Original Article

30-day postoperative sepsis risk factors following laminectomy for intradural extramedullary tumors

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Background: Posterior laminectomy (LA) for resection of intradural extramedullary tumors (IDEMTs) is associated with postoperative complications, including sepsis. Sepsis is an uncommon but serious complication that can lead to increased morbidity and mortality, prolonged hospital stays, and greater costs. Given the susceptibility of a solid tumor patients to sepsis-related complications, it is important to recognize IDEMT patients as a unique population when assessing the risk factors for sepsis after laminectomy.

Methods: The study design was a retrospective cohort study. Adult patients undergoing LA for IDEMTs from 2012 to 2018 were identified in the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database. Baseline patient characteristics/comorbidities, operative and hospital variables, and 30-day postoperative complications were collected.

Results: Of 2,027 total patients undergoing LA for IDEMTs, 38 (2%) had postoperative sepsis. On bivariate analysis sepsis was associated with superficial surgical site infection [odds ratio (OR) 11.62, P<0.001], deep surgical site infection (OR 10.67, P<0.001), deep vein thrombosis (OR 10.75, P<0.001), pulmonary embolism (OR 15.27, P<0.001), transfusion (OR 6.18, P<0.001), length of stay greater than five days (OR 5.41, P<0.001), and return to the operating room within thirty days (OR 8.72, P<0.001). Subsequent multivariate analysis identified the following independent risk factors for sepsis and septic shock: operative time ≥50th percentile (OR 2.11, P=0.032), higher anesthesia class (OR 1.76, P=0.046), dependent functional status (OR 2.23, P=0.001), diabetes (OR 2.31, P=0.037), and chronic obstructive pulmonary disease (OR 3.56, P=0.037).

Conclusions: These findings can help spine surgeons identify high-risk patients and proactively deploy measures to avoid this potentially devastating complication in individuals who may be more vulnerable than the general elective spine population.

Keywords: Postoperative complications; spine; intradural-extramedullary spinal cord neoplasms; laminectomy; sepsis

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Introduction

Intradural extramedullary tumors (IDEMTs) comprise 30% of intraspinal neoplasms in adults (1). Posterior laminectomy is the preferred approach to achieve adequate visualization of the entire spinal canal and exposure of the lesion necessary for aggressive gross total resection (2,3). According to the Healthcare Cost and Utilization Project Nationwide Inpatient Sample, an estimated 490,000 laminectomies were performed annually from 2001–2011 (4). Given the susceptibility of solid tumor patients to infection (5-8), it is important to recognize IDEMT patients as a unique population when assessing complications after laminectomy. For example, autonomic dysregulation, adjuvant immunosuppressive therapy, frequent hospital visits, and general frailty are all factors that may render IDEMT patients more susceptible to infectious complications (9-12).

Sepsis is an uncommon but serious infectious complication following surgery for spinal tumors (13). The systemic inflammatory response can lead to multi-organ dysfunction, which severely compromises postoperative recovery and drastically increases the risk of morbidity and mortality (14). Sepsis is significantly correlated with discharge to a non-home facility after laminectomy for IDEMT resection and is also a common reason for 30- and 90-day readmission after spine tumor surgery (15,16). Further, prolonged hospital stays and complex multidisciplinary management of septic patients create a considerable source of financial strain on the U.S. healthcare system, costing an estimated $20.3 billion annually (17). As with other infectious complications, solid tumor patients are particularly vulnerable to sepsis and septic shock (18,19).

Given the prevalence of IDEMTs, the widespread implementation of posterior laminectomy, and the significant clinical and economic burdens posed by postoperative sepsis, it is important to better understand the underlying modifiable risk factors. To date, we are not aware of any studies assessing risk factors for postoperative sepsis specifically following laminectomy for IDEMTs. The aim of this study is to determine the incidence and risk factors for 30-day sepsis following laminectomy for IDEMTs using data from the 2012–2018 American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) databases. We present the following article in accordance with the STROBE reporting checklist (available at https://jss.amegroups.com/article/view/10.21037/jss-22-22/rc).

Methods

Data source and cohort selection

Data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) during 2012 to 2018 was used to conduct this retrospective cohort study (20). ACS-NSQIP is an extensive risk-adjusted national database containing 30-day postoperative morbidity and mortality outcomes. It includes data contributions from clinical abstractors from approximately 700 hospitals varying in size, socioeconomic location, and academic affiliation. Collected data encompasses more than 150 demographic, preoperative, intraoperative, and 30-day postoperative variables (21). An extensive number of quality improvement programs based on the ACS-NSQIP database have been repeatedly validated by many studies and deemed successful (22-24).

Individuals included in this study were selected based on the criteria of being an adult patient ≥18 years old who underwent elective excisional laminectomy for resection of IDEMTs spinal tumors. Current Procedural Terminology codes used were 63280, 63281, and 63282 for laminectomy of cervical, thoracic, and lumbar IDEMTs respectively. The recommended sample size to detect a 5% difference in the incidence of sepsis between any two subgroups with 80% power and a 95% confidence level was 400–500 per subgroup. In order to account for smaller subgroups after controlling for comorbidities, the maximum available sample size (n=2,027) was selected with minimal additional risk. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Variable definitions

Preoperative variables included were age (>65), gender, obesity [body mass index (BMI) ≥35 kg/m^2], smoking status (within 1 year of surgery), diabetes mellitus (DM) with oral agents or insulin, functional status (unknown, independent or partially/totally dependent ≤30 days before surgery), history of chronic obstructive pulmonary disease (COPD), dyspnea (at rest or moderate exertion), cardiac comorbidity (history of congestive heart failure or hypertension requiring medication ≤30 days before surgery), renal insufficiency (history of renal failure or currently on dialysis), weight loss (>10% loss body weight in last 6 months), steroid use for chronic condition, and pre-operative physical health status [American Society of Anesthesiologists (ASA) classification 1–4].

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Table 1 Sepsis complication by location of intradural extramedullary tumor laminectomy

Location	No sepsis complication	Sepsis complication	Rate
Cervical	375	8	2%
Thoracic	851	17	2%
Lumbar	763	13	2%
Total	1,989	38	2%

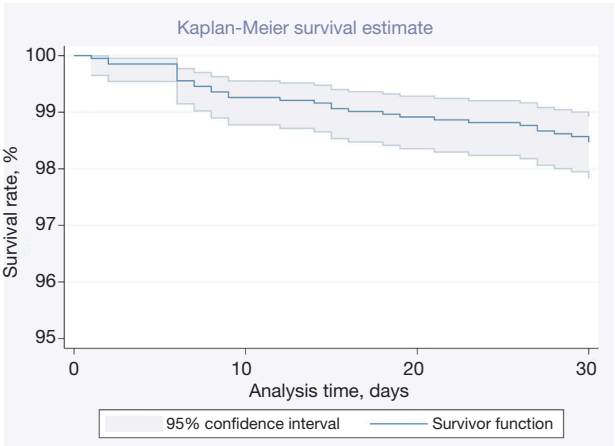

Figure 1 Kaplan Meier survival curve of days to sepsis related complications.

Operative variables included tumor location (cervical, thoracic or lumbar), operative time, and use of general anesthesia as the principal anesthesia technique.

Post-operative variables included mortality, prolonged length of stay (LOS) (>5 days), wound complication (superficial or deep surgical site infection), sepsis complication (including septic shock), cardiac complication (cardiac arrest requiring cardiopulmonary resuscitation or myocardial infarction), venous thromboembolism (VTE) (deep vein thrombosis or pulmonary embolism), neurological complications (cerebrovascular accident or stroke), progressive renal insufficiency, intraoperative or postoperative transfusion red blood cell transfusion, and unplanned reoperation (related to the initial procedure). Sepsis is defined by the systemic inflammatory response syndrome (SIRS) criteria in addition to either a positive blood culture, purulence or positive culture from a wound noting the site as cause of sepsis, or pre-operative condition of infection or bowel infarction leading to surgery. Septic shock is defined as sepsis in addition to documented organ and/or circulatory dysfunction.

Statistical analysis

All statistical analyses were performed using Stata (Version 17). Bivariate statistics were performed on pre-operative patient characteristics and demographics, risk factors, and major post-operative outcomes. Chi-square, and analysis of variance were used to evaluate association between various risk factors and outcomes as appropriate. Multivariable logistic regression was performed in order to control for patient factors and outcomes. Kaplan Meier survival curve was plotted for days to sepsis. Odds ratios (OR) were calculated with a 95% confidence interval (CI). For all analyses, a P value <0.05 was considered significant. All patients had complete data.

Results

The NSQIP database search yielded a total of 2,027 patients undergoing laminectomy for intradural extramedullary tumor, of whom 38 (2%) had sepsis (*Table 1*). The locations of laminectomies were then examined. There were 383 cervical laminectomies with 8 (2%) associated cases of sepsis related complications, 868 thoracic laminectomies with 17 (2%) associated sepsis related complications, and 776 lumbar laminectomies with 13 (2%) associated sepsis related complications. The mean days to sepsis was found to be 13 days (38 patients). The Kaplan Meier survival curve is plotted on *Figure 1*.

Associated preoperative demographic and clinical variables

Patients with or without sepsis related complications had similar age, mean BMI, gender (P>0.05). Patients with or without sepsis had similar rates of smoking, hypertension history, steroid use, bleeding disorder, dyspnea, and likelihood of general anesthesia (P>0.05). Those patients with sepsis had a high likelihood of greater anesthesia class (P=0.026), prolonged operative times (P=0.014), being functionally dependent (21.1% *vs.* 0.5%; P<0.001), diabetic

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(28.9% *vs.* 12.5%; P=0.003) and diagnosed with COPD (10.5% *vs.* 2.6%; P=0.003) (*Table 2*).

Associated postoperative outcomes

We also identified sepsis related complications to be associated with superficial surgical site infection (OR 11.62, 95% CI: 0.03–47.12; P<0.001), deep surgical site infection (OR 10.67, 95% CI: 2.74–41.52; P<0.001), deep vein thrombosis (OR 10.75, 95% CI: 3.65–31.60; P<0.001), pulmonary embolism (OR 15.27, 95% CI: 4.36–53.50; P<0.001), transfusion (OR 6.18, 95% CI: 2.75–13.88; P<0.001), length of stay >5 days (OR 5.41, 95% CI: 2.30–12.71; P<0.001), and return to operating room within 30 days (OR 8.72, 95% CI: 4.06–18.75; P<0.001) (*Table 3*).

Multivariable adjusted risk factor analysis

Multivariate analysis adjusted for all available baseline characteristics and comorbidities. Patients with incidence of sepsis related complications generally have an ASA class ≥3 (OR 1.76, 95% CI: 1.01–3.07; P=0.046), partially or totally dependent functional status (OR 2.23, 95% CI: 1.38–3.62; P=0.001), DM (OR 2.31, 95% CI: 1.05–5.08; P=0.037), COPD (OR 3.56, 95% CI: 1.18–5.08; P=0.037), and operative time in the 50th percentile or higher (OR 2.11, 95% CI: 1.06–4.19, P=0.032) (*Table 4*).

Discussion

We conducted a retrospective analysis of 2,027 spine surgery patients from the 2012–2018 ACS NSQIP databases to determine the risk factors for 30-day postoperative sepsis and septic shock following laminectomy for IDEMTs. The overall incidence of sepsis related complications among this patient population was 2% (38 total patients) and did not vary based on location of the tumor. Higher ASA classification, dependent functional status, DM, COPD, and prolonged operative time were found to be independent risk factors for sepsis related complications after laminectomy. Additional postoperative morbidities associated with sepsis related complications surgical site infection (SSI), deep venous thrombosis (DVT)/pulmonary embolism, transfusion, length of stay greater than five days, and return to the operating room within 30 days.

Posterior laminectomy has been associated with a host of secondary complications including structural instability, increased pain, and postoperative kyphosis (2,25). To date, however, the postoperative sepsis related complications after laminectomy for IDEMTs has not been well studied. Our findings are generally consistent with previously published data demonstrating a 2.9–3% incidence of sepsis for patients undergoing any surgical procedure for either primary or secondary spinal tumors, including laminectomy, corpectomy, and/or fusion (13,26). However, the reported incidence of sepsis related complications after elective spine surgery for non-oncologic indications is generally lower (0.23–2.5%) (27-30), likely due to the immunologic complexity and systemic burden of cancer (26). More broadly, sepsis related complications are seen in 2.3–5% of patients undergoing any type of surgery, suggesting that laminectomy for IDEMT may not contribute additional risk of sepsis compared to other surgical procedures (31).

The mean time to diagnosis of sepsis in our study was 14 days. This is generally consistent with previously published findings, which demonstrate a median time to diagnosis of 13 days after surgery for spinal tumors (26), 12 days after adult spinal deformity surgery (32), 10.5 days after anterior cervical discectomy and fusion (ACDF) (29), and 9 days after posterior lumbar fusion (PLF) (29). Of note, delayed diagnosis of sepsis and septic shock is significantly associated with profound mortality as high as 30–50% (33,34). Interestingly, our data did not show a correlation between sepsis related complications and mortality, although an increased risk of death has been well-described in spine surgery patients who develop postoperative sepsis (27). We did find that septic patients incurred a higher likelihood of suffering from other major complications, however. Bleeding requiring transfusion, prolonged length of stay, and reoperation within 30 days have been reported to occur at a significantly higher rate among spine surgery patients who develop sepsis (13,27,28). This is consistent with the clinical course of sepsis, which frequently escalates to multi-organ dysfunction and severe drops in blood pressure requiring vasopressors and vigilant in-patient monitoring.

Though we are not aware of any studies investigating the risk of sepsis after laminectomy for IDEMTs, there is a large body of evidence outlining the risk factors for infectious complications after general spine surgery. The ASA physical status classification system is designed to broadly describe the severity of a patient's disease and comorbidities prior to anesthesia. Although not a risk stratification system in and of itself, numerous studies have reported ASA classification as an important predictor of various postoperative complications (35). Higher ASA classification has been

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Table 2 Patient characteristics and demographic variables

Patient characteristics	No sepsis complication		Sepsis complication		P value
	n	%	n	%	
Total	1,989		38		
Cervical	375	18.9	8	21.1	0.862
Thoracic	851	42.8	17	44.7	
Lumbar	763	38.4	13	34.2	
Age, years (mean)	55		55		0.508
BMI (mean)	29		28		0.317
Male	903	45.4	21	55.3	0.227
Female	1,086	54.6	17	44.7	
ASA Class 1	77	3.9	0	0.0	0.026
ASA Class 2	805	40.5	10	26.3	
ASA Class 3	1,007	50.6	23	60.5	
ASA Class 4	96	4.8	5	13.2	
Smoking	289	14.5	7	18.4	0.501
Functional status, independent	1,865	93.8	28	73.7	<0.001
Functional status, dependent	10	0.5	8	21.1	
Functional status, totally dependent	15	0.8	2	5.3	
Functional status, unknown	9	0.5	0	0.0	
Diabetes	248	12.5	11	28.9	0.003
Chronic obstructive pulmonary disease	52	2.6	4	10.5	0.003
Congestive heart failure	3	0.2	0	0.0	0.811
Hypertension	786	39.5	18	47.4	0.327
Renal failure	0	0.0	0	0.0	
Dialysis	4	0.2	0	0.0	0.782
Weight loss	20	1.0	0	0.0	0.534
Steroid use	132	6.6	3	7.9	0.758
Bleeding disorder	35	1.8	0	0.0	0.409
Dyspnea at rest	4	0.2	0	0.0	0.936
Dyspnea at mod exertion	66	3.3	1	2.6	0.936
General anesthesia	1,982	99.6	38	100.0	0.998
Operative time, min (mean)	213.6305		249.7105		0.014

BMI, body mass index; ASA, American Society of Anesthesiologists.

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Table 3 Associated post-operative outcomes

Post-operative outcomes	Odds ratio	Lower 95% CI bound	Upper 95% CI bound	P value
Superficial surgical site infection	11.62	0.03	47.12	<0.001
Deep surgical site infection	10.67	2.74	41.52	<0.001
Cardiac arrest	9.50	0.87	103.09	0.06
Renal insufficiency	21.78	0.98	482.26	0.05
Deep vein thrombosis	10.75	3.65	31.60	<0.001
Pulmonary embolism	15.27	4.36	53.50	<0.001
CVA or stroke	8.61	0.79	93.67	0.08
Mortality	3.68	0.73	18.64	0.12
Transfusion	6.18	2.75	13.88	<0.001
Length of stay >5 days	5.41	2.30	12.71	<0.001
Return to OR	8.72	4.06	18.75	<0.001

CI, confidence interval; CVA, cerebrovascular accident; OR, operating room.

Table 4 Risk factors after multivariable logistic regression

Risk factors for sepsis	Odds ratio	Lower 95% CI bound	Upper 95% CI bound	P value
ASA class	1.76	1.01	3.07	0.046
Functional status	2.23	1.38	3.62	0.001
Diabetes	2.31	1.05	5.08	0.037
Chronic obstructive pulmonary disease	3.56	1.18	5.08	0.037
Hypertension	0.79	0.38	1.64	0.532
High operative time (≥50th percentile)	2.11	1.06	4.19	0.032

CI, confidence interval; ASA, American Society of Anesthesiologists.

previously identified as an independent predictor of SSI and sepsis after both general spine and spinal tumor surgery (26,36-38). Functional status is a measure of preoperative dependency in performing normal daily activities. Dependent functional status has also been reported to be a risk factor for major complications including sepsis after elective adult deformity spine surgery and spinal tumor surgery (26,27). ASA classification and preoperative functional status are easily evaluable patient factors that can allow surgeons to risk stratify patients before operating. In high-risk patients, such as those with higher ASA status and advanced dependency, more aggressive measures to mitigate the risk of infectious complications may be warranted. Alternatively, if certain comorbidities can be treated in a timely manner (e.g., DM and COPD), delaying surgery may be a viable option so long as spinal cord compression is not a concern. Intraoperatively, mindful minimization of surgical duration can reduce the risk of sepsis and other infectious complications after spinal procedures (27,38).

Diabetes is a well-known risk factor for infection and sepsis after spinal surgery, including surgery for spinal tumors (27,38,39). As expected, our data similarly demonstrated that sepsis was an independent predictor of sepsis related complications after laminectomy. Interestingly, obesity was not significantly associated with postoperative sepsis in our study, although a growing body of evidence suggests a correlation between obesity and infection risk (40-42). Although the reasons underpinning this observation were not readily apparent in the NSQIP data, it may be due, at least in part, to the fact that the baseline metabolic profiles of cancer patients are typically vastly altered from those of healthy counterparts. Another

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well-described metabolic factor driving risk of infection after spine surgery is serum albumin level, a surrogate measure of nutritional status (43,44). Although we did not investigate albumin level in our study, nutritional intake should be deemed adequate before surgery for patients undergoing laminectomy for IDEMTs. In general, it is important to ensure patients are in a stable metabolic state before spine surgery. Although weight loss should be encouraged for obese patients, prior literature suggests that excessive unintentional weight loss preoperatively may also be an independent risk factor for sepsis after spine surgery (27).

Unsurprisingly, postoperative SSI (OR 23.3; 95% CI: 8.6–63.7), pneumonia (OR 5.8; 95% CI: 2.2–15.2) and urinary tract infection (OR 14.7; 95% CI: 5.96–36.1) were all significantly associated with increased odds of sepsis (P<0.001) (13). There are a number of simple measures that can be taken to combat the morbidity and mortality associated with infection and subsequent sepsis related complications. Orthopaedic literature suggests that decolonization with chlorhexidine bath or other topical antibiotics the night before surgery is highly efficacious in reducing the risk of infection with challenging organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) (45-48). There is evidence that intrawound irrigation with Betadine (povidone-iodine) may reduce infection rates after spinal surgery, although support for topical intrawound vancomycin powder is lacking (49,50). Ensuring the implementation of other, more standard practices such as redosing antibiotics intraoperatively, postoperative antibiotic protocol, double gloving, and limiting traffic through the OR is also critical for spine surgeons to optimize outcomes (51). However, surgeons should be weary to reserve the most extreme prophylactic measures for high-risk patients only, so as to avoid the emergence of antibiotic resistant bacterial strains.

There are a number of other well-described risk factors of infection and sepsis related complications that did not correlate with sepsis in our study. Among these, the most commonly reported is prolonged operative time, which has been described extensively as a predictor of infectious complications including sepsis after spine surgery (26,27,43,52). Older age and male sex have also been identified as independent predictors of sepsis after elective adult deformity spine surgery and spinal tumor surgery, although neither sex nor age were associated with sepsis in our patient cohort (26,27,38,53). One variable that we did not investigate was history of systemic inflammatory response syndrome (SIRS), which is a part of the diagnosis of sepsis (13,26). Smoking is another well-known risk factor for infection after spine surgery (54). However, we did find that COPD, but not smoking, was significant correlated with sepsis related complications.

This study is not without limitations. Prophylactic measures to minimize SSI risk and therefore risk of sepsis related complications were not recorded in the NSQIP database and therefore could not be accounted for in this study. Specific considerations associated with IDEMTs such as tumor subtype and meningitis, as well as operative considerations such as minimally invasive versus open approaches and levels operated, were also not recorded and could not be analyzed in the context of sepsis (55). Mounting evidence supports the use of minimally invasive techniques in spine surgery, which are associated with equivalent or superior patient outcomes in addition to reduced risk of infectious and other complications including sepsis (56,57). Estimated blood loss is another pertinent operative variable that was not available in the NSQIP database, although occurrence of blood transfusion may serve as a surrogate measure of high-volume blood loss for the purposes of this study. Similarly, patients with IDEMTs may suffer from a host of other comorbidities related to their cancer, including prior treatment especially for metastatic disease. It stands to reason that disruption of the native immune environment with chemotherapy or immunotherapy is a likely confounding variable for the occurrence of infectious complications including sepsis. The highly variable immune status of these patients, as well as the nature of their cancer, are major comorbid factors that were not included in this data. Additionally, the NSQIP database is limited to reporting complications that occur within a 30-day postoperative period. Although previous studies suggest that the onset of sepsis is typically within the first three weeks after surgery, our data would not have included any events that occurred beyond this 30-day window and may therefore underestimate the true incidence of sepsis related complications. Nevertheless, the findings of this study are likely applicable to most U.S. hospitals and in-patient spine surgery services, given our utilization of the broadly generalizable and validated NSQIP database (22-24).

Despite limitations, this study provides a novel assessment of the incidence and risk factors for postoperative sepsis related complications following laminectomy for IDEMTs using a large, U.S.-based patient

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population. Here, we report an overall incidence of 2% and identify four independent predictors of sepsis: higher ASA classification, dependent functional status, DM, and COPD. Further, we report that SSI, DVT/PE, transfusion, length of stay greater than five days, and return to the operating room within thirty days are additional major complications that correlate with sepsis and septic shock. These findings can help spine surgeons identify high-risk patients and proactively deploy measures to avoid this potentially devastating complication. Further research may help elucidate the relationship between cancer and sepsis risk, as this is a major comorbidity that distinguishes our patient sample from those who undergo elective spine procedures.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jss.amegroups.com/article/view/10.21037/jss-22-22/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jss.amegroups.com/article/view/10.21037/jss-22-22/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was deemed non-human subjects research and therefore exempt from review by institutional review board of Johns Hopkins University.

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