RT delivered in fractionated doses successfully provides local control of radiosensitive tumors and has been the mainstay treatment for decades. However, these effects are limited by poor control of radioresistant tumors and risk of radiation-induced injury to the spinal cord with repeat dosing.^{3,4} Alternatively, stereotactic radiosurgery (SRS) allows the delivery of high-dose radiation in a single stage or hypofractionated stages with minimal exposure to surrounding tissues that may be conformed around the spinal cord.⁵⁻⁷

With the advent of SRS, the development of separation surgery emerged. Separation surgery—re-creation of a minimum amount of space of 2- to 3-mm margins between the tumor and the spinal cord to allow for safe postoperative SRS—avoids the morbidity of extensive tumor debulking and reconstruction.⁸⁻¹⁰ This strategy has allowed for the exploration of minimally invasive surgery (MIS) approaches with the goals of reducing blood loss, muscle disruption, pain, and recovery time.¹¹ Systematic reviews by Pennington et al. and Zuckerman et al. exploring MIS for spinal metastases found that patients treated with MIS tended to achieve these goals with fewer complications.^{12,13} However, the included studies varied significantly with technique, and few focused specifically on comparing MIS versus open separation surgery for MESCC. They also lacked a detailed description of surgical technique. Furthermore, the utility of intraoperative stereotactic navigation in the resection of spinal tumors has been shown,¹⁴ but its value in MIS separation surgery is still emerging. Here, we provide an overview of our MIS technique for separation surgery with intraoperative stereotactic navigation and compare our experience between open and MIS approaches for providing circumferential separation and allowing safe postoperative SRS.

Methods

Study Design and Patient Selection

This is a single-institution, retrospective comparative study of patients undergoing either MIS or standard open surgery for separation and stabilization of spinal metastases. A chart review was performed over a 10-year span between July 2009 and June 2019. Patients with metastatic spinal disease who received circumferential separation via laminectomy and a transpedicular approach to debulk ventral epidural disease as well as instrumented stabilization, through either an open or MIS approach, were included in this study. Patients were excluded from this study if they were younger than 18 years of age and if they underwent more-invasive tumor debulking with anterior column reconstruction, including cage placement, as this was not consistent with the intended goal of separation surgery.

Diagnosis of metastatic disease was confirmed through

histopathological analysis performed on intraoperatively obtained specimens. Indications for separation surgery were determined by the NOMS decision framework, which includes the algorithm of neurological, oncological, mechanical, and systemic principles.¹⁵ Patients with hematological malignancies underwent surgery for neurological deficits due to cord compression with an unknown preoperative diagnosis, including nondiagnostic biopsies. Patients who were diagnosed with solitary plasmacytoma were treated with postoperative radiotherapy with curative intent, and, although their tumors were not radioresistant, the patients were still included in our analysis.^{16,17} Patients were discussed at a multidisciplinary tumor board conference in nonemergency cases.

Collected patient data included age at surgery, sex, presence of medical comorbidities, BMI, preoperative and postoperative Karnofsky Performance Scale (KPS) score, neurological status (assessed by the Frankel scale), Spine Instability Neoplastic Score (SINS), and Tokunashi score. Operative data included operative time, estimated blood loss, need for red blood cell transfusion, number of levels fused, and postoperative radiation doses. Outcome data included complication rates, 6-month mortality, and neurological status.

Minimally Invasive Tubular Transpedicular Decompression and Percutaneous Instrumentation

A detailed description of the minimally invasive tubular transpedicular decompression technique has been described previously, including in an operative video.^{18,19} In brief, patients are placed prone on a Jackson table with padding of all pressure points. It is essential that the patient is secured with additional tape and straps to minimize patient movement on the table for navigation accuracy, as well as to allow for more degrees of rotation of the bed to facilitate an increased medial trajectory. A Mayfield head holder is occasionally used for lesions approaching the upper thoracic spine, to allow for use of the rigid arm in fixation of the reference array. In midthoracic cases, an additional incision and spinous process clamp are used. In thoracolumbar and lumbar cases, rigid fixation is obtained using a hip pin. Stereotactic intraoperative navigation is used to plan appropriate paramedian incisions for placement of percutaneous pedicle screws and to determine the entry point for access to the tumor. Pedicle screws are generally placed first, with preference to utilize a system without K-wires to avoid risk of inadvertent advancement, especially in regions of compromised bone integrity.

After pedicle screw placement, a minimally invasive tubular retraction system is inserted under stereotactic guidance. For the thoracic levels, the transverse process is used for docking to provide an appropriately medial trajectory (Fig. 1). After placement of the tubular retractor, we expose the ipsilateral lamina and facet joint. After exposure and identification of the facet joint, the inferior articulating process is removed, exposing the underlying superior articulating process. A bilateral laminotomy via a unilateral approach is performed over the involved level to ensure adequate posterior decompression as well as to visualize the thecal sac (Fig. 2). The superior articulating process is then drilled down to access the foramen, and

FIG. 1. A: Demonstration of docking with the tubular retractor system using the navigated pointer with the rigid arm. **B:** Confirmation of final position and removal of tubular dilators. **C and D:** Real-time axial (C) and sagittal (D) stereotactic images demonstrating docking onto the transverse process of the involved level.

the exiting nerve root is identified. Attention is then turned toward identifying the pedicle at the involved level, and a transpedicular corridor is created to access the epidural space medially and anteriorly. Stereotactic navigation is used to guide the surgeon toward achieving circumferential decompression. Pathologic specimens of the tumor are collected for histological analysis. For decompression anterior to the cord, a partial corpectomy is utilized to create space for a downgoing curette to push the residual tumor away anteriorly into the vertebral body. Care is taken to remain below the posterior longitudinal ligament to avoid any injury to the ventral spinal cord. A Woodson dissector is used to carefully ensure that there is no further ventral compression. A final O-arm image can be obtained to confirm circumferential decompression in the case of osteoblastic bony spinal cord compression (Fig. 3). Rods are placed percutaneously, and satisfactory hardware placement is confirmed by radiography. In cases of osteoblastic lesions requiring only a unilateral approach for sufficient decompression, a short fusion construct was performed.

Statistical Analysis

Statistical analyses were performed using R version 4.0.3 (The R Foundation), where the average values for all parameters were compared between groups, and assessed by multivariate ANOVA, with Tukey post hoc analysis for parametric variables and the chi-square test for binary variables. Significance was set at $p < 0.05$.

Results

Characteristics of the 41 patients who underwent either

FIG. 2. Left: Intraoperative view after an over-the-top decompression and facetectomies were performed, leaving the involved pedicle (arrow) isolated. **Right:** A downgoing curette is used below the level of the posterior longitudinal ligament (arrow). A partial corpectomy allows for residual tumor to be pushed away anteriorly into the vertebral body.

FIG. 3. A: Preoperative CT scan demonstrating blastic prostate metastasis with asymmetrical involvement of the left pedicle. **B:** Preoperative axial MR image demonstrating high-grade spinal cord compression. **C:** Intraoperative CT scan demonstrating satisfactory ventral decompression through a unilateral transpedicular approach. **D:** Postoperative anteroposterior radiograph of percutaneously placed short-segment instrumentation.

MIS or standard open surgery, including both urgent and nonurgent clinical presentations (i.e., more than 48 hours from symptom onset), are presented in Table 1. Pathologies were similar among both groups, including breast, prostate, and lung being the most common, with other diagnoses of plasmacytoma, renal cell carcinoma, hepatocellular carcinoma, cholangiocarcinoma, uterine leiomyosarcoma, colon adenocarcinoma, and adenocarcinoma of unknown origin. There were 17 patients in the MIS group and 24 in the open surgery group. The average age of the

TABLE 1. Patient characteristics

	Open Surgery	MIS	p Value
Male sex, %	62.5	70.6	0.84
Mean age, yrs	56.6	65.5	0.02*
Comorbidities, %			
Type 2 diabetes	20.83	29.41	0.79
Hypertension	45.83	58.82	0.62
Coronary artery disease	4.17	17.65	0.37
Chronic kidney disease	12.50	11.76	1.00
Chronic lung disease	4.17	11.76	0.76
Chronic liver disease	4.17	11.76	0.76
Mean BMI	28.4	26.4	0.19
Mean preop KPS score	63.0	75.9	0.02*
Mean preop Frankel grade†	4.3	4.5	0.31
Mean SINS	11.0	9.4	0.09
Mean Tokuhashi score	8.6	8.8	0.84

*p < 0.05.

† Grades A–E are represented as 1–5.

FIG. 4. Comparison of preoperative and postoperative KPS scores between open surgery and MIS groups. Bars represent the mean and the error bars the SD. *p < 0.05; ns = not significant.

MIS group was significantly greater than that of the open surgery group (65.5 vs 56.6 years, $p = 0.02$). The preoperative KPS score of the open group was significantly lower than that of the MIS group, with an average of 63.0 versus 75.9, respectively ($p = 0.02$), corresponding to an overall less functional population. This was also evidenced by the higher proportion of emergency procedures performed in the open group (9 of 24 patients vs 0 of 17 patients, $p =$

TABLE 2. Operative parameters, patient outcomes, and radiotherapy treatment

	Open Surgery	MIS	p Value
No. of levels fused	6.5	5.8	
Length of surgery, mins	405	380	0.69
Estimated blood loss, mL	783	430	0.02*
Packed red blood cells transfused, mL	325	216	0.36
Postop length of stay, days	12.3	13.2	0.75
Complications, n (%)	3 (13)	1 (6)	0.87
6-mo mortality, n (%)	2 (8)	0	0.63
Postop KPS score	76.7	80.0	0.52
Change in KPS score	13.8	4.1	0.03
Postop Frankel grade†	4.7	4.6	0.74
Change in Frankel grade	0.43	0.18	0.23
Postop radiation dose, Gy	26.5 ± 6.9	23.5 ± 5.0	0.084
Days until start of RT	43.1 ± 20.3	32.8 ± 15.6	0.069
Long-term follow-up (minimum 1 yr)			
No. of patients	15	16	
Average follow-up, yrs	2.8	4.1	
Local recurrence, n (%)	3 (20)	2 (12.5)	

Values are presented as the mean or mean ± SD unless otherwise noted.

*p < 0.05.

† Grades A–E are represented as 1–5.

0.004). Preoperative comorbidities, BMI, Frankel grade, and Tokuhashi score were similar between the two groups. The SINS was slightly higher in the open group, but not significantly.

Outcomes are summarized in Table 2. The number of levels fused and operative parameters, including length of surgery, were similar, except the average estimated blood loss for the open surgery group was significantly higher than that for the MIS group (783 mL vs 430 mL, $p = 0.02$). However, this did not appear to impact the average amount of packed red blood cells transfused (325 mL vs 216 mL, $p = 0.36$). Postoperatively, the open group demonstrated significantly greater improvement in KPS scores, such that the preoperative difference between groups was no longer significant (Fig. 4).

The open surgery group experienced 3 complications, including 2 wound infections and 1 return to the operating room for revision of a pedicle screw, while the MIS group had 1 wound infection. No patients developed radiation-related wound breakdown. The open surgery group had 2 deaths within 60 days, though these were due to coexisting problems. Finally, postoperatively 23.5% of patients in the MIS group improved neurologically on the Frankel grade, 64.7% remained the same, and 11.8% deteriorated, while 41.7% of patients in the open group improved, 45.8% remained the same, and 12.5% deteriorated (Fig. 5). It is noteworthy, however, that all patients in the MIS group scored Frankel grade D or E, while 6 of the 24 open surgery patients scored Frankel grade C, where the most

FIG. 5. Comparison of preoperative and postoperative Frankel scale grades between the open surgery (left) and MIS (right) groups.

significant improvement was appreciated. Furthermore, there was no significant difference between groups as pertaining to Frankel grade, in particular with regard to deterioration.

Postoperative radiation doses were available for 18 patients in the open group and 14 patients in the MIS group. In the open surgery group, 12 patients (66.7%) received 20–40 Gy in 5–6 fractions, 5 patients (27.8%) received 24–30 Gy in 3–4 fractions, and 1 patient (5.5%) received a single dose of 18 Gy. In the MIS group, 5 patients (35.7%) received 20–35 Gy in 5–6 fractions, 8 patients (57.1%) received 24–30 Gy in 3–4 fractions, and 1 patient (7.1%) received a single dose of 24 Gy. The mean dose in the open group was 26.5 ± 6.9 Gy, and that in MIS was 23.5 ± 5.0 Gy ($p = 0.084$). Time until start of RT was slightly less in the MIS than the open surgery group (32.8 ± 15.6 days vs 43.1 ± 20.3 days, $p = 0.069$). This included 4 patients in the MIS group who underwent RT during the same admission as surgery.

Long-term results (a minimum of 1-year follow-up) were available for the majority of patients (Table 2). In the open surgery group, 3 of the 15 (20%) patients with long-term follow-up were found to have recurrence at the site of surgery with MESCC compared with 2 of the 16 (12.5%) patients treated with MIS technique. Two of these recurrences arose in patients with highly malignant uterine leiomyosarcomas, and the others occurred in hepatocellular, renal cell, and colon adenocarcinoma. No patient in either group developed hardware failure requiring revision surgery.

Discussion

The term “separation surgery” is credited to Lilyana Angelov and Edward Benzel at the Cleveland Clinic to designate a procedure in which tumor resection is limited to decompression of the spinal cord to create enough space to provide a safe target for spine SRS.²⁰ Moulding et al. introduced the concept to the literature in 2010 by demonstrating the effectiveness of high-dose adjuvant SRS after surgical decompression and stabilization to achieve local disease control and preserve neurological function.²¹ As such, the integration of limited cytoreductive surgery with

postoperative radiosurgery in the treatment of spinal metastatic tumors has led to a shift in surgical goals.²² More-invasive surgeries that carry increased risk of complications and surgical morbidity, such as staged thoracotomy or retroperitoneal approaches, corpectomies with anterior column reconstruction, or spondylectomies with wide excision, are now less frequently utilized.^{10,23,24} Because of the advancements in technique, including less local tissue disruption and a potentially faster rate of recovery while maintaining safe targets for high-dose radiotherapy, MIS has become the new state-of-the-art treatment for MESCC.^{8,25,26} In this study, we have demonstrated that, although there was a trend toward faster time to starting radiation treatment in the MIS group, there were similar postoperative radiotherapy doses among both groups, with no increased rate of local recurrence and no occurrences of hardware failure.

Furthermore, the prediction of patient outcomes regarding survival and quality of life after surgery remains challenging despite numerous prognostic scores that attempt to stratify patients into risk groups.^{27–30} MIS techniques may be able to expand our patient population to include those who are considered candidates for surgery despite stratification into a higher risk group. In recent studies, patients with metastatic spinal disease treated with MIS approaches tended to have decreased blood loss, shorter inpatient stays, and fewer complications compared with patients undergoing open procedures while maintaining similar outcomes in regard to pain, neurological improvement, and function.¹² The results presented herein demonstrate overall noninferiority of MIS as compared with open separation surgery for metastatic spinal disease despite a tendency toward use of the latter in an older population.

Similar to other studies, our results were biased against using MIS techniques in patients with emergency presentation, i.e., within 24 hours of developing profound weakness. Lau and Chou also reported that the time of surgery dictated the choice of mini-open versus an open approach; scheduled cases during elective hours had the necessary staff and navigation support needed for MIS, whereas patients presenting at night or on the weekend were relegated to an open approach.³¹ Conversely, Miscusi et al. demon-

TABLE 3. Candidates for minimally invasive separation surgery

Potential Candidates	Contraindications	Relative or Institutional Considerations
Access to a multidisciplinary spinal oncology team offering postop adjuvant SRS	Life expectancy <3 mos	Older age or multiple medical comorbidities
Life expectancy >3 mos	More than 2-level involvement	Access to intraoperative stereotactic navigation
1- or 2-level involvement	Anterior & middle column involvement or need for anterior column reconstruction*	Emergency presentation requiring off-hours (night or weekend) surgical intervention
Absence of gross instability denoted by a SINS <13*		

* In the presence of a pathologic fracture or mechanical instability where anterior column reconstruction is required, an open or mini-open approach for transpedicular corpectomy and anterior cage placement should be employed.

strated an effective use of the MIS technique for patients with acute presentation due to high-grade MESCC causing myelopathy, with a significant improvement in terms of blood loss, operation time, days in bed, and decreased length of stay compared with a retrospective control group of patients who underwent open surgery.³² In a previous prospective propensity score–matched analysis, the MIS group again was found to have the advantage of less blood loss, lower rate of blood transfusion, lower average units of blood transfused, and shorter hospital stays.³³

Our results demonstrate a significantly lower average estimated blood loss for the MIS group; however, this did not appear to significantly impact the average amount of packed red blood cells transfused or the length of stay. Of note, all abovementioned studies included patients who required anterior column reconstruction, performed via either open surgery or MIS, which was often through a mini-open or hybrid approach.^{31–33} As such, our results, which focused on separation surgery with only limited resection and stabilization among both groups, demonstrated a total lower rate of blood loss, need for blood transfusion, and postoperative length of stay for both open and MIS groups compared with the results of prior studies. Additionally, length of stay in our MIS cohort was confounded by several patients receiving inpatient RT during the same admission as surgery.

Another factor that may have influenced blood loss is the nature of performing a limited resection. Typically, bleeding is better controlled once the majority of the tumor is removed; however, this is by definition not the goal in separation surgery. Here, the objective is to create sufficient space around the neural elements to allow for safe postoperative RT and not a gross-total resection. This means blood loss must be well controlled throughout the surgery, especially for vascular tumors like hepatocellular and renal cell carcinoma. Hemostasis is made even more difficult during MIS access with a limited surgical field. Considerations for preoperative embolization should always be discussed with the interventional radiologist,³⁴ and, at our institution, all hypervascular tumors are embolized. In addition, we use a series of hemostatic maneuvers to control bleeding. A 4- or 6-mm coarse diamond burr is used during creation of the transpedicular corridor and partial corpectomy as it cauterizes while drilling, which aids in hemostasis.¹⁹ A combination of Avitene, Gelfoam, and other thrombin-mixed hemostatic agents can also be very useful. This may require several rounds of application before adequate control is achieved. In addition, we gener-

ally overlay the tumor edges with Surgicel at the end of the procedure. As the degree of tumor resection between the two techniques was similar, the MIS technique is able to achieve significantly less blood loss through minimizing bleeding during exposure.

Stereotactic navigation is becoming more widespread in its utilization and can be a valuable intraoperative adjunct.³⁵ Its effectiveness during MIS to allow surgeons greater understanding of bony and soft-tissue anatomy through limited incisions and exposure, as well as minimizing radiation exposure, has been demonstrated.^{23,36} Its unique contribution during MIS separation surgery lies in the abnormal anatomy inherent to tumoral invasion.^{14,18,37} Thus, the use of guidance to identify the abnormal anatomy and determine the extent of resection is indispensable. Final imaging with intraoperative CT scanning can verify complete ventral decompression. Additionally, navigation offers higher accuracy in the placement of pedicle screws, specifically for patients with metastatic disease who often have poor bone quality and are potentially at higher risk of pedicle breach or fractures.³⁸ The limited perspective of a tubular retractor system without stereotactic navigation, and fluoroscopically placed K-wires for percutaneous pedicle screws in the setting of metastatic spinal infiltration with abnormal and poor bony integrity, warrants reconsideration.

The data presented herein demonstrate overall equivalent perioperative complication and morbidity of MIS as compared with open separation surgery for MESCC. There are, however, certain limitations to this study. The main drawbacks are related to the retrospective nature of this study as well as the limited cohort. There was also selection bias in performing emergency surgery with a conventional open approach, which resulted in a lower preoperative functional performance score in the open group as well as potentially slightly higher rate of complications. Additionally, the open group tended to have higher SINS, more levels fused, and the surgery was more likely to cross a junction, either cervicothoracic or thoracolumbar. Table 3 lists considerations for best candidates for MIS separation surgery according to various reports and qualitative reviews.^{12,13,27,39,40} Other variables, such as opioid consumption, days in bed, pain scores, and quality-of-life patient-reported outcome measures, were not available in our retrospective review. These factors may have been influenced by the choice of open or MIS approach but unfortunately were unable to be assessed. However, our results uniquely demonstrate the potential for MIS separation surgery to

decrease morbidity and allow for the faster delivery of RT with similar rates of local control and stabilization compared with open separation surgery.

Conclusions

MIS separation surgery for metastatic MESCC is a safe and effective approach for decompression and stabilization compared with standard open separation surgery, and it significantly reduced blood loss during surgery. Although there was a trend toward a faster time to starting radiation treatment in the MIS group, both groups received similar postoperative radiotherapy doses, with similar rates of local recurrence and hardware failure. An increased ability to perform MIS in emergency settings as well as larger, prospective studies are needed to determine the potential benefits of MIS over standard open separation surgery.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Yassari, Echt, Stock, Nasser. Acquisition of data: Echt, Hamad, Holland, Nasser. Analysis and interpretation of data: Echt, Stock, Der. Drafting the article: Yassari, Echt, Stock, De la Garza Ramos, Hamad, Holland, Cezayirli. Critically revising the article: Yassari, Echt, Stock, De la Garza Ramos, Cezayirli, Nasser, Yanamadala. Reviewed submitted version of manuscript: Yassari, Echt, Stock, De la Garza Ramos, Yanamadala. Statistical analysis: Echt, Stock, De la Garza Ramos, Der. Administrative/technical/material support: Yassari. Study supervision: Yassari.

Correspondence

Reza Yassari: Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY. ryassari@montefiore.org.