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Timing and Outcomes of Abdominal Surgery in Neutropenic Patients

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Abstract

Background Surgery in neutropenic patients is challenging due to both atypical manifestations of common conditions and higher perioperative risk. We sought to describe the outcomes of neutropenic patients undergoing abdominal surgery and to identify factors contributing to morbidity and mortality.

Methods A retrospective chart review was performed for all patients neutropenic in the 24-hours prior to an abdominal operation at our institution between 1998 and 2017. The primary and secondary outcomes were 30-day mortality and morbidity, respectively. The chi-square test and two-tailed Student's *t* test were used for univariable comparisons (non-parametric tests used when appropriate). To determine the optimal threshold of absolute neutrophil count (ANC) to discriminate 30-day mortality, we maximized the Youden index (*J*).

Results Amongst 237 patients, mortality was 11.8% (28/237) and morbidity 54.5% (130/237). Absolute neutrophil count < 500 cells/μL (50% vs. 20.6%, $P < 0.01$) and perforated viscus (35.7% vs. 14.8%, $P = 0.01$) were associated with mortality. Perforated viscus (25.4% vs. 7.5%) was also associated with morbidity. Urgent operations were associated with higher morbidity (63.6% vs 34.7%, $P < 0.001$) and mortality (16.4% vs 1.4%, $P = 0.002$) when compared to elective operations. Transfer from an outside hospital (22.3% vs. 11.2%, $P = 0.02$) and longer median time from admission to operation (2 days (IQR 0–6) vs. 1 day (IQR 0–3), $P < 0.01$) were associated with morbidity. An ANC threshold of 350 provided the best discrimination for mortality.

Conclusions Elective surgery in the appropriately chosen neutropenic patient is relatively safe. For patients with obvious surgical pathology, we advocate for earlier operation and a lower threshold for surgical consultation in an effort expedite the diagnosis and necessary treatment.

Keywords General surgery · Neutropenia · Outcomes research

Introduction

Neutropenia, generally defined as an absolute neutrophil count (ANC) of less than 1500 cells/μL, is uncommon in the general population but may be caused by a variety of factors in hospitalized patients including chemotherapy, lymphoproliferative disorders, idiosyncratic drug reactions, immunodeficiency and autoimmune syndromes, and sepsis.[1–3] Chemotherapy-associated neutropenia is more common amongst oncology patients, with prevalence reported between 11 and 89.8%, depending on the primary oncologic diagnosis and chemotherapeutic regimen.[4–6] The consequences of neutropenia can be severe and include an increased risk for potentially life-threatening organ system infections, breaks in chemotherapeutic administration, and neutropenic enterocolitis (NE).[1,2]

Abdominal pathology in neutropenic patients poses a diagnostic dilemma for the general surgeon due to atypical manifestations of common conditions in this population, as well as the need to consider rare and often life-threatening pathology that generally does not present in otherwise immunocompetent patients.[7–9] The decision whether to operate on patients with neutropenia is complicated and requires the

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consideration of multiple factors including the patient's hemodynamic stability, severity of their condition, underlying comorbidities, prognosis, and goals of care. Higher rates of infectious perioperative complications are expected, and postoperative mortality rates have been reported as high as 41%.[10] Understandably, this is a difficult patient population to study and treatment decisions are often based on anecdotal experience; the literature guiding practice is limited to case series within small populations, the largest of which reported on the outcomes of surgical intervention in 18 patients.[7,8,10–12] Although our series is also retrospective in nature, we sought to use our extensive experience in dealing with this patient cohort to describe the outcomes of neutropenic patients who underwent abdominal surgery and to identify factors contributing to morbidity and mortality.

Methods

Patient Identification

We conducted a single-institution retrospective review of consecutive patients from 1998 to 2017 who were neutropenic in the 24-hours prior to the index abdominal operation of their hospitalization. This study was approved by the Partners Healthcare Institutional Review Board (Protocol 2006P001280) and informed consent was waived. Abdominal operations were initially identified based on Current Procedural Terminology (CPT) coding (40,490–40,700, 38,100–38,200), which yielded 17,000 patients. Python was used to identify 821 unique patients at Brigham and Women's Hospital who had a low neutrophil count on the day of, or the day prior to the index operation based upon laboratory data in our institutional data registry. Chart review was performed to identify patients with neutropenia in the 24-hours prior to surgery and exclude patients who were neutropenic intra- or immediately post-operatively. A final cohort of 237 patients was identified. Reoperations occurring during the same hospitalization (e.g., reoperation after a "damage control" operation or other staged procedure) were not included as separate observations because our focus was on the initial decision to operate on these complex patients. Patients with distinct index operations during separation hospitalizations were included as separate events. Abdominal surgery was defined as any operation or intervention through the abdominal wall including (1) any intervention or operation on the alimentary tract from the gastroesophageal junction to the end of the rectum, including open and laparoscopic gastrostomy and jejunostomy tubes, and (2) any operation involving the omentum, peritoneum, liver, spleen, pancreas, abdominal lymph nodes, intraabdominal abscesses, abdominal masses, and retroperitoneal space. Urogenital operations, endoscopic interventions, drainage of abscesses or collections by interventional radiology, and visceral organ transplantations were excluded from analysis. Neutropenia was identified either as (1) a directly measured absolute neutrophil count (ANC) < 1500 cells/μL, (2) using the measured percentage of polymorphonuclear leukocytes (PMNs) for a given white blood cell (WBC) count to calculate the ANC, or (3) by extrapolation for patients with a white blood cell (WBC) count of ≤ 2500 assuming PMNs comprised 60% of the WBC volume (institutional reference 48–76%).

Chart Review

Chart review of the selected patients was used to confirm those patients who were neutropenic in the 24-hours prior to their abdominal operation. For patients with more than one white blood cell count prior to their operation, the most recent WBC prior to surgery was utilized for analysis. Etiology of neutropenia was categorized as follows: (1) idiopathic/no identifiable cause; (2) chemotherapy as treatment for any systemic malignancy or condition; (3) pharmacological immunosuppression, e.g., after solid organ transplantation; (4) primary disease process (e.g., hematological conditions without chemotherapy, myelodysplastic syndromes); and (5) sepsis. Patients were characterized based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) as having mild (ANC ≤ 1500 cells/μL), moderate (500 ≤ ANC < 1000 cells/μL), or severe (ANC < 500 cells/μL) neutropenia.[3]

Primary and secondary outcomes were 30-day mortality and 30-day morbidity, respectively. Morbidity was defined as ≥ 1 complication identified on chart review based on, but not exclusive to, the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) tracked outcomes and what was ascertainable on chart review (Table 1).[13] For complications, total number of complications as well as the number of patients with ≥ 1 complication in each group were described and compared. In cases of mortality, complications prior to death were also used in morbidity calculations and comparisons.

Elective operations were defined as those in which patients presented from home and were associated with no time constraint on completion. Urgent or emergent operations included all other observations and predominantly stemmed from in-hospital surgical consultations or life-threatening intraabdominal pathology (e.g., perforated viscous, non-resolving small bowel obstruction).

Statistical Analysis

Baseline features of the population were tabulated according to the primary and secondary end points as described previously. The chi-square test and two-tailed Student's *t* test were used to evaluate the association between categorical and

Table 1 Reviewed post-operative morbidities for neutropenic patients

Readmission within 30 days	Pulmonary embolus (PE)
Reoperation	Ventilator dependence > 48 h
Hospitalization > 30 days	Acute or acute on chronic renal failure
Superficial surgical site infection (SSI)	Urinary tract infection (UTI)
Deep or organ space surgical site infection	Cerebrovascular accident (CVA)
Wound dehiscence	Myocardial infarction (MI)
Pneumonia	Blood product transfusion
Unplanned intubation	Enterocutaneous fistula (ECF) formation
Deep vein thrombus (DVT)	

continuous variables, respectively, and the outcomes of interest. Non-parametric tests were used when appropriate. Missing data were handled using a complete case approach. A two-tailed value of $P < 0.05$ was considered statistically significant. To determine the optimal threshold of ANC to discriminate 30-day mortality, we maximized the Youden index (J), a statistic that equally weights sensitivity and specificity. Data were analyzed using SAS (SAS Institute, Inc., Cary, NC) and R 3.5.0.

Results

Demographics

From 1998 to 2017, we identified 237 index abdominal operations in neutropenic patients at our institution. Median age at the time of admission was 56 years old, and females comprised 54.9% (130/237) of the patient population. Of the operations, 69.6% (165/237) were urgent or emergent and 75.1% (178/237) were performed open (vs. laparoscopic). Median time from admission to operation was 1 day (range 0–73 days) and median hospital length of stay (LOS) postoperatively was 8 days (range 0–345 days). Median ANC was 990 cells/μL (range 0–1490 cells/μL) with 24.1% being classified as having mild, 27% as having moderate, and 48.9% as having severe neutropenia. The predominant cause of neutropenia was chemotherapy in 46.4% (110/237), followed by idiopathic in 19.4% (46/237), pharmacologic immunosuppression in 18.1% (43/237), primary disease driving neutropenia in 11.8% (28/237), and sepsis in 4.2% (10/237). Of these patients, 84% (199/237) had concomitant anemia, 57.4% (136/237) concomitant thrombocytopenia, and 53.2% (126/237) had both anemia and thrombocytopenia. The operative diagnosis was small bowel obstruction (SBO) in 17.7% (42/237) and perforated viscous in 17.3% (41/237) of patients, respectively. Common etiologies for perforation were idiopathic, cancer-related, complicated diverticulitis, and due to gastric or duodenal ulcers. 19.4% (46/237) received granulocyte colony stimulating factor (GCSF) during their hospitalization.

Mortality

For our primary end point, 28 patients (11.8%) suffered 30-day mortality (Table 2). Comparing the characteristics of patients between the mortality and no-mortality groups, urgent operations (27/28, 96.4% vs. 138/209, 66%, $P < 0.01$), severe neutropenia with ANC < 500 cells/μL (14/28, 50% vs. 43/209, 20.6%, $P < 0.01$), perforated viscous (10/28, 35.7% vs. 31/209, 14.8%, $P = 0.01$), and GCSF use during their hospitalization (10/28, 35.7% vs. 36/209, 17.2%, $P = 0.02$) were each significantly associated with mortality (Fig. 1). The etiology of neutropenia was significantly associated with mortality ($P = 0.0496$) with sepsis being the largest magnitude etiological risk factor (RR 2.72, 95% CI 0.99–7.53) (Table 3). We found an ANC of 350 cells/μL was the best

Table 2 Baseline characteristics stratified by mortality

Variable	Mortality	No mortality	P
Overall	28 (12)	209 (88)	
Age	56 (44–67)	59 (47–71)	0.40
Female	14 (50)	116 (55)	0.58
Urgent/emergent	27 (96)	138 (66)	< 0.01
Open	24 (86)	154 (74)	0.17
ANC			< 0.01[a]
0–500	14 (50)	43 (21)	
500–1000	7 (25)	57 (27)	
> 1000	7 (25)	109 (52)	
Etiology			0.050
Chemotherapy	14 (50)	96 (46)	
Idiopathic	1 (4)	45 (22)	
Immunosuppression	7 (25)	36 (17)	
Progression of primary disease	3 (11)	25 (12)	
Sepsis	3 (11)	7 (3)	
Small bowel obstruction	4 (14)	38 (18)	0.79
Perforation	10 (36)	31 (15)	0.01
Outside transfer	8 (29)	33 (16)	0.11
GCSF	10 (36)	36 (17)	0.02
Any cytopenia	25 (89)	184 (88)	> 0.99
Anemia	24 (86)	175 (84)	> 0.99
Thrombocytopenia	20 (71)	116 (55)	0.11
Anemia and thrombocytopenia	19 (68)	107 (51)	0.10
Days to operation	1 (0–4)	1 (0–7)	0.77
Hospital LOS	10 (6–20)	9 (2–19)	0.10
Post-operative LOS	8 (4–14)	3 (1–10)	< 0.01

Number (%) or median (interquartile range)

[a] Cochran–Armitage trend test

threshold for discrimination of 30-day mortality (Fig. 2). This threshold had a sensitivity of 50% and specificity of 85%.

Morbidity

One hundred and thirty of 237 patients (54.8%) experienced at least one 30-day morbidity for a total of 360 morbidity observations (Tables 4 and 5). Male sex (68/130, 52.3% vs. 39/107, 36.4%, $P = 0.01$), urgent operations (105/130, 80.8% vs 60/107, 56.1%, $P < 0.01$), open operations (108/130, 83.1% vs. 70/107, 65.4%, $P < 0.01$), bowel perforation (33/130, 25.4% vs. 8/107, 7.5%, $P < 0.01$), GCSF use (34/130, 26.3% vs. 12/107, 11.2%, $P < 0.01$), and a concomitant cytopenia were each significantly associated with 30-day morbidity.

Additionally, transfer from an outside hospital (OSH) (29/130, 22.3% vs. 12/107, 11.2%, $P = 0.02$) and longer median time from admission to operation (2 (IQR 0–6) vs. 1 (IQR 0–3), $P < 0.01$) were both associated with morbidity.

Urgent vs. Elective Operations

Of the 237 operations, 165 were urgent or emergent (69.6%). These non-elective operations were associated with significantly higher mortality (27/165, 16.4% vs 1/72, 1.4%, $P = 0.002$) and morbidity (105/165, 63.6% vs 25/72, 34.7%, $P < 0.001$) and were more likely to be performed open (132/165, 80% vs 46/72, 63.9%), had a lower median ANC (820.40 [IQR 350–1250] vs 1211 [IQR 876.15–1393.37], $P < 0.001$), and were more likely to receive GCSF during their hospitalization (40/165, 24.2% vs 6/72, 8.3%, $P = 0.008$) (Table 6). They were more likely to be transferred from an OSH (39/165, 23.6% vs 2/72, 2.8%, $P < 0.001$) and had a longer time period from admission to operation and both hospital and postoperative length of stay.

Table 3 Association between etiology of neutropenia and mortality

Etiology	Relative risk[a]	95% CI
Idiopathic	0.15	0.02–1.10
Chemotherapy	1.15	0.58–2.3
Immunosuppression	1.50	0.68–3.31
Primary disease process	0.89	0.29–2.77
Sepsis	2.72*	0.99–7.53

[a] Each separately compared with all other etiologies

For elective operations, 25 of 72 patients (34.7%) experienced ≥ 1 reportable morbidity, for a total of 45 reportable occurrences. Of these, 3 were hospitalizations >30 days, 8 were readmissions within 30 days, and 12 were transfusions (Table 4). For 7 of 25 patients, their only morbidity was transfusion.

Discussion

In this study, we report on the largest series of neutropenic patients to have undergone abdominal surgery in the current published literature. As expected, overall mortality and morbidity rates, 11.8% and 54.8%, respectively, were significantly higher than published rates in the general population for both elective and emergency abdominal operations.[13–15] Few studies have described the outcomes of surgery in neutropenic patients. In a retrospective analysis of neutropenic patients with abdominal pain for whom the surgical service was consulted, Badgwell and colleagues reported that the most frequent pathological diagnosis was NE in 28%, though the diagnosis remained uncertain. Thirty-day mortality was 30%, and although only 9 patients (15%) ultimately underwent

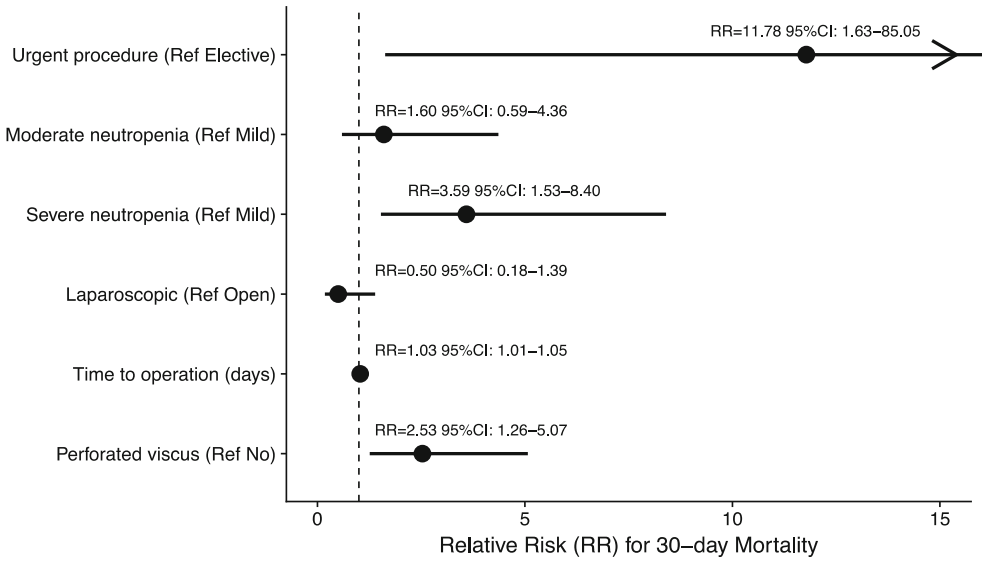

Fig. 1 Unadjusted predictors of 30-day mortality. Moderate neutropenia = 500 ≤ ANC < 1000 cells/μL; severe neutropenia = ANC < 500 cells/μL. RR relative risk

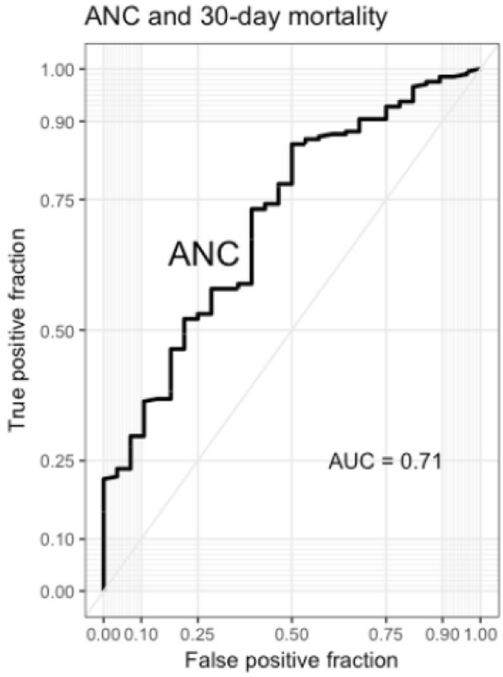

Fig. 2 Receiver operating characteristic (ROC) for ANC and 30-day mortality

surgical intervention, a lack of surgical intervention was associated with increased mortality.[7]

Predictors of both morbidity and mortality included surgical urgency, bowel perforation, and GCSF administration. Male sex, open operations, and concomitant anemia or thrombocytopenia were also associated with increased morbidity. Urgency, likely a surrogate for hemodynamic instability and/or other confounding clinical factors, has been shown to be a predictor of mortality in the general population as well.[15] Anecdotally, the threshold to operate on neutropenic patients is significantly higher and it is not surprising that 96.4% of mortalities occurred following urgent operations, many of which may have been last resort "rescue" attempts.

In-hospital mortality after surgery for intestinal perforation has been reported as high as 13.1% in the general population, whereas Cauley and colleagues found that oncology patients have substantially higher 30-day mortality after surgery for intestinal perforation (34%); this increased mortality was demonstrated in our findings with a 24.4% overall mortality after surgery for perforation.[16,17] In the neutropenic patient population, which includes predominantly oncology patients, both on and off chemotherapy, and the immunosuppressed, an operation for a perforated viscous can be immediately lifesaving, irrespective of their overall prognosis. Obviously, the morbidity associated with this operation is an important consideration; however with over 75% 30-day survival, these patients can still gain substantial benefit from surgical intervention.

Table 4 Frequency of morbidities

Variable	Overall	Elective	Urgent/emergent	*P*
Overall	237	72	165	
Any complication	130 (55)	25 (34.7)	105 (63.6)	< 0.001
Reoperation	32 (14)	4 (5.6)	28 (17.1)	0.032
In-hospital at 30 days	31 (13)	3 (4.2)	28 (17.0)	0.013
30-day readmission	49 (21)	8 (11.1)	41 (24.8)	0.026
Superficial surgical site infection	21 (9)	6 (8.3)	15 (9.1)	> 0.99
Deep surgical site infection	19 (8)	0 (0.0)	19 (11.5)	0.006
Dehiscence	7 (3)	1 (1.4)	6 (3.6)	0.601
Pneumonia	34 (14)	3 (4.2)	31 (18.8)	0.006
Intubation	26 (11)	3 (4.2)	23 (13.9)	0.047
Pulmonary embolism	1 (0.4)	0 (0.0)	1 (0.6)	> 0.99
Ventilator	36 (15)	2 (2.8)	34 (20.6)	0.001
Acute kidney injury	28 (12)	1 (1.4)	27 (16.4)	0.002
Urinary tract infection	6 (3)	0 (0.0)	6 (3.6)	0.234
Cerebrovascular accident	3 (1)	0 (0.0)	3 (1.8)	0.603
Coma	0 (0)	0 (0)	0 (0)	> 0.99
Myocardial infarction	2 (1)	0 (0.0)	2 (1.2)	0.868
Transfusion	47 (20)	12 (16.7)	35 (21.2)	0.529
Deep venous thrombosis	11 (4)	1 (1.4)	10 (6.1)	0.216
Enterocutaneous fistula	7 (3)	1 (1.4)	6 (3.6)	0.601
ANC, median [IQR]		1211 [876, 1393]	820 [350, 1250]	< 0.001

Number (%) or median (interquartile range)

Table 5 Baseline characteristics stratified by morbidity

Variable	Morbidity	No morbidity	*P*
Overall	130 (55)	107 (45)	
Age	57 (45–67)	54 (43–69)	0.55
Female	62 (48)	68 (64)	0.01
Urgent/emergent	105 (81)	60 (56)	< 0.01
Open	108 (83)	70 (65)	< 0.01
ANC			0.13[a]
0–500	35 (27)	22 (21)	
500–1000	37 (28)	27 (25)	
> 1000	58 (45)	58 (54)	
Etiology			0.03
Chemotherapy	60 (46)	50 (47)	
Idiopathic	19 (15)	27 (25)	
Immunosuppression	32 (25)	11 (10)	
Progression of primary disease	13 (10)	15 (14)	
Sepsis	6 (5)	4 (4)	
Small bowel obstruction	19 (15)	23 (21)	0.17
Perforation	33 (25)	8 (7)	< 0.01
Outside transfer	29 (22)	12 (11)	0.02
GCSF	34 (26)	12 (11)	< 0.01
Any cytopenia	123 (95)	86 (80)	< 0.01
Anemia	118 (91)	81 (76)	< 0.01
Thrombocytopenia	83 (64)	53 (50)	0.03
Anemia and thrombocytopenia	78 (60)	48 (45)	0.02
Days to operation	2 (0–6)	1 (0–3)	< 0.01
Hospital LOS	16 (9–31)	6 (3–11)	< 0.01
Post-operative LOS	10.5 (7–22)	5 (2–8)	< 0.01
Mortality	18 (14)	10 (9)	

Number (%) or median (interquartile range)

[a] Cochran–Armitage trend test; continuous variable, $P = 0.03$, Mann–Whitney *U* test

The use of GCSF was a predictor of both morbidity and mortality. As it relates to postoperative outcomes, neutrophils are implicated in both host defense and wound healing through microbicidal action and chemokine-induced epithelialization and the absence of these effects may be implicated in both infectious and surgical site related complications, including anastomotic leaks and dehiscence.[18] GCSF, which is often administered preoperatively in an attempt to stimulate neutrophil production, is likely a surrogate for the patient's severity of illness several days prior to the operation and underlying immunological compromise, rather than a causative factor contributing to morbidity and mortality.[19–21]

Against a backdrop of baseline inferior outcomes after abdominal surgery for neutropenic patients, two potentially modifiable factors were identified. Open operations were associated with poorer outcomes, highlighting a benefit in using a laparoscopic approach when feasible. Transfers from an outside hospital (OSH) and delays from admission to operation were associated with increased rates of morbidity, but not mortality. Lack of mortality difference was potentially confounded by the high relative proportion of urgent operations and an inability to delay surgery in these patients. Mortality was higher amongst patients transferred from an OSH; however, the small sample size may have been underpowered to detect a statistical significance. These findings have also been reported in general surgical populations; McIsaac and colleagues demonstrated that delays in non-cardiac emergency surgical operations were significantly associated with an increase in mortality.[21] Amongst, older, higher risk patients with a greater number of comorbidities, delays in surgical intervention for perforated viscous were associated with increased morbidity and mortality postoperatively.[16] Moreover, inter-hospital transfer has been associated with adverse postoperative outcomes but may be regarded both as a metric of patient illness severity and a cause for delays from diagnosis to definitive surgical management.[22,23] Although anecdotally, some clinicians may be hesitant to operate on neutropenic patients with obvious surgical pathology; given the substantial survival benefit with surgery and the risks associated with operative delays, such fear should be realistically balanced against the obvious consequences of delaying or not performing a definitive intervention.

In conducting this study, we hoped to describe this population to better guide providers faced with the dilemma of whether to operate on a neutropenic patient, both electively and urgent/emergently. Patients with severe neutropenia (< 500 cells/μL) did have a higher risk of mortality and this must be balanced against the impact of operative delays; however, the individual contributions of each to overall outcome are difficult to determine. Certain patients do necessitate "watchful waiting" and/or non-operative management such as those with neutropenic enterocolitis without perforation or contained intraabdominal abscess amenable to percutaneous drainage.

We found that an ANC of 350 cells/μL was the best threshold for discriminating mortality and may help guide decision-makers prior to surgical intervention. We sought to divide neutropenia into a binary variable (greater or less than 350 cells/μL) for interpretability, however acknowledge that operative risk is based on an ANC continuum. Some operations may be more or less affected by neutropenia due to impaired wound healing or infectious risk; however, ultimately, the classically defined operative threshold of 500 cells/μL may be too stringent for all patients.

A subgroup of our study population included 72 elective operations which included hernia repairs, laparoscopic feeding jejunostomy tubes, and cholecystectomies. The patients had higher ANCs than their urgent and emergent counterparts and their operations were relatively safe, with one mortality in a pancytopenic patient who underwent a diagnostic splenectomy and hepatic segmentectomy but ultimately died from

Table 6 Outcomes by urgency

Variable	Elective	Urgent/emergent	*P*
Overall	72	165	
Age	55.50 [44.00, 68.00]	56.00 [45.00, 67.00]	0.903
Female	41 (56.9)	89 (53.9)	0.775
Morbidity	25 (34.7)	105 (63.6)	< 0.001
Mortality	1 (1.4)	27 (16.4)	0.002
Open	46 (63.9)	132 (80.0)	0.013
ANC	1211.00 [876.15, 1393.37]	820.40 [350.00, 1250.00]	< 0.001
ANC			< 0.001
0–500	7 (9.7)	50 (30.3)	
500–1000	16 (22.2)	48 (29.1)	
> 1000	49 (68.1)	67 (40.6)	
Etiology			0.046
Chemotherapy	31 (43.1)	79 (47.9)	
Idiopathic	14 (19.4)	32 (19.4)	
Immunosuppression	13 (18.1)	30 (18.2)	
Progression of primary disease	14 (19.4)	14 (8.5)	
Sepsis	0 (0.0)	10 (6.1)	
Outside transfer	2 (2.8)	39 (23.6)	< 0.001
GCSF	6 (8.3)	40 (24.2)	0.008
Any cytopenia	65 (90.3)	144 (87.3)	0.66
Anemia	61 (84.7)	138 (83.6)	0.986
Thrombocytopenia	43 (59.7)	93 (56.4)	0.735
Anemia and thrombocytopenia	39 (54.2)	87 (52.7)	0.95
Days to operation	1.00 [0.00, 3.25]	1.00 [1.00, 5.00]	0.007
Hospital LOS	6.50 [3.75, 11.50]	12.00 [7.00, 23.00]	< 0.001
Post-operative LOS	5.00 [3.00, 8.25]	9.00 [4.00, 16.00]	< 0.001

Continuous as median [IQR]

Aspergillus pneumonia-related septicemia. Although 34.7% of these patients experienced some form of reportable morbidity, 23/45 observations were non-life threatening, including 30-day readmissions, and hospital stay > 30 days. Twelve patients received a transfusion which is not unexpected given the high rate of concomitant thrombocytopenia and anemia. When removing transfusions, which is not unexpected in neutropenic or pancytopenic patients, morbidity fell to 25% (18/72). The remainder of more serious complications were infrequent in nature, the most common being superficial surgical site infections. Overall, it appears that elective abdominal surgery is relatively safe in the appropriately chosen neutropenic patient.

There are several limitations to this study. First, this was a descriptive study with observational data and intrinsic potential for bias and data were available only as part of routine clinical care. As such, data such as daily clinical status changes, dates and times of medication administration (e.g., GCSF), and physical examination changes are unknown. As such, the goal of this study was to provide a descriptive overview of this under-studied population, rather than to determine causal relationships. Second, while we report a "best" ANC threshold for discriminating mortality, we acknowledge that operative risk is based on an ANC continuum and note the risks of dichotomization. Some operations may be more or less affected by neutropenia due to impaired wound healing or infectious risk. Ultimately, the classically defined operative threshold of 500 cells/μL may be too stringent for all patients. Third, the patients included in this study were admitted to a quaternary care center and these results may not be generalizable. Finally, because we restricted our study to patients undergoing operations, we cannot quantify the value (or lack thereof) of surgical intervention compared with no intervention; however, multiple series have demonstrated the association between non-operative medical management and adverse outcomes for neutropenic and oncologic patients with surgical pathology.[7,10,24]

In conclusion, given the findings reported in our study and accepting the baseline increased risk of postoperative morbidity and mortality, we advocate for early consideration of operation on patients with obvious surgical pathology, presumably as soon as the diagnosis is made. Surgical consultation

should be sought with a lower threshold in neutropenic patients in the hopes that a multidisciplinary approach may expedite the diagnosis and necessary treatment.

Author Contribution All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship.

Compliance with Ethical Standards

This study was approved by the Partners Healthcare Institutional Review Board (Protocol 2006P001280) and informed consent was waived.

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References

1. Lustberg MB. Management of neutropenia in cancer patients. Clin Adv Hematol Oncol. 2012;10(12):825–6.
2. Dale DC. Understanding neutropenia. Curr Opin Hematol. 2014;21(1):1–2.
3. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE). Version 4.0. Bethesda, MD: National Cancer Institute; 2009.
4. Hashiguchi Y, Kasai M, Fukuda T, Ichimura T, Yasui T, Sumi T. Chemotherapy-induced neutropenia and febrile neutropenia in patients with gynecologic malignancy. Anticancer Drugs. 2015;26(10):1054–60.
5. Jolis L, Carabantes F, Pernas S, et al. Incidence of chemotherapy-induced neutropenia and current practice of prophylaxis with granulocyte colony-stimulating factors in cancer patients in Spain: a prospective, observational study. Eur J Cancer Care (Engl). 2013;22(4):513–21.
6. Fujiwara T, Kenmotsu H, Naito T, et al. The incidence and risk factors of febrile neutropenia in chemotherapy-naïve lung cancer patients receiving etoposide plus platinum. Cancer Chemother Pharmacol. 2017;79(6):1229–1237.
7. Badgwell BD, Cormier JN, Wray CJ, et al. Challenges in surgical management of abdominal pain in the neutropenic cancer patient. Ann Surg. 2008;248(1):104–9.
8. Starnes HF, Moore FD, Mentzer S, Osteen RT, Steele GD, Wilson RE. Abdominal pain in neutropenic cancer patients. Cancer. 1986;57(3):616–21.
9. Chow EJ, Bishop KD. Painless neutropenic enterocolitis in a patient undergoing chemotherapy. Curr Oncol. 2016;23(5):e514-e516.
10. Wade DS, Douglass H, Nava HR, Piedmonte M. Abdominal pain in neutropenic patients. Arch Surg. 1990;125(9):1119–27.
11. Chirletti P, Barillari P, Sammartino P, et al. The surgical choice in neutropenic patients with hematological disorders and acute abdominal complications. Leuk Lymphoma. 1993;9(3):237–41.
12. Glenn J, Funkhouser WK, Schneider PS. Acute illnesses necessitating urgent abdominal surgery in neutropenic cancer patients: description of 14 cases and review of the literature. Surgery. 1989;105(6):778–89.
13. American College of Surgeons. National Surgical Quality Improvement Program. User Guide for the 2014 ACS NSQIP Participant Use Data File (PUF). Chicago, IL: American College of Surgeons; October 2015.
14. Tolstrup MB, Watt SK, Gögenur I. Morbidity and mortality rates after emergency abdominal surgery: an analysis of 4346 patients scheduled for emergency laparotomy or laparoscopy. Langenbecks Arch Surg. 2017;402(4):615–623.
15. Massarweh NN, Legner VJ, Symons RG, Mccormick WC, Flum DR. Impact of advancing age on abdominal surgical outcomes. Arch Surg. 2009;144(12):1108–14.
16. Khuri SF, Henderson WG, Depalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. Ann Surg. 2005;242(3):326–41.
17. Al-qurayshi Z, Srivastav S, Kandil E. Postoperative outcomes in patients with perforated bowel: early versus late intervention. J Surg Res. 2016;203(1):75–81.
18. Cauley CE, Panizales MT, Reznor G, et al. Outcomes after emergency abdominal surgery in patients with advanced cancer: Opportunities to reduce complications and improve palliative care. J Trauma Acute Care Surg. 2015;79(3):399–406.
19. Nathan C. Neutrophils and immunity: challenges and opportunities. Nat Rev Immunol. 2006;6(3):173–82.
20. Schaefer H, Engert A, Grass G, et al. Perioperative granulocyte colony-stimulating factor does not prevent severe infections in patients undergoing esophagectomy for esophageal cancer: a randomized placebo-controlled clinical trial. Ann Surg. 2004;240(1):68–75.
21. Schneider C, Von aulock S, Zedler S, Schinkel C, Hartung T, Faist E. Perioperative recombinant human granulocyte colony-stimulating factor (Filgrastim) treatment prevents immunoinflammatory dysfunction associated with major surgery. Ann Surg. 2004;239(1):75–81.
22. Mcisaac DI, Abdulla K, Yang H, et al. Association of delay of urgent or emergency surgery with mortality and use of health care resources: a propensity score-matched observational cohort study. CMAJ. 2017;189(27):E905-E912.
23. Lucas DJ, Ejaz A, Haut ER, Spolverato G, Haider AH, Pawlik TM. Interhospital transfer and adverse outcomes after general surgery: implications for pay for performance. J Am Coll Surg. 2014;218(3):393–400.
24. Suresh K, Gouveia CJ, Kern RC, Cramer JD. The Association of External Transfer Status with Adverse Outcomes in Otolaryngology. Otolaryngol Head Neck Surg. 2018;194599817753611.
25. Villar HV, Warneke JA, Peck MD, Durie B, Bjelland JC, Hunter TB. Role of surgical treatment in the management of complications of the gastrointestinal tract in patients with leukemia. Surg Gynecol Obstet. 1987;165(3):217–22.