Enhanced Recovery After Surgery-Based **Perioperative Protocol for Head and Neck Free Flap Reconstruction**



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Caitlin Bertelsen, MD¹, Kevin Hur, MD¹, Margaret Nurimba¹, Janet Choi, MD, MPH¹, Joseph R. Acevedo, MD¹, Anna Jackanich¹, Uttam K. Sinha, MD¹, Amit Kochhar, MD¹, Niels Kokot, MD¹, and Mark Swanson, MD¹

Abstract

Objectives. Evaluate an enhanced recovery after surgery (ERAS)-based free flap management protocol implemented at our center.

Study Design. Prospective cohort study of patients after implementation of an ERAS-based perioperative care protocol for patients undergoing free flap reconstruction of the head and neck as compared with a historical control group.

Setting. Tertiary care academic medical center.

Participants and Methods. All patients undergoing free flap reconstruction were prospectively enrolled in the ERAS protocol group. A retrospective control group was identified by randomly selecting an equivalent number of patients from a records search of those undergoing free flap surgery between 2009 and 2015. Blood transfusion, complications, 30-day readmission rates, intensive care unit (ICU) and hospital length of stay, and costs of hospitalization were compared.

Results. Sixty-one patients were included in each group. Patients in the ERAS group underwent less frequent flap monitoring by physicians and had lower rates of intraoperative (70.5% vs 86.8%, P = .04) and postoperative (49.2% vs 27.2%, P = .026) blood transfusion, were more likely to be off vasopressors (98.3% vs 50.8%, P < .01) and ventilator support (63.9% vs 9.8%, P < .01) at the conclusion of surgery, and had shorter ICU stays (2.11 vs 3.39 days, P =.017). Length of stay, readmissions, and complication rates did not significantly differ between groups.

Conclusion. ERAS-based perioperative practices for head and neck free flap reconstruction can reduce time on the ventilator and in the ICU and the need for vasopressors, blood transfusions, and labor-intensive flap monitoring, without adverse effects on outcomes.

Keywords

free flap, perioperative care, early awakening, enhanced recovery after surgery

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ead and neck cancer resection with free flap reconstruction requires labor-intensive surgery and a prolonged recovery period. Perioperative management of these patients has historically been highly variable and is often based on single-institution experience and surgeon preference.

The Enhanced Recovery After Surgery Society has encouraged the development of evidence-based perioperative care guidelines, which have been implemented across several surgical specialties.^{1,2} In keeping with the goals of the society, a consensus review and recommendations for patients undergoing head and neck surgery with free flap reconstruction were recently published.³ Among factors addressed were the use of perioperative antibiotics and anticoagulation, acute fluid management including blood transfusions, the frequency and nature of flap monitoring, early mobilization, and postoperative care in the intensive care unit (ICU).

¹Caruso Department of Otolaryngology–Head and Neck Surgery, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

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Corresponding Author:

Mark Swanson, MD, Caruso Department of Otolaryngology-Head and Neck Surgery, Keck School of Medicine of USC, 1450 San Pablo Street, Suite 5100, Los Angeles, CA 90033, USA. Email: Mark.Swanson@med.usc.edu



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Prior to and concurrent with the development of these guidelines, enhanced recovery after surgery (ERAS) protocols have been implemented and evaluated to a limited extent in head and neck oncologic surgery. These studies have focused on assessing compliance with protocol elements^{4,5} and complication rates.^{6,7} Data remain limited regarding perioperative outcomes such as hospital and ICU length of stay (LOS), hospitalization costs, and readmission rates, and further study is warranted. Here, we evaluate the effects of implementing an ERAS-based perioperative care protocol for patients undergoing free flap reconstruction after head and neck cancer resection at a tertiary care medical center.

Methods

Patient Selection

Under a study protocol approved by the institutional review board at the University of Southern California (HS-17-00810), patients undergoing free flap surgery at our institution for reconstruction of defects of the head and neck were prospectively enrolled after ERAS protocol implementation. A retrospective control group was selected from patients undergoing free flap reconstruction at our institution between 2009 and 2015. The control cohort was generated by selecting an equivalent number of patients with a random number generator.

Historical Free Flap Perioperative Management

Prior to ERAS protocol implementation, patients undergoing free flap reconstruction were managed as follows. Fluid and blood products, as well as vasoactive medications, were administered intraoperatively at the discretion of the anesthesiologist.

Patients were admitted to the ICU postoperatively and kept sedated on the ventilator overnight. Systolic blood pressure was maintained strictly between 110 and 160 mm Hg with the use of crystalloids, colloids, and continuous infusions of vasoactive medications if necessary. Patients were transferred to the stepdown unit after being weaned from ventilatory support and vasoactive medications, per discretion of the inpatient rounding team. Patients underwent in-person flap monitoring by a resident at least every 6 hours for the first 24 hours postoperatively. Doppler flap monitoring was performed by nursing hourly in the ICU and every 2 to 4 hours in the stepdown unit. Blood products were administered for target hemoglobin of 10 g/dL.

Antiemetics were given routinely, and feeding via a nasogastric or gastric tube was initiated when patients expressed hunger. This was typically continued at a constant rate of 10 to 15 mL/h for 24 hours and then increased to the patient's goal rate as determined by a registered dietitian. When tolerating the goal rate, patients transitioned to bolus feeds and were typically discharged on this regimen, with return to oral intake as outpatients.

Oral aspirin (325 mg) was administered preoperatively. Postoperative anticoagulation consisted of aspirin (81 mg daily) and prophylactic doses of subcutaneous heparin or enoxaparin. Prophylactic broad-spectrum antibiotics were administered for 7 days.

Postoperative pain control was typically opioid based. Patient-controlled analgesia was used for the first postoperative day; oral and parenteral narcotic medications were subsequently given as needed. For patients with a history of preoperative opioid use or chronic pain, the acute pain service was consulted for assistance with pain management.

New ERAS-Based Free Flap Perioperative Care Protocol

The ERAS-based protocol was implemented at our center in October 2017. In this protocol, patients undergoing tracheotomy were removed from ventilator support at the conclusion of surgery, prior to leaving the operating room. Prophylactic tracheotomy was avoided when feasible, in accordance with consensus guidelines advocating this practice.³ These determinations were made per surgeon judgment based on the defect itself, comorbidities, and body habitus. Patients with limited oral cavity resections were sedated and intubated overnight to be extubated on postoperative day 1. Patients undergoing lateral skull base resections and reconstruction with no involvement of the aerodigestive tract also did not undergo tracheotomy and were extubated in the operating room.

Intra- and postoperative use of vasopressors was reserved for significant hypotension (systolic blood pressure <90 mm Hg), for symptomatic anemia, or by evidence of poor flap perfusion, such as slow rate of bleeding on pinprick or weak Doppler signal. Fluid management was directed toward maintaining normovolemia. Blood transfusions in the absence of significant blood loss were avoided. These changes in management were implemented per communication with the anesthesiologist, who was primarily responsible for enacting them intraoperatively.

All patients were admitted to the ICU postoperatively and transferred to the stepdown unit the next morning if there were no acute events. Patients underwent Doppler flap monitoring by nursing hourly in the ICU and every 2 hours in the stepdown unit until 72 hours postoperatively; after that point, flap monitoring was performed every 4 hours by nursing. Residents performed in-person flap monitoring every 12 hours. Blood transfusions were administered for goal hemoglobin of 7 g/dL in the absence of symptomatic anemia, evidence of flap compromise, or cardiac comorbidity. Patients with cardiac comorbidities were transfused with a threshold of 9 g/dL. This was done on the basis of recommendations from the critical care literature that transfusions be administered for hemoglobin thresholds of 7 g/dL and that a restrictive transfusion strategy does not increase morbidity⁸; however, in patients with cardiac comorbidities, lower thresholds are associated with increased cardiac risk, and a more liberal transfusion threshold (>8 g/dL) is supported.⁹ Patients were prescribed perioperative prophylactic broad-spectrum antibiotics for 24 hours.

Anticoagulation and enteral feeding practices did not change. In this version of the ERAS protocol, pain management was also unchanged from historical practices.

Data Collection, Outcomes, and Measures

Medical records were reviewed for relevant demographic and clinical variables. Prior surgery was defined as head and neck oncologic surgery and did not include diagnostic procedures such as operative biopsy. Flap complications were defined as partial or complete flap loss or anastomotic failure requiring revision. Infectious complications were defined as positive wound cultures or radiographic evidence of infection requiring antibiotics. Fistulas were counted separately as nonflap and noninfectious complications. Data were gathered prospectively after protocol implementation and by chart review for the retrospective control group. Billing records were queried to obtain cost information, including total charges for cost to the hospital of hospitalization, as well as ICU, ward, and blood bank charges. All monetary figures for costs were adjusted to 2018 dollars with data from the Bureau of Labor Statistics.¹⁰

Statistical Analysis

Descriptive analysis was conducted to examine differences in sociodemographic characteristics and hospital course between patients in the historical control group and the ERAS group. A multivariable linear regression model, with hospital stay as the dependent variable, was created by using candidate pre- and intraoperative variables that were significant (P < .05) from univariable analysis, in addition to the study arm variable (ERAS vs control group). All results in the multivariable model are reported as odds ratios with 95% CIs. All data were imported into RStudio for statistical analysis.

Results

A total of 61 eligible patients were included in each group. Mean age in the control group was 67.8 years versus 59.6 years in the ERAS group (P < .001). Distribution of ethnicities and history of smoking were comparable between groups; there was a higher proportion of heavy alcohol users in the ERAS group (26.2% vs 6.7%, P = .01). Prior surgery or radiation in the head and neck was comparable between groups, as was the prevalence of various medical comorbidities. Patient characteristics are summarized in **Table 1**.

Intraoperative details are summarized in **Table 2**. Fewer patients in the ERAS group underwent tracheostomy (50.8% vs 77.0%, P < .001) or gastrostomy tube (50.8% vs 70.5%, P = .01) placement at the time of surgery. The proportion of patients undergoing these procedures prior to surgery was comparable between groups. The tumor histologies were comparable between groups, as were the types of flaps. Of note, 1 patient in the control group underwent a latissimus dorsi free flap versus none in the ERAS group. Additionally, 1 patient in the control group underwent a scapula free flap and none in the control group.

Estimated blood loss (EBL) was comparable between the control and ERAS groups; however, patients in the ERAS group were less likely to receive blood transfusions: intraoperative (70.5% vs 86.8%, P = .047) or postoperative (53% vs 43%, P = .026; mean: 0.61 vs 1.44 units, P = .016). Transfusion rates did not differ on the basis of age, race, sex, smoking or alcohol consumption history, radiation or surgical history, diabetes, kidney disease, anemia, or gastrostomy or tracheostomy placement. Patients with a history of heart disease were more likely to undergo transfusion than those without (100% vs 75.7%, P = .039). Patients who received intraoperative transfusions had higher EBL than those who did not (913 vs 463 ml, P < .001); there was no difference in EBL between patients who did and did not receive postoperative transfusions (783 vs 839 mL, P = .569).

Postoperative details are shown in **Table 3**. A greater proportion of the ERAS group was off vasopressors (98.3% vs 50.8%, P < .001) and ventilator support (63.9% vs 9.8%, P < .001) at the conclusion of surgery and spent fewer days in the ICU (2.11 vs 3.39 days, P = .017). LOS (10 days for the ERAS group vs 8.85 days for the control group, P =.346), 30-day readmission rate (16.4% for the ERAS group and 13.1% for the control group, P = .828), rates of flaprelated complications, total flap loss, and complications requiring reoperation did not differ between groups. There was no difference in rates of infectious complications between groups.

Table 4 compares costs between control and ERAS cohorts. Total costs, ICU costs, and ward costs did not differ between groups. Blood bank costs were significantly lower for the ERAS group (mean: \$1353 vs \$2455, 95% CI for difference: \$501-\$1701).

Table 5 depicts results of multivariable analysis. On univariable analysis, factors associated with increased hospital stay across both cohorts included history of tracheostomy prior to surgery (P = .043), placement of tracheostomy (P = .005) or gastrostomy tube (P < .001) at the time of surgery, length of ICU stay (P < .001), need for mechanical ventilation postoperatively (P < .001), and an infectious (P < .001) or flap-related (P = .01) complication.

On multivariable analysis controlling for potential preand intraoperative confounding variables, previous head and neck cancer surgery was associated with shorter LOS (P =.016), and undergoing tracheostomy concurrently with surgery was associated with longer LOS (P < .001).

Discussion

ERAS protocols have been found to reduce LOS and postoperative morbidity across surgical specialties.^{1,11} At our institution, a new perioperative protocol for patients undergoing head and neck free flap reconstruction was developed according to recently published ERAS recommendations.³ Patients undergoing surgery after protocol implementation were less likely to undergo tracheostomy or gastrostomy tube placement or receive a blood transfusion during or after surgery. They were also more likely to be off vasopressor or ventilator support at the conclusion of surgery,

Table 1. Patient Characteristics.

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	3	0	0.0	2	3.3	.026ª

Abbreviations: COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; ERAS, enhanced recovery after surgery. ${}^{a}P \leq .05$.

Table 2. Intraoperative Data.

	ERAS pi	ERAS protocol		Control	
	No.	%	No.	%	P value
Tracheostomy prior to surgery					
Yes	I	1.6	5	8.2	
No	60	98.6	56	91.8	.21
Tracheostomy during surgery					
Yes	31	50.8	47	77.0	
No	30	49.2	14	23.0	.004 ^a
Gastrostomy tube prior to surgery					
Yes	6	9.8	8	13.1	
No	55	90.2	53	86.9	.78
Gastrostomy tube during surgery					
Yes	31	50.8	43	70.5	
No	30	49.2	18	29.5	.041ª
Concurrent tumor resection					
No	3	4.9	7	11.5	
Yes	58	95.1	54	88.5	.32
Tumor type					
Salivary gland	I	1.6	I	1.6	
Sarcoma	0	0.0	I	1.6	
Cutaneous	8	13.1	0	0.0	
SNUC	I	1.6	0	0.0	
SCC	44	72.1	48	78.7	
Other	7	11.5	6	9.8	.07
Flap type					
ALT	18	29.5	21	34.4	
Fibula	12	19.7	11	18.0	
Latissimus	0	0.0	I	1.6	
RFFF	30	49.2	28	45.9	
Scapula	I	1.6	0	0.0	.67
EBL, mean, mL	759.18		855.13		.33
Intraoperative transfusion					
Yes	43	70.5	53	86.9	
No	18	29.5	8	13.1	.05ª
Off vasopressors at end of surgery					
No	60	98.4	31	50.8	
Yes	I	1.6	28	45.9	<.001ª
Off ventilator at end of surgery					
Yes	39	63.9	6	9.8	
No	22	36.1	55	90.2	<.001ª

Abbreviations: ALT, anterolateral thigh; EBL, estimated blood loss; ERAS, enhanced recovery after surgery; RFFF, radial forearm free flap; SCC, squamous cell carcinoma; SNUC, sinonasal undifferentiated carcinoma.

 $^{a}P \leq .05.$

and they spent fewer days in the ICU. LOS, hospital costs, readmissions, and rates of infectious and flap-related complications did not differ between groups. To our knowledge, this is the first study to combine early awakening and a shortened ICU stay with other elements of the ERAS guidelines. The ERAS group did have a small increase in the rate of complications requiring return to the operating room that was not statistically significant. Given the small sample size, it is possible that our study was underpowered to detect a difference in rates of these infrequent events.

Historically, perioperative management has involved labor-intensive monitoring and prolonged use of vasoactive, antimicrobial, and anticoagulant medications, as well as long ICU and hospital stays. A 2007 national survey of institutions performing free flaps in the head and neck revealed the use of various postoperative monitoring practices, including

Table 3. Postoperative Data.

	ERAS protocol		Control		
	No.	%	No.	%	P value
LOS	10		8.85		.346
ICU, d	2.11		3.39		.017 ^a
Postoperative ventilator, d	0.721		2.084		<.001ª
Postoperative transfusion					
Yes	17	27.9	30	49.2	
No	44	72.1	31	50.8	.026 ^a
Postoperative units transfused, mean	0.61		1.44		.016ª
Infectious complication					
No	49	80.3	52	85.2	
Yes	12	19.7	9	14.8	.631
Flap complication					
No	54	88.5	56	91.8	
Yes	5	8.2	5	8.2	>.999
Flap survival					
No	4	6.6	3	4.9	
Yes	57	93.4	58	95.1	>.999
Complication requiring reoperation					
No	53	86.9	58	95.1	
Yes	8	13.1	3	4.9	.114
30-d readmission					
No	51	83.6	52	85.2	.828
Yes	10	16.4	8	13.1	
Alive at 30 d					
No	2	3.3	5	8.2	.430
Yes	55	90.2	55	90.2	
Data missing	4	6.5	I	1.6	

Abbreviations: ERAS, enhanced recovery after surgery; ICU, intensive care unit; LOS, length of stay.

 $^{a}P \leq .05.$

observation of color, pinprick, bleeding rate, capillary refill, measurement of surface temperatures, and implantable Doppler monitors.¹² The same study reported a mean post-operative ICU stay of 2.44 days, with up to 5 planned ICU days at some institutions. Interestingly, a more recent similarly conducted study reported a slightly higher flap success rate for patients admitted to the general floor than to the ICU.¹³ Other studies have shown that eliminating routine ICU admission after free flap surgery is safe¹⁴ and can lower cost and overall LOS without increasing complication rates.¹⁵

There is also evidence that rapid awakening after free flap surgery reduces complications relative to planned overnight mechanical ventilation.¹⁶⁻¹⁸ Given this evidence, we sought to reduce the duration of postoperative mechanical ventilation and limited the planned ICU stay to the first night postoperatively. We observed no increase in flap failures or complication rates upon enacting these changes, corroborating observations by others.

In-person monitoring by physicians is another component of free flap perioperative care. Kovatch et al reported that postoperative monitoring of free flaps by residents ranged from every 4 hours to every 12 hours by residents.¹³ In the era of duty hour restrictions and physician burnout, there has been an effort to reduce the frequency of flap monitoring by residents. One recent study showed no difference in rates of flap salvage or flap loss among groups undergoing monitoring every 4, 8, or 12 hours.¹⁹ Our study found that implementation of a new ERAS protocol decreased frequency of physician monitoring from every 6 hours to every 12 hours with no change in flap failure rates.

Similarly, no consensus exists regarding transfusion thresholds for patients undergoing head and neck free flap reconstruction. Many physicians have used hemoglobin levels of 10 g/dL or a hematocrit level of 30% as a transfusion threshold based on evidence that tissue perfusion is optimized at these levels²⁰; however, practice patterns vary widely.¹³ Recent data suggested that liberal use of blood transfusions is associated with adverse perioperative outcomes, such as myocardial infarction, congestive heart failure, respiratory distress, pneumonia, and wound dehiscence.²¹ Other studies have shown decreased survival^{22,23} and increased rate of recurrence²³ in patients with head and neck cancer undergoing blood transfusion, theoretically due to

Table 4. Descriptive	e Statistics of	Hospital	Costs for	Control	and ERAS	Groups.
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	Charges, l		
	Control	ERAS	B (95% CI) ^a
Total			
Mean	87,350	86,793	-557 (-19,149 to 18,034)
Median	74,292	68,008	
IQR	64,663-95,941	61,082-84,941	
ICU			
Mean	14,540	11,161	-3380 (-8907 to 2148)
Median	10,788	7871	
IQR	7397-14,391	4053-12,047	
Ward			
Mean	13,025	21,109	8084 (-811 to 16,980)
Median	10,545	13,286	
IQR	8024-15,638	11,055-18,246	
Blood bank			
Mean	2455	1353	$-1101 (-1701 to -501)^{b}$
Median	1807	1104	
IQR	1082-3172	539-1997	

Abbreviations: ERAS, enhanced recovery after surgery; ICU, intensive care unit; IQR, interquartile range.

^aB coefficient: Mean differences in each cost category between control and ERAS groups in adjusted 2018 US dollars, based on univariable regression models. ^b95% CI does not include 0.

 Table 5. Multivariable Analysis of Associations With Increase in Length of Hospitalization.

	Coefficient	SE	95% CI	P value
Race				
African American	1.185	0.125	0.928-1.514	.17
Asian	1.551	0.093	1.294-1.860	<.001ª
Hispanic/Latino	0.792	0.094	0.659-0.953	.01ª
Other	1.545	0.167	1.114-2.142	<.01ª
Caucasian	Ref			
Prior surgery				
Yes	0.794	0.794	0.690-0.913	<.01ª
No	Ref			
Tracheostomy				
Yes	1.360	0.088	1.145-1.616	<.001ª
No	Ref			
PEG surgery				
Yes	0.900	0.086	0.769-1.066	.22
No	Ref			
Arm				
ERAS	1.130	0.076	0.974-1.312	.11
Control	Ref			
Alcohol use				
Daily	1.121	0.101	0.919-1.367	.26
Occasional	0.930	0.083	0.791-1.093	.38
None	Ref			

Abbreviations: ERAS, Enhanced Recovery After Surgery; PEG, percutaneous endoscopic gastrostomy; Ref, reference.

 $^{a}P \leq .05.$

immunomodulatory effects of blood products. Importantly, rates of flap failure and flap-related complications were comparable between patients who did and did not undergo transfusion, as well as between patients who were transfused per a restrictive strategy versus liberal one.²¹

In developing our new perioperative care protocol, we sought to minimize harm from unnecessary blood transfusions by setting a restrictive transfusion threshold. We found that mean EBL did not differ between patients, with the ERAS group having a lower rate of blood transfusions. There was no difference in rates of flap complications, which further supports a restrictive transfusion strategy. Importantly, the difference between cohorts in blood transfusions is likely more reflective of new postoperative management than changes in intraoperative blood transfusions. This practice changed over time toward more restrictive intraoperative management as well. There was no observed difference in multifactorial endpoints, such as cost and LOS. While our care pathway may have had some effect on these variables, other less controllable factors, such as insurance-related and social issues, often contribute to hospitalization length and cost. Specifically, delays in hospital discharge due to the need to find, and obtain insurance authorization for, skilled nursing or subacute placement may negate the potential benefits of the ERAS pathway on LOS. These factors may be future targets for process improvements aimed at reducing LOS. Interestingly, we found on multivariable analysis that prior treatment for head and neck cancer was associated with shorter LOS, perhaps due to patient and family familiarity with wound and tracheostomy care and supplies. Thus, preoperative patient education and discharge planning may be one additional method of reducing LOS and cost. Since the conclusion of this study, we have augmented our ERAS protocol by standardizing pathways for anesthetic use, intraoperative blood transfusions, perioperative pain management, and nutrition. It is possible that these additions will result in improvements in cost and LOS.

While the ERAS and historical cohorts were well matched for sex and racial composition, comorbidities, tumor histology, and types of free flaps, one important limitation is the lack of matching in terms of age and performance status. This may be due to a difference in payer mix, as the ERAS group was treated post–Affordable Care Act, which allowed a higher proportion of younger, non–Medicare insured patients to be seen at our institution. Another possible explanation is the changing demographic of patients with head and neck cancer, with those with human papilloma virus–related tumors generally of younger age.

Additionally, the retrospective nature of the comparator arm of this study raises the possibility of information bias due to the lack of availability of information in the medical record. An additional limitation is the fact that this study did not have the duration of follow-up necessary to assess oncologic outcomes or functional results of reconstruction associated with the new protocol. Finally, as mentioned earlier, cost and LOS of hospitalization after free flap surgery are often affected by logistical and insurance-related issues, such as authorization for home health supplies, which were difficult to measure and control.

Conclusions

Evidence-based ERAS protocols can reduce ventilator days, ICU LOS, vasopressor use, and blood transfusions. Additionally, labor-intensive flap monitoring can be scaled back without adverse effects on near-term perioperative outcomes. Further modifications and advanced discharge planning may help reduce hospital costs and LOS.

Author Contributions

Caitlin Bertelsen, primary author, data collection, data analysis, study design; Kevin Hur, data collection, statistical analysis; Margaret Nurimba, data collection, statistical analysis, study design; Janet Choi, data collection, statistical analysis, study design; Joseph R. Acevedo, data collection, statistical analysis, study design; Anna Jackanich, data collection, statistical analysis; Uttam K. Sinha, study design, editing; Amit Kochhar, study design, editing; Niels Kokot, study design, editing; Mark Swanson, principal investigator, study design, editing, analysis.

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