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Direct Endoscopic Necrosectomy Versus Step-Up Approach for Walled-Off Pancreatic Necrosis:

Comparison of Clinical Outcome and Health Care Utilization

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Abstract

Objectives—Infected walled-off pancreatic necrosis (WOPN) is a complication of acute pancreatitis requiring intervention. Surgery is associated with considerable morbidity. Percutaneous catheter drainage (PCD), initial therapy in the step-up approach, minimizes complications. Direct endoscopic necrosectomy (DEN) has demonstrated safety and efficacy. We compared outcome and health care utilization of DEN versus step-up approach.

Methods—This was a matched cohort study using a prospective registry. Twelve consecutive DEN patients were matched with 12 step-up approach patients. Outcomes were clinical resolution after primary therapeutic modality, new organ failure, mortality, endocrine or exocrine insufficiency, length of stay, and health care utilization.

Results—Clinical resolution in 11 of 12 patients after DEN versus 3 of 12 step-up approach patients after PCD ($P < 0.01$). Nine step-up approach patients required surgery; 7 of these experienced complications. Direct endoscopic necrosectomy resulted in less new antibiotic use, pulmonary failure, endocrine insufficiency, and shorter length of stay ($P < 0.05$). Health care utilization was lower after DEN by 5.2:1 ($P < 0.01$).

Conclusions—Direct endoscopic necrosectomy may be superior to step-up approach for WOPN with suspected or established infection. Primary PCD generally delayed definitive therapy. Given the higher efficacy, shorter length of stay, and lower health care utilization, DEN could be the first-line therapy for WOPN, with primary PCD for inaccessible or immature collections.

Keywords

pancreatic necrosis; endoscopic necrosectomy; endoscopy; step-up approach

Acute pancreatitis is the most common gastroenterological cause for inpatient admission in the United States with more than 270,000 admissions annually and a resulting expenditure of approximately $2.6 billion dollars per annum.[1] Necrosis of the pancreatic parenchyma or

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the peripancreatic fat complicates acute pancreatitis in approximately 20% of patients, 30% of whom develop infected necrosis.[2,3] Without radiological, endoscopic, or surgical intervention, infected necrosis has a mortality rate approaching 100%.[4,5] Early disease recognition, aggressive supportive care, and therapeutic management of necrosis have been shown to dramatically improve outcomes.[6,7] When possible, intervention is delayed to allow liquefaction of necrosis and maturation of the collection to form walled-off pancreatic necrosis (WOPN). Encapsulation facilitates drainage and debridement and reduces procedural risk.[8] Nevertheless, the interventions themselves can cause substantial morbidity, and selection of the optimal therapeutic modality is important to affect resolution and minimize complications.

Minimally invasive and open surgical necrosectomy for infected necrosis has a 47% to 72% complication rate.[9–11] The PANTER trial demonstrated that a step-up approach of percutaneous catheter drainage (PCD), with subsequent minimally invasive surgical necrosectomy if needed, was superior to initial open surgical necrosectomy.[12] However, many patients subsequently required surgical necrosectomy. Direct endoscopic necrosectomy (DEN) is a relatively new technique that involves drainage and endoscopic debridement through the gastric or duodenal wall.[13] Direct endoscopic necrosectomy has been shown to be superior to endoscopic drainage alone for treatment of WOPN, with resolution in 88% versus 45%, respectively.[14] Additionally, the PENGUIN trial demonstrated that DEN resulted in reduced overall inflammatory state and lower rates of new-onset multiorgan failure and major complication compared with surgical necrosectomy.[15]

Although the step-up approach with initial PCD has been shown to avoid much of the morbidity associated with early surgical necrosectomy, the PANTER trial relied heavily on PCD as a primary modality, and DEN was not evaluated.[12] We hypothesize that DEN will result in more frequent and more rapid clinical resolution of symptomatic WOPN than primary PCD, yielding better clinical outcome and lower health care utilization.

METHODS

All procedures were performed at Brigham and Women's Hospital (Boston, Massachusetts). Institutional Review Board approval was obtained.

Study Design

This matched cohort study was performed using a prospective clinical registry. Twenty-four patients were included. Twelve consecutive patients from January 2009 to December 2010 were included in the DEN group. Patients undergoing a step-up approach with primary PCD were identified from the same registry and matched 1:1 with DEN patients based on collection size and Charlson Comorbidity Index, a prospectively validated metric. Follow-up data collection continued until March 2012. Inclusion criteria were diagnosis of acute pancreatitis based on the Atlanta classification and presence of symptomatic WOPN with suspected or confirmed infected necrosis.[16] Included patients had fever, leukocytosis, positive fluid aspirate Gram stain, and/or positive blood cultures. Patients with other prior intervention for WOPN were excluded. All patients had computed tomography (CT) of the

abdomen and pelvis within 5 days before the procedure. Charlson Comorbidity Index was calculated at the time of the first procedure. The following data were collected: baseline demographics, radiological features of the collections (content, volume, location, wall thickness, CT severity index), and microbiologic culture data.

Procedures

Endoscopic Necrosectomy—All procedures were performed by a single endoscopist using a standardized technique. General anesthesia and carbon dioxide insufflation were used. Linear endoscopic ultrasound with Doppler (GIF UC-240P; Olympus, Tokyo, Japan) was employed to localize the site of WOPN entry and avoid vascular injury. The posterior gastric wall was punctured using a 19-gauge Fine Needle Aspiration (FNA) needle (Cook, Winston-Salem, NC). Walled-off pancreatic necrosis contents were aspirated and sent for Gram stain and culture. Contrast was injected into the cavity, replacing all fluid removed. A 0.035-in ×440 cm guidewire was inserted into the cavity under fluoroscopic visualization. The Fine Needle Aspiration needle was removed. A 4- to 6-mm Hurricane balloon (Boston Scientific, Natick, MA) was inserted over the guidewire with the stiffening stylet in place and dilated until waist obliteration. This was then repeated with an 18-19-20 mm balloon controlled radial expansion (Boston Scientific). No electrocautery was used during WOPN entry. The echoendoscope was then replaced with either a large single-channel or a double-channel endoscope (GIF XTQ-160 or GIF 2T-160; Olympus). The endoscope was advanced into the collection and all fluid in the cavity aspirated. Endoscopic debridement of necrotic tissue was performed during the initial procedure in all cases. Debridement was carried out using Roth nets, large forceps, cold snares, and occasionally hot snares until all removable debris was extracted. Irrigation was performed with 1 to 2 L warmed Bacitracin-saline solution (25,000 units/L). Three 10 French double-pigtail stents (Solus; Cook, Bloomington, IN) were left in place. No nasocystic drains were placed. Follow-up endoscopy was performed for repeat necrosectomy or stent removal as indicated.

Percutaneous Catheter Drainage—Conscious sedation was administered. With the use of cross-sectional imaging to avoid injury to vasculature and organs, a percutaneous needle was placed into the necrotic collection. Fluid was aspirated and sent for Gram stain and culture. The catheter tract was dilated over a 0.035-in guidewire. A drainage catheter (Flexima; Boston Scientific, Natick, MA) was inserted over the guidewire. All liquefied necrotic tissue was aspirated. Irrigation was started the next day with 0.9% saline solution every 4 to 8 hours. The collection was followed with repeat cross-sectional imaging. If collection size was no longer decreasing with irrigation, the drains were repositioned or additional drains were placed at the discretion of the radiologist. Those patients with lack of response to drainage or with clinical signs or symptoms of infection or abdominal pain were taken to surgery at the discretion of the surgical team.

Surgical Necrosectomy—Surgical technique was at the discretion of the attending surgeon and included both open and minimally invasive approaches. In general, the lesser sac was approached through the greater omentum between the stomach and the colon. Adhesions were lysed as necessary. All necrotic material was removed with care to avoid injury to vasculature and adjacent structures. A Jackson-Pratt drain was left in place.

Outcomes

The primary outcome was clinical resolution of symptomatic WOPN after the primary therapeutic modality. Clinical resolution was defined as resolution of primary symptom and absence of abdominal pain, nausea, vomiting, fever, leukocytosis, and sepsis. Secondary outcomes were new-onset organ failure, mortality during the procedure or before clinical resolution, length of stay (LOS), inpatient health care utilization, and development of endocrine or exocrine insufficiency. Organ failure was defined as per the Marshall scoring system used in the Atlanta classification of acute pancreatitis.[17,18] Respiratory failure was present if PO_2/FIO_2 was 300 or lower. Renal failure was present if serum creatinine was 1.9 or higher. Circulatory failure was present if systolic blood pressure was less than 90 mm Hg and unresponsive to fluid administration. Multiorgan failure was present if two or more organ systems were in failure 48 hours or longer. Endocrine insufficiency was defined as need for insulin or antidiabetic medication during the follow-up period. Exocrine insufficiency was defined as a need for pancreatic enzymes during the follow-up period. Procedural complications were defined as bleeding requiring transfusion, capsule perforation, fistula formation, wound infection, air embolism, and venous thromboembolism. Patients who achieved clinical resolution and were asymptomatic were not subjected to repeat cross-sectional imaging.

Health Care Utilization

Charges were used as a proxy. The ratio of charges between groups was calculated to provide a charge-independent metric for differential utilization. Hospital-associated charges were obtained from the Partners Healthcare Finance Department. Professional fees were calculated based on the 2010 Medicare fee schedule for metropolitan Boston. All relevant charges for endoscopic necrosectomy and percutaneous drainage were included. Charges for procedural medications, materials, professional fees, facility fees, anesthesia, imaging, and follow-up endoscopy for stent retrieval were incorporated. Additionally, all charges during inpatient hospitalization were categorized, including room and nursing, ventilation, laboratory studies, physical therapy, occupational therapy, speech therapy, cardiology, hemodialysis, radiology (other than the percutaneous drainage procedure), endoscopy (other than endoscopic necrosectomy), pathology, blood bank, nutrition, and medications.

Statistics

Statistics are reported as mean ± standard error. Student *t* test was used to compare means and the Fisher exact test was used to compare proportions. *P* values 0.05 or lower were considered significant. The statistical analyses were performed using Statistical Analysis Software 9.3 (SAS Institute, SAS, Arlington, VA).

RESULTS

There was no significant difference in baseline characteristics between the DEN and step-up cohorts as summarized in Table 1. Patients commonly had alcohol-induced and gallstone-induced pancreatitis. Illness severity was similar between groups. No patient in the DEN group was in organ fa6ilure before primary therapy; one patient undergoing the step-up

approach was in renal failure. Imaging characteristics, including CT severity index, were similar between groups.

Primary modality results are listed inTable 2. Direct endoscopic necrosectomy patients each underwent 1.4 ± 0.2 necrosectomies. Percutaneous catheter drainage patients underwent significantly more procedures (2.0 ± 0.2 catheter placements, $P = 0.015$). Procedural complications occurred in 1 of 12 after DEN (bleeding) versus 1 of 12 after PCD (wound infection). Clinical resolution occurred in 11 of 12 DEN patients with DEN alone versus 3 of 12 step-up approach patients after PCD ($P = 0.0028$). During the postprocedure course, significantly fewer patients in the DEN group required intravenous (IV) antibiotics ($P = 0.003$). In addition, intensive care unit (ICU) LOS was significantly shorter ($P = 0.04$). One patient in the step-up group died with pulseless electrical activity arrest 28 days after PCD. This patient was on a non-ICU floor receiving IV antibiotics, but not vasopressors or total parenteral nutrition (TPN), and did not have organ failure.

Secondary modality results are listed in Table 3. One DEN patient of 12 patients proceeded to PCD (after 26 weeks). The procedure was required because of a persistent collection that was not endoscopically accessible, with evidence of infection. No complications occurred. Nine of 12 patients in the step-up approach group proceeded to minimally invasive surgical necrosectomy after 3.4 ± 0.9 weeks for persistent signs or symptoms of infection; each had one surgical intervention. Collections were culture-positive in 6 of 9 patients. Seven of the 9 patients undergoing surgical necrosectomy experienced a total of 8 complications, with 6 patients experiencing bleeding requiring transfusion and 1 developing both wound infection and enterocutaneous fistula. In the DEN group, PCD placement resulted in clinical resolution. In the step-up approach, all 9 patients undergoing surgical necrosectomy achieved resolution after one procedure. During the postprocedure course, all 9 patients in the step-up approach group required IV antibiotics, and most had organ failure (2 patients remained in organ failure; 3 developed new organ failure). There was no additional mortality.

The overall outcome of DEN and the step-up approach are listed in Table 4. Direct endoscopic necrosectomy required fewer procedures to achieve clinical resolution ($P = 0.0006$). Complications occurred in 1 of 12 patients in the DEN group versus 7 of 12 patients completing the step-up approach ($P = 0.027$). Direct endoscopic necrosectomy resulted in less new IV antibiotic use, less pulmonary failure, and shorter ICU and floor LOS ($P < 0.05$). All surviving patients had documented outpatient follow-up with similar duration between groups. Direct endoscopic necrosectomy also resulted in a lower rate of new endocrine insufficiency ($P = 0.01$).

A total of 12,882 charges were individually categorized across both cohorts (Table 5). Total charge for the primary modality until resolution or need for secondary modality was significantly lower after DEN ($P = 0.015$). Charges for the secondary modality were also lower in the DEN group. Charges for related outpatient procedures, including radiology and endoscopy for stent removal, were higher in the DEN group. Only 1 patient in the step-up approach needed imaging after discharge. Nevertheless, total charges were significantly lower after DEN by a ratio of 5.2:1 ($P = 0.0003$). The primary factors resulting in higher

utilization in the step-up approach were ICU and room charges, ventilation, antibiotics, radiology, TPN, blood transfusion, and albumin.

DISCUSSION

This study suggests that DEN may be superior to the step-up approach for management of WOPN with suspected or established infection. Clinical resolution after DEN in this study was 92% versus 25% after initial PCD ($P = 0.003$), with 75% of step-up patients requiring surgical intervention. These resolution and surgical intervention rates are consistent with published randomized trials.[9,15]

After the primary intervention, three patients in the step-up approach developed organ failure compared to none in the DEN group. After the second intervention, an additional 2 patients in the step-up approach developed organ failure. Additionally, patients in the step-up approach required significantly more TPN, IV antibiotics, ICU care, and floor care, especially when surgical intervention was taken into account. Given the higher rates of postprocedural morbidity and organ failure in the step-up pathway, it follows that step-up therapy was associated with greater health care utilization by a ratio of 5.2:1. These findings are consistent with the PANTER trial, in which a majority of patients proceeded to surgical necrosectomy after ineffective PCD.

In this study, primary PCD likely delayed definitive therapy with subsequent negative consequences, including evidence of persistent culture-positive infection in the majority of patients undergoing secondary surgical intervention, significantly higher rate of IV antibiotic use, and longer ICU LOS. Additionally, once definitive surgical therapy was performed, most patients experienced organ failure, which added to both LOS and utilization. Conversely, early and safe definitive therapy with DEN resulted in less organ failure and sepsis, and shorter LOS, avoiding the high cost of ICU care. Additionally, DEN appears to shift utilization to the outpatient setting, resulting in lower aggregate utilization.

This study had notable strengths. Clinical outcomes were consistent with published randomized trials. Unlike prior trials, the primary and secondary modalities were examined independently, allowing distinct characterization of outcome and utilization between PCD and surgical necrosectomy. Additionally, the number of charges categorized was both large and comprehensive and provided insight into which specific elements of care were most highly utilized. There were, however, limitations. Patients managed on the surgical service were more likely to enter the step-up pathway, whereas patients managed on the medical service were more likely to undergo DEN as initial management. This may have reflected potential referral bias. Although randomization could address this limitation, randomizing patients with WOPN to the step-up approach may not be appropriate given the published high effectiveness and low morbidity of DEN.[15,16] Randomized trials currently in progress should report outcomes after each therapeutic modality and health care utilization data. The cost of long-term complications, such as endocrine and exocrine insufficiencies after necrosectomy, was also not evaluated in this study. However, this would likely have amplified the observed utilization differences between DEN and the step-up approach. Additionally, charges were assumed to be proportional to health care utilization; however,

the same charge scale was applied to both groups, allowing direct and comprehensive comparison of utilization. Finally, only direct hospital charges were measured; loss of the ability to perform daily activities and time lost from work are major personal and societal costs that were not captured.

In summary, direct endoscopic necrosectomy may be superior to the step-up approach for primary management of patients with symptomatic WOPN. Given higher efficacy, lower morbidity, shorter LOS, and lower health care utilization, DEN could be the first-line therapeutic modality. The step-up approach using initial PCD remains useful in patients with immature necrotic collections, or collections that are inaccessible by DEN.

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TABLE 1

Baseline Characteristics

	DEN (n = 12)	SUA (n = 12)
Patient Characteristics		
Sex	8 M/4 F	9 M/3 F
Age	58.9 ± 3.9	53.3 ± 3.0
BMI	27.0 ± 1.4	29.5 ± 2.2
Endocrine insufficiency	3	1
Exocrine insufficiency	1	0
Etiology of pancreatitis		
Alcohol	3	3
Gallstone	7	5
Hypertriglyceridemia	0	1
Post-endoscopic retrograde cholangiopancreatography	0	1
Unknown	2	2
Illness Severity		
Charlson comorbidity	2.5 ± 0.7	2.3 ± 0.4
APACHE II	10.1 ± 1.1	9.4 ± 1.2
Serum albumin, mg/dL	3.1 ± 0.2	2.7 ± 0.2
TPN use	3	2
White blood cells, thousands/μL	10.3 ± 1.8	12.2 ± 1.1
Positive blood culture	1	1
IV antibiotic use	9	11
Vasopressor use	0	0
Organ failure	0	1 (renal)
Multiple organ failure	0	0
Radiological Characteristics		
Collection size, mL	1306 ± 508	1354 ± 449
CT severity index	8.3 ± 0.8	7.8 ± 0.8
Encapsulation		
Good	7	6
Fair	5	6
Septations		
None	9	9
Few	3	1
Many	0	2
Air in collection	3	3

$P < 0.05$ for difference between DEN and SUA.
ERCP indicates endoscopic retrograde cholangiopancreatography.

TABLE 2

Primary Modality Results

Procedural Experience				
	DEN (n = 12)		**SUA (n = 12)**	
Time from onset to initial procedure, wk	7.2 ± 1.8		5.2 ± 1.0	
Procedures per patient *	1.4 ± 0.2 DEN		2.0 ± 0.2 PCD	
Fluid culture positive	8		6	
Postprocedure Experience				
	Before	**After †**	**Before**	**After †**
TPN	3	0	2	3
IV antibiotic use ‡	9	3 §	11	11
Vasopressor use	0	0	0	1
Organ failure	0	0	1	2
Pulmonary	0	0	0	2
Circulatory	0	0	0	1
Renal	0	0	1	1
Multiple organ failure	0	0	0	1
ICU LOS, days *	0.2		5.4 ± 2.5	
Floor LOS, days	5.0 ± 1.4		11.6 ± 3.4	
Clinical resolution ‡	11/12		3/12	
Mortality	0/12		1/12	

* $P < 0.05$ for difference between DEN and SUA.

† Versus baseline.

‡ $P < 0.01$ for difference between DEN and SUA.

§ If significant change versus baseline.

NC indicates no change.

TABLE 3

Secondary Modality Results*

Procedural Experience				
	DEN (n = 1)		SUA (n = 9)	
Timing from onset to secondary procedure (weeks after primary)	26.3		3.4 ± 0.9	
Procedures per patient	1.0 PCD		1.0 surgery†	
Positive fluid culture	1		6	
Complications	0		8	
Postprocedure Experience				
	Before	**After‡**	**Before**	**After‡**
TPN	0	0	3	5
IV antibiotic use	0	0	9	9
Vasopressor use	0	0	1	1
Organ failure	0	0	2	5
Pulmonary	0	0	2	5
Circulatory	0	0	1	1
Renal	0	0	1	1
Multiple organ failure	0	0	1	1
ICU LOS, days	0		10.3 ± 3.9	
Floor LOS, days	3.0		18.9 ± 5.8	
Clinical resolution	1		9	
Mortality	0		0	

*P value not calculated for SUA versus DEN as n = 1 in DEN group.

†Nine patients had one surgical necrosectomy each.

‡Versus primary modality.

TABLE 4

Overall Procedural Experience

Procedural Experience				
	DEN (n = 12)		SUA (n = 12)	
Total procedures *	1.5 ± 0.3		2.8 ± 0.2	
Positive fluid culture	8		8	
Complications †	1		8	
Postprocedure Experience				
	Before	After ‡	Before	After ‡
TPN §	3	0	2	6
Positive blood culture	1	1	1	0
IV antibiotic use *	9	3 ‖	11	12
Vasopressor use	0	0	0	2
Organ failure	0	0	1	5
Pulmonary §	0	0	0	5
Circulatory	0	0	0	1
Renal	0	0	1	1
Multiple organ failure	0	0	0	1
ICU LOS, days §	0.2		11.9 ± 4.6	
Floor LOS, days §	5.3 ± 1.4		23.6 ± 6.5	
Clinical resolution	12		11	
Mortality	0		1	
Outpatient Experience ¶				
Follow-up duration, y	1.9 ± 0.3		2.5 ± 0.8	
New endocrine insufficiency †	0		7	
New exocrine insufficiency	3		5	
Mortality	0		0	

* $P < 0.001$ for difference between DEN and SUA.

† $P < 0.01$ for difference between DEN and SUA.

‡ Versus baseline.

§ $P < 0.05$ for difference between DEN and SUA.

‖ If significant change versus baseline.

¶ n indicates 11 in the SUA group.

TABLE 5

Categorized Charges (USD)

	Primary Modality		
	DEN (n = 12)	**SUA (n = 12)**	**SUA:DEN ratio**
Procedure professional *	1511 ± 225	2194 ± 203	1.4:1
Theatre, instruments, recovery	8830 ± 1435	7945 ± 1927	0.9:1
Anesthesia	459 ± 353	828 ± 128	1.8:1
ICU and ventilation †	650	36,225 ± 15,896	55.7:1
Floor and nursing	13,774 ± 4365	27,911 ± 7860	2.0:1
Radiology ‡§	2861 ± 1303	16,761 ± 3666	5.9:1
Labs, pathology *	3494 ± 950	19,738 ± 3797	5.6:1
Pharmacy *	1160 ± 514	12,199 ± 2647	10.5:1
Blood bank †	275 ± 139	4791 ± 1982	17.4:1
Nutrition †	100 ± 87	2957 ± 1248	29.6:1
Physical, speech therapy †	58 ± 39	871 ± 294	15.0:1
Hemodialysis	0	1173 ± 1109	—
Cardiology	0	785 ± 431	—
Endoscopy ‖	0	420 ± 243	—
Total †	33,172 ± 7268	134,796 ± 26,312	4.1:1
	Secondary Modality ¶		
	DEN (n = 1)	**SUA (n = 9)**	
Procedure professional	1053	2882	
Theatre, instruments, recovery	2118	23,874 ± 3205	
Anesthesia	235	4419 ± 940	
ICU and ventilation	0	62,439 ± 18,241	
Floor and nursing	5553	39,973 ± 8266	
Radiology §	0	14,248 ± 3207	
Labs, pathology	1945	30,572 ± 5574	
Pharmacy	953	22,439 ± 3681	
Blood bank	0	5682 ± 1463	
Nutrition	0	5534 ± 1524	
Physical, speech therapy	0	2139 ± 555	
Hemodialysis	0	0	
Cardiology	0	541 ± 555	
Endoscopy ‖	0	0	
Total	11,857 §	214,489 ± 36,670 †	
	Total Charges		

	DEN (n = 12)	SUA (n = 12)	SUA:DEN Ratio
Procedure professional	1607 ± 308	4352 ± 494	2.7:1
Theatre, instruments, recovery†	8830 ± 1435	23,552 ± 4574	2.7:1
Anesthesia‡	481 ± 351	4308 ± 959	9.0:1
ICU and ventilation†	650	72,699 ± 27,500	>100:1
Floor and nursing‡	14,279 ± 4233	63,473 ± 10,941	4.4:1
Radiology*§	2861 ± 1303	24,746 ± 5261	8.6:1
Labs, pathology*	3671 ± 909	38,910 ± 6966	10.6:1
Pharmacy*	1247 ± 502	25,037 ± 5554	20.1:1
Blood bank*	275 ± 139	9751 ± 2172	35.4:1
Nutrition‡	100 ± 87	6262 ± 2324	62.3:1
Physical, speech therapy*	58 ± 39	2122 ± 633	36.6:1
Hemodialysis	0	1173 ± 1109	—
Cardiology†	0	1084 ± 554	—
Endoscopy‖	0	458 ± 240	—
Inpatient total*	34,023 ± 6910	282,364 ± 52,821	8.3:1
Outpatient	22,769 ± 14,002	208#	<1:100
Total*	53,956 ± 17,392	282,572 ± 52,821	5.2:1

*$P < 0.001$ for difference between DEN and SUA.

†$P < 0.05$ for difference between DEN and SUA.

‡$P < 0.01$ for difference between DEN and SUA.

§Radiology charges do not include fees related to percutaneous catheter drainage.

‖Endoscopy charges do not include fees related to endoscopic necrosectomy.

¶P value not calculated as n indicates 1 in DEN group.

#$n = 11$.