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What Do Our Patients Really Know About Dialysis and End Stage Kidney Disease

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University of Nebraska Medical Center

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What Do Our Patients Really Know About Dialysis and End Stage Kidney Disease

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Up-Regulation of Tumor Suppressor MicroRNA LET-7 in Inflammatory Bowel Disease is a Novel Molecular Marker for Induction of Disease Remission

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Mentor: Peter Mannon

Program: Internal Medicine

Type: Original Research

Background: Precise molecular signatures of successful inflammatory bowel disease (IBD) treatment response would help establish benchmarks for and reveal critical components of inflammation control. We assessed let-7 microRNA (miRNA) up-regulation as a molecular marker for successful induction of disease remission, using it to map the transcriptional dynamics of IBD-associated cytokines. We postulate that refractoriness to therapy, including anti-tumor necrosis factor α (anti-TNF α) drugs, in certain patients may be due to inability to express let-7 miRNAs following lowered serum TNF α levels.

Methods: RNA-Seq library of colonic biopsies (n=51, ulcerative colitis, n=28, Crohn's disease) was aligned in a descending order of linked serum TNF α concentrations. Active/inactive disease states were defined using SCCAI or HB scores. Serum cytokines were measured using a multiplex assay.

Results: Serum inflammatory cytokine levels (IFN γ , IL-18, TNF α) were inversely related to let-7 miRNA expression but TNF α levels were not significantly different among groups. Among active IBD patients with serum-TNF α <15pg/ml, only 40% exhibited let-7 miRNA up-regulation. Multi-dimensional scaling analysis of genome-wide expression profiles revealed a striking transitional linkage pattern between this group and the inactive IBD group within the principal component space, supportive of an association of let-7 miRNA up-regulation with successful induction of remission (Figure 1).

Conclusion: We believe let-7 miRNA up-regulation may be an important molecular marker to predict movement toward inflammation control in active IBD patients undergoing treatment. The heterogeneity of let-7 miRNA expression is consistent with the unpredictable response to current IBD treatments and restoring its expression might confer the anti-inflammatory effects it shows in murine colitis and in vitro models.

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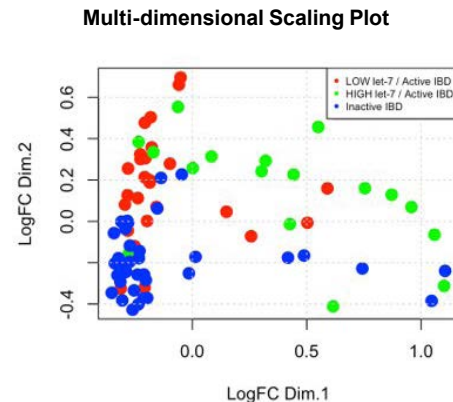


Figure 1. Principle component analysis of whole genome RNA profiles in active IBD with “high” let-7 and “low” let-7, and inactive IBD patient groups. The “high” group is in green and “low” group is in red. All inactive IBD patients are labeled blue. A striking transitional linkage pattern between let-7 expressing active IBD group (green) and inactive IBD group (blue) within the principal component space is present, supportive of an association of let-7 miRNA up-regulation with successful induction of remission.

Comparison of Outcomes for Patients Admitted from the Emergency Department with Focal vs Multifocal Pneumonia

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Mentor: Aaron Barksdale

Program: Emergency Medicine

Type: Original Research

Background: There is a paucity of research analyzing the outcome differences between community acquired multifocal vs focal pneumonia in patients admitted from the emergency department (ED). We aimed to discover in-hospital patient mortality and morbidity outcome differences when comparing focal vs multifocal pneumonia. A secondary objective investigated other commonly assessed factors that may also contribute to these outcomes.

Methods: A retrospective chart review at a single urban academic medical center.

ED admission patients between 9/1/2012 to 2/29/2020 diagnosed with community acquired pneumonia were included. Outcomes included death at discharge, hospital length of stay (LOS), ICU admission, mechanical ventilation, and ventilation days. Models included: age, race, gender, structural lung disease, abnormal labs (WBC>12, Procalcitonin >2, Lactic acid >2), and abnormal vital signs. P-value of < 0.05 was considered statistically significant.

Results: A total of 2610 subjects were included (1368 focal, 1242 multifocal). There was a significant difference in multifocal pneumonia for in-hospital death (7.9% vs 3.3%, p< 0.0001), ICU admission (24.4% vs 16.7%, p< 0.0001), mechanical ventilation (13.8% vs 6.7%, p< 0.0001), and median LOS

(4 vs 3 days, p< 0.0001). A subset of 1730 subjects with complete data were included in multivariate analysis. Multifocal pneumonia was 1.99 (p=0.0007) times the odds of in-hospital death. Increased age, elevated lactate, elevated procalcitonin, and increased respiratory rate were also statistically significant for in-hospital death.

Conclusion: Multifocal pneumonia had nearly double the in-hospital mortality rate, increased LOS, and ventilator requirement compared to focal pneumonia. Elevated lactate, procalcitonin, age, and respiratory rate are also independently associated with in-hospital death.

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Outcomes in Intravenous to Oral Antimicrobial Therapy in Beta-Hemolytic Streptococcus Species

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Mentor: Jasmine R. Marcelin

Program: Infectious Disease

Type: Original Research

Background: Uncomplicated bloodstream infections (uBSI) often receive prolonged courses of intravenous (IV) antibiotics, increasing risk for catheter-associated complications and hospitalization costs. β -hemolytic Streptococcus spp. BSI are common and have reliable susceptibility to oral antibiotics. Clinically improving patients without persistent BSI and controlled source of infection are candidates for oral antimicrobial therapy (OAT) but despite anecdotal practice, there are few studies affirming this practice in gram-positive uBSI. We evaluated IV to OAT transitions for treating β -hemolytic streptococcal uBSI.

Methods: This retrospective cohort study included adult patients hospitalized 1/1/2013 - 12/31/2019 diagnosed with β -hemolytic Streptococcus uBSI. Patients with complicated source of BSI were excluded. We compared outcomes in patients treated with IV only to those transitioned to OAT including: 30-day mortality, antimicrobial therapy, length of stay (LOS), BSI relapse, 30-day rehospitalization, and adverse drug events. Fisher's exact test was used for categorical variables; Mann-Whitney test and independent t-test for continuous variables.

Results: A total of 238 Streptococcus BSI were included (83 excluded as complicated, pediatric, or outpatient). OAT was used in 153

Table 1. Demographics and outcomes comparing IV only and OAT cohorts.

	IV only	IV to OAT	IV only	IV to OAT
Demographics				
Gender*				
Female	28/89 (33%)	74/153 (48%)		
Male	57/89 (67%)	79/153 (52%)		
Race				
Native American	2/89 (2%)	3/153 (2%)		
Asian	0/89	1/153 (1%)		
Black	12/89 (14%)	19/153 (12%)		
White	66/89 (78%)	122/153 (80%)		
Hispanic	5/89 (6%)	7/153 (5%)		
Unknown	0/89	1/153 (1%)		
Insurance				
Private	16/89 (20%)	24/153 (16%)		
Medicare	45/89 (55%)	98/153 (64%)		
Medicaid	10/89 (12%)	10/153 (11%)		
Self-pay	11/89 (13%)	13/153 (9%)		
Age (Years)				
Median (IQR)	62 (23)	65 (25)		
Mean	59.8	61.2		
		p=0.278		
Pitt Bacteremia Score				
Median (IQR)	3(3)	1(1)		p<0.0001
Outcomes				
30-day mortality				
	11/89 (13%)	3/153 (2%)		p=0.0009
Recurrence of infection				
	1/89 (1%)	9/153 (6%)		p=0.17
30-day rehospitalization				
	19/89 (24%)	30/153 (20%)		p=0.50
Length of stay (Days)				
Median (IQR)	7.5 (10.5)	5(4)		
Mean	12.3	6.5		
		p<0.0001		

IV= intravenous, OAT= oral antimicrobial therapy, IQR= interquartile range

*No patients identified as non-binary in this study

(64%). Cohort demographics were similar (Table 1). LOS was shortened in OAT cohort with median of 5 (interquartile range 4) vs. 7.5 (10.5) (p<0.0001). Patients transitioned to OAT finished antibiotic course outpatient more frequently (93 vs. 61% p<0.001). Thirty-day mortality was decreased in OAT cohort (2% vs. 13% p<0.0001). Adverse events were not statistically different.

Conclusion: Opportunities exist to modify management of uBSI. For β -hemolytic Streptococcus uBSI, OAT was associated with decreased length of stay without adverse clinical outcomes.

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Clinically Significant Hypotension in Patients Undergoing Thoracoscopic Lobectomy: A Single-center, Retrospective Analysis of Thoracic Epidural Analgesia Versus Liposomal Bupivacaine Intercostal Nerve Blockade

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Mentor: Karin Trujillo

Program: General Surgery

Type: Original Research

Background: Minimally invasive video-assisted thoracoscopic surgery (VATS) is the standard of care for early-stage lung cancers.

Thoracic epidural analgesia (TEA) is the gold standard for postoperative analgesia, although the associated sympathetic blockade can elicit hypotension requiring intervention. Liposomal bupivacaine intercostal nerve blockade (ICNB) has been utilized as a viable alternative with fewer side effects including hypotension. However, its impact on the

frequency of interventions is not known. Our objective was identifying the incidence of postoperative hypotension and quantify the interventions between ICNB and TEA in patients undergoing VATS lobectomy for malignancy.

*Names in bold type indicate presenting author.

Methods: Patients who underwent VATS lobectomy for malignancy at a single institution between 2018-2021 were reviewed. Those with a history of chronic opioid use, previous thoracic surgery, history of atrial fibrillation, and congestive heart failure were excluded. The primary outcome was episodes of clinically significant hypotension (systolic blood pressure <90mmHg) requiring intervention.

Results: A total of 155 patients were identified, 110 (71%) receiving TEA and 45 (29%) receiving ICNB. There were no demographic differences between the groups. Overall, 30% of patients in the TEA group had at least one clinically significant episode requiring intervention compared to 9% for ICNB (p=0.005). The most common interventions are shown in Table 1. There was no difference in average oral morphine

Table 1. Interventions performed for clinically significant hypotensive episodes

	LB group (n=4)	TEA group (n=33)
Intravenous fluid bolus		
1 episode	0	15
2 episodes	3	6
3 episodes	0	4
4+ episodes	1	3
Vasopressor initiation	0	17
Change in epidural concentration		1
Change in epidural rate		7
Premature discontinuation of epidural		1

milligram equivalents between the groups, although patients in the ICNB group utilized more non-opioid adjuncts.

Conclusion: Hypotension requiring intervention that is associated with thoracic epidurals should warrant consideration

of local anesthetic blockade to streamline postoperative management and utilize fewer hospital resources for equivalent postoperative analgesia.

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Predictors of Trauma Patients Leaving Against Medical Advice

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Mentor: W. T. Hillman Terzian

Program: General Surgery

Type: Original Research

Background: Discharge against medical advice (AMA) affects 1-2% of hospital admissions. We aimed to assess risk factors for AMA discharge within the University of Nebraska Medical Center population.

Methods: We performed a retrospective audit of our level 1 trauma center database between 2015 and 2021. We collected patient demographics and other information on their hospitalization. We performed a binary logistic regression to assess whether risk factors commonly cited in literature for leaving AMA—such as gender, race, age, self-

pay, alcohol and drug use, ISS, and trauma mechanism—were predictive of leaving AMA. We created a heat map based on patient zip codes to assess if patients coming from specific areas were more likely to leave AMA.

Results: We identified 18,850 patients. On analysis, when controlling for gender and race, we found that the commonly cited risk factors for leaving AMA were not risk factors in our population. Our heat map showed that the highest-concentrated area of patients leaving AMA came from a socially disparate population-dense area of Northeast Omaha that is also the only part of the county with limited health-care facilities (Figure 1).

Conclusion: Risk factors traditionally associated with leaving AMA were not significant risk factors in our trauma

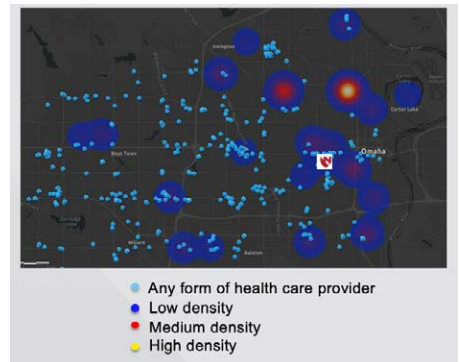


Figure 1: Heat map demonstrating the zip codes in Omaha with the highest percentage of AMA discharges plotted with locations of currently existing health care facilities of any type.

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Analyzing Predictive Factors for Pathologic Complete Response for Locally Advanced Rectal Cancer

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Mentor: Sean Langenfeld

Program: General Surgery

Type: Original Research

Background: Neoadjuvant chemoradiation (NACRT) is the standard of care for locally advanced rectal cancers with a significant

number of patients achieving a complete pathologic response (pCR) on final pathology ranging from 10-30%. However, these previous studies mostly comprise single-institution reports and have conflicting results. This study's purpose was to analyze the association between patient characteristics, tumor characteristics, and rates of pCR.

Methods: The National Surgical Quality Improvement Program proctectomy-targeted database was utilized to identify all patients from 2016-2020 who underwent NACRT followed by proctectomy with curative intent for T3-4N0-2 rectal cancers. The independent samples t-test, Wilcoxon Rank Sum test, Chi-Square, and Fischer's exact test were used for comparative analysis.

Results: Out of the total 2,777 patients, 330 (11.9%) demonstrated pCR on final pathology. Pretreatment N0 staging was associated with a higher rate of pCR (17.3%) when compared to N1 (5.4%, OR 3.647, 95% CI 2.661-4.998, $p < 0.001$) and N2 (6.4%, OR 3.059, 95% CI 1.980-4.725, $p < 0.001$). Patients clinically staged at T3N0 had the greatest percentage of patients with no residual tumor (17.8%), followed by T4N0 (14.2%), which was a higher response rate than T3N1 and T3N2 patients (5.6% and 6.8%, respectively) (Table 1). Gender, age, race, weight and smoking status did not impact rates of pCR. Tumor height was also not predictive of pCR.

Conclusion: Pretreatment nodal staging is an important predictive factor for pathologic complete response following neoadjuvant chemoradiation treatment. pCR rates did not appear to be associated with tumor location, patient demographics, or pretreatment medical diagnoses.

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Table 1. Complete Pathologic Response Rates by TN Staging.

pCR Rates by TN Staging				
Pretreatment TN Stage		Pathologic Complete Response		
Frequency	Row Pct	Yes	No	Total
T3	N0	226 (17.8%)	1043 (82.2%)	1269
T3	N1	45 (5.6%)	756 (94.4%)	801
T3	N2	21 (6.8%)	290 (93.2%)	311
T4	N0	30 (14.2%)	181 (85.8%)	211
T4	N1	5 (4.1%)	116 (95.9%)	121
T4	N2	3 (4.7%)	61 (93.3%)	64
Total		330 (11.9%)	2447 (88.1%)	2777

Incidence and Outcomes of Acute Appendicitis during the COVID-19 Pandemic

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Mentor: Aaron Barksdale

Program: Emergency Medicine

Type: Original Research

Background: Prior research described links between COVID-19 and myocardial injury, venous thromboembolism, and acute kidney injury, but a paucity of literature investigating correlations between COVID-19 and surgical emergencies, specifically appendicitis. We hypothesized a difference in outcomes and complications in COVID-19 infected patients with acute appendicitis. The objective of this study was to compare the incidence and outcomes of appendicitis in patients with and without SARS-CoV-2 infection.

Methods: Retrospective chart review at an academic medical center, with approximately

64,000 annual Emergency Department (ED) visits. Adults with appendicitis and COVID-19 infection between 4/01/2020-2/28/2022 were included. A random convenience sample of non-COVID-19 infected subjects and appendicitis was included. Outcome measures included perforation, post-operative infection, ED length of stay (LOS), ED presentation to initiation of surgery (time), ICU admission, hospital LOS, and return ED visits. Mean and median described age and LOS. Fisher's exact test compared associations between patient characteristics/outcomes with COVID status. Wilcoxon rank sum compared age and LOS with COVID status. P-value < 0.05 was considered statistically significant.

Results: A total of 210 patients (22 COVID/188 non-COVID) were included, with no

difference between age, gender, or race. A statistically significant increase was observed in median ED LOS in COVID-19 positive patients (7.5 vs. 5.0 hours, $p=0.0031$), but none between groups regarding perforation, post-operative infection, ICU admission, hospital LOS, or ED return visits was observed.

Conclusion: There was no statistically significant difference in appendicitis outcome measures in COVID-19 patients apart from ED LOS. Additionally, there was no increased incidence of perforation, ICU admission, or post-operative infections.

<https://doi.org/10.32873/unmc.dc.gmerj.5.1.014>

What Do Our Patients Really Know About Dialysis and End Stage Kidney Disease

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Mentors: Jay Hawkins, Jonathan Hall, Felipe Naranjo

Program: Internal Medicine

Type: Original Research

Background: As part of dialysis cares, dialysis patients receive education on dialysis and how they can impact their own health. Despite efforts at education, patients experience problems related to electrolytes and volume management. This raises the question, "how successful are current

education strategies and how can they be further improved?" With the numerous dialysis patients in the United States, education is an important avenue for many patients care.

Methods: Patients at the Center Street Fresenius Dialysis Center were surveyed on

their knowledge and satisfaction with dialysis cares as well as preferred learning modalities. The survey included 29 multiple choices, yes/no, Likert Scale, and free response questions. Surveys were administered in English and Spanish. Assistance completing the survey was provided to consenting patients with visual impairment or other barrier to independent completion.

Results: Twenty-five of 40 patients completed the survey including 4 partial

responses. Seven questions exhibited a correct response rate of less than 60%. These questions pertained to anemia, volume overload, constipation medications, and how both the kidney and dialysis contribute to patients' health.

Conclusion: This survey identified several opportunities for improved patient education. Based on survey responses, educational pamphlets and videos are being created and disseminated to patients with the intention of

repeating surveys thereafter. If educational material improves patient knowledge, further investigation into its impact on outcome measures – interdialytic weight gain and serum phosphorous levels – ought to be pursued. Since dialysis education ought to be standardized across centers, interventions resulting in improvement in patient knowledge may be transferable to other centers.

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Standardized Approach to Managing Adhesive Small Bowel Obstructions Reduces Hospital Length of Stay on the Emergency General Surgery Service

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Mentor: W. T. Hillman Terzian

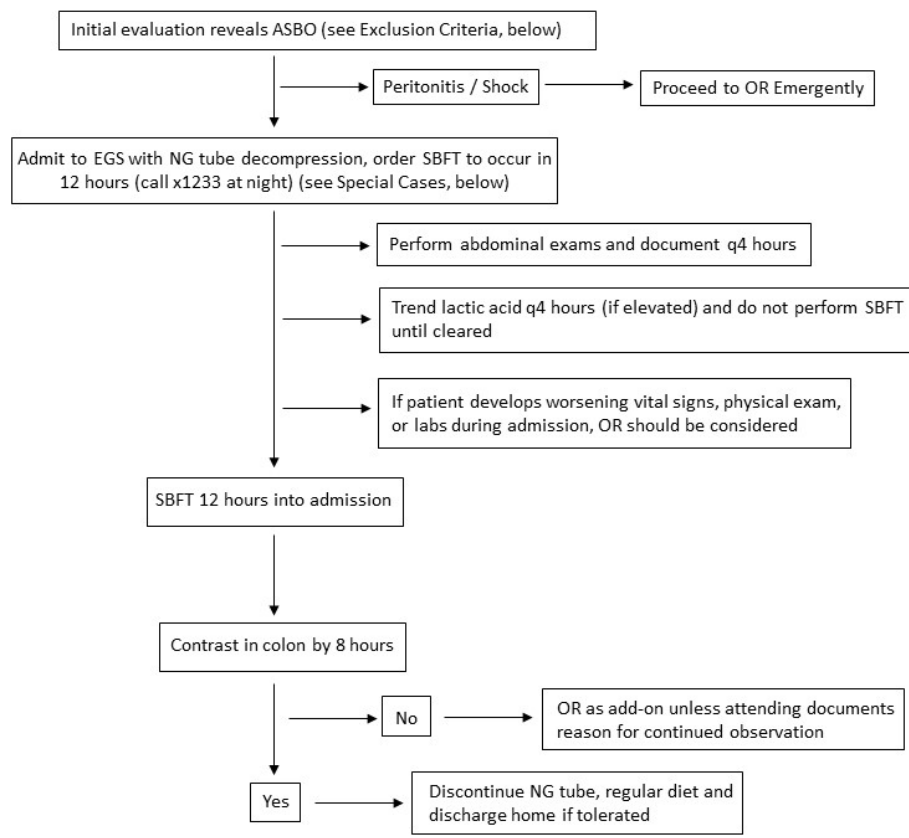
Program: General Surgery

Type: Original Research

Background: The water-soluble contrast challenge (WSCC) has become the standard approach for differentiating operative from non-operative adhesive small bowel obstructions (ASBOs). An ingestible radiopaque contrast medium is followed by serial abdominal radiographs. Although well-described in theory, there are no resources available to guide administration of the WSCC, and management of ASBOs is usually dictated by individual surgeon practice. We hypothesized that a standardized approach to the WSCC would decrease hospital length of stay (LOS) and improve resource utilization.

Methods: We developed an evidence-based pathway for managing ASBOs (Figure 1) on our emergency general surgery (EGS) service at UNMC. Inclusion criteria was patients admitted with a presumed ASBO. Exclusion criteria was built into the pathway and included patients presenting within six weeks of abdominal surgery and specific medical or surgical conditions. We retrospectively compared hospital LOS for patients admitted two years prior to implementation of our pathway (PRE) vs patients admitted for six months after implementation of the pathway (POST). Comparison of proportions was calculated using χ^2 test.

Results: A total of 153 patients were included (120 in the PRE group, 33 in the POST group). The mean LOS was 4.7 days in the PRE group vs 2.7 days in the POST group ($p = 0.02$), a reduction in LOS by two days.



Exclusion Criteria – do not use this pathway if any of the following apply:

- Recent abdominal surgery (within six weeks)
- History of gastric bypass (admit to MIS)
- History of Crohn's / Ulcerative colitis (admit to colorectal)
- Large bowel obstruction or evidence of carcinomatosis
- Obstruction itself is directly caused by hernia of any kind
- Patient actively followed by surgical oncology or on chemoradiation (admit to surgical oncology)

Special Cases – if any of the following apply, discuss with attending before proceeding down pathway:

- Worrisome findings on imaging or labs—including, but not limited to, the following: closed-loop obstruction, high-grade obstruction, "whirl sign," mesenteric twisting, stranding, or thickening, poor or absent bowel wall enhancement, pneumatosis, portal venous gas, free fluid, lactic acidosis, leukocytosis, electrolyte abnormalities
- Obliterative peritonitis ("hostile abdomen") with known dense adhesions
- Virgin abdomen (carries 10% chance of occult malignancy causing obstruction despite CT scan report)

Figure 1. UNMC – Emergency General Surgery (EGS) Adhesive Small Bowel Obstruction (ASBO) Management Pathway.