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Impact of Transfusion Threshold on Infectious Complications After Ileal Pouch-Anal Anastomosis

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Abstract
Background This study was conducted to investigate the impact of different hemoglobin level-based transfusion practices on infectious complications after surgery for ulcerative colitis.
Methods Patients who underwent ileal pouch-anal anastomosis for ulcerative colitis between January 2008 and December 2013 were identified and divided into four groups: group 1 with hemoglobin≥10 and group 2 with hemoglobin≥7 and <10 g/dL who did not receive transfusion and group 3 with hemoglobin≥7 and <10 and group 4 with hemoglobin<7 g/dL who received transfusion. Clinical characteristics and septic complications within postoperative 30 days were compared.
Results There were 237, 341, 40, and 20 patients in groups 1, 2, 3, and 4, respectively. All the groups were comparable regarding perioperative characteristics except for age, gender, preoperative albumin and hemoglobin levels, and operative blood loss. The rates of overall septic complications were 18.6, 26.7, 47.5, and 40 % in the groups 1, 2, 3 and 4, respectively. In multivariate analysis, compared to group 2, group 3 was associated with an increased likelihood of developing organ/space (odds ratio (OR)= 4.34, p=0.004) and overall surgical site infections (SSIs) (OR=2.81, p= 0.01).
Conclusion Blood transfusion decided based on a perioperative hemoglobin (Hgb) level above 7 mg/dL is associated with higher overall and organ/space SSIs.

Keywords Transfusion threshold · Postoperative infections · Ulcerative colitis · Surgery

Introduction

Ileal pouch-anal anastomosis (IPAA) has been accepted as the treatment of choice for most patients with ulcerative colitis. Blood transfusions are frequently required for this group of patients due to increased incidence of perioperative anemia and/or blood loss resulting from a major operative procedure inclusive of pelvic dissection.[1] However, studies have shown that blood transfusion is an independent risk factor for infectious complications after colorectal surgery,[2,3] possibly due to the immunosuppressive effects of the transfused blood.[2,4] In addition to this, blood transfusion has been reported to impair the healing of intestinal anastomosis and increase the rate of anastomotic leak.[5,6]

In the perioperative setting, blood transfusion is generally not indicated in otherwise healthy patients if hemoglobin (Hgb) level is above 10 g/dL. The traditional practice to transfuse patients when the Hgb level dropped below 10 g/dL has been questioned in a variety of clinical settings.[7–9] It is suggested that in patients without advanced coronary artery disease, transfusions can be withheld in the presence of Hgb level as low as 7 g/dL with the goal of minimizing exposure to transfusion (restrictive strategy).[10–12] Also, this restrictive strategy is reported to be associated with a significant

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reduction in the rates of infections.[9,11] However, the effects of the lower Hgb threshold of 7 mg/dL for administering transfusions on any change in the infectious complications and anastomotic leak after IPAA or any other colorectal surgery are not known. Therefore, the aim of this study was to investigate the impact of different Hgb level-based transfusion practices on these complications in patients with ulcerative colitis undergoing IPAA procedure.

Patients and Methods

Patients who underwent surgery for ulcerative colitis (UC) between January, 2008 and December, 2013 were identified from an IRB-approved, prospectively maintained institutional ileal pouch database. We attempted to control some of the variables by choosing a group of patients with the same disease, undergoing the same operation. Therefore, patients who underwent either total proctocolectomy or completion proctectomy and IPAA with diverting ileostomy were deemed eligible for the study. Exclusion criteria included emergency surgery, including surgery for fulminant colitis or compromised colon, a preoperative septic focus, American Society of Anesthesiologists (ASA) class 4, serious cardiac disease defined by Canadian Cardiovascular Society angina classification[13] ≥grade 3, blood transfusion within 1 month before surgery, and re-operation for a non-septic event during the same hospitalization period.

In order to demonstrate an association between different blood transfusion practices with postoperative infectious complications, patients were classified into four groups based on the perioperative lowest Hgb level and transfusion status: group 1 with Hgb level ≥10 g/dL and group 2 with Hgb level ≥7 and <10 g/dL who did not receive transfusion and group 3 with Hgb level ≥7 and <10 g/dL and group 4 with Hgb level <7 g/dL who received transfusion. In addition to the exclusion criteria provided above, patients in group 3 who required transfusions due to clinical symptoms and/or hemodynamic instability secondary to anemia or hypovolemia were excluded. Hemodynamic instability was defined as heart rate>100/min and/or systolic blood pressure<90 mm Hg. The threshold Hgb level of 7 g/dL for transfusion was chosen based on a recent meta-analysis reported by Carless et al.[12] There were no patients with a perioperative lowest Hgb level ≥10 g/dL who received transfusion. Also, all the patients with a Hgb level <7 g/dL were transfused. Group 1 served as a control group, and clinical and perioperative characteristics and postoperative septic complications were compared among the four groups.

Medical records of all included patients were retrospectively reviewed. Data collected included age, gender, body mass index (BMI), ASA class, smoking status, co-morbidities, and preoperative albumin and Hgb levels. Information regarding medications used within the 2 months preceding surgery included steroids and immunosuppressive drugs including biologics. Surgical factors evaluated included surgeon, type of operative procedure (completion proctectomy and IPAA or total proctocoloectomy and IPAA) and approach (open or laparoscopy), anastomotic technique (stapled or hand-sewn), type of pouch constructed (J- or S-pouch), operative time, and blood loss.

The primary outcomes were anastomotic leak and organ/space surgical site infections (SSIs), and secondary outcomes were overall SSIs and overall infectious complications. All the complications were defined as having occurred within 30 days after surgery. Overall infectious complication was defined as the presence of at least one complication which included any SSI (superficial, deep, or organ/space), anastomotic leak (AL), pouch leak, pouch fistula/sinus, urinary tract infections, pneumonia, and sepsis. Anastomotic or pouch leaks were defined as clinically apparent leak sign (such as the emission of gas, pus, or feces from the pelvic drain) or extravasation of an endoluminally administered water-soluble contrast medium according to the computed tomography postoperatively or prior to ileostomy closure. The diagnosis of SSIs was made based on the definitions stated in the guidelines reported by the CDC's NNIS system.[14]

Statistical Analysis

Preoperative, operative, and postoperative variables were compared among the four groups. Categorical variables were reported as frequencies and percentages. Continuous variables were reported as mean and standard deviations. Comparisons of the groups were performed using the Pearson's chi-squared test or Fisher's exact test with respect to categorical data and the Wilcoxon rank sum test with respect to quantitative data. Logistic regression analysis was used to assess multivariable associations between potential risk factors and the postoperative complications. Results are presented as odds ratios (ORs) with 95 % confidence intervals (CI). All tests were performed at a significance level of 0.05. SAS 9.3 software (SAS Institute, Cary, NC) was used for all analyses.

Results

The database yielded 802 patients during the 6-year study period. Six hundred and thirty-eight patients (366 [57.4 %] males) with a mean age of 39.0±13.1 years met the inclusion criteria. There were no patients with a perioperative lowest Hgb level ≥10 g/dL who received transfusion. Also, all the patients with a Hgb level <7 g/dL were transfused. There were 237 (37.1 %), 341 (53.4 %), 40 (6.2 %), and 20 (3.2 %) patients in groups 1, 2, 3, and 4, respectively.

The preoperative characteristics of the four groups are provided in Table 1. The mean age was the highest in group 3

Table 1 Comparison of preoperative characteristics among the study groups

Preoperative characteristics	Study groups				*P* value
	Group 1 (Hgb≥10 non-transfused) *n*=237	Group 2 (Hgb≥7 and <10 non-transfused) *n*=341	Group 3 (Hgb≥7 and <10 transfused) *n*=40	Group 4 (Hgb<7 transfused) *n*=20	
Age, mean (SD)	37.2 (12.9)	40.2 (13.2)	41.0 (13.7)	36.1 (11.0)	0.03
Gender, male, *n* (%)	183 (77.2)	155 (45.5)	15 (37.5)	13 (65.0)	<0.001
BMI, mean (SD)	25.9 (4.3)	25.8 (5.0)	26.1 (4.5)	25.1 (3.9)	0.89
ASA status, *n* (%)					0.26
1	5 (2.1)	5 (1.5)	0 (0)	0 (0)	
2	196 (82.7)	260 (76.2)	34 (85.0)	14 (70.0)	
3	36 (15.2)	76 (22.3)	6 (15.0)	6 (30.0)	
Diabetes mellitus, *n* (%)	8 (3.4)	13 (3.8)	5 (12.5)	1 (5.0)	0.06
Smoking, *n* (%)					0.33
Never or former	225 (94.9)	321 (94.1)	37 (92.5)	17 (85.0)	
Current	12 (5.1)	20 (5.9)	3 (7.5)	3 (15.0)	
Cardiac disease, *n* (%)	13 (5.5)	20 (5.9)	6 (15.0)	1 (5.0)	0.13
Hypertension, *n* (%)	36 (15.2)	45 (13.2)	7 (17.5)	5 (25.0)	0.46
Vascular disease, *n* (%)	27 (11.4)	34 (10.0)	6 (15.0)	3 (15.0)	0.71
Renal disease, *n* (%)	13 (5.5)	38 (11.1)	5 (12.5)	2 (10.0)	0.11
Liver disease, *n* (%)	8 (3.4)	13 (3.8)	3 (7.5)	1 (5.0)	0.65
Lung disease, *n* (%)	33 (13.9)	43 (12.6)	9 (22.5)	1 (5.0)	0.23
Cerebrovascular disease, *n* (%)	1 (0.42)	6 (1.8)	2 (5.0)	0 (0)	0.11
Other diseases, *n* (%)	57 (24.1)	94 (27.6)	13 (32.5)	6 (30.0)	0.62
Preop albumin level, g/dL, mean (SD)	4.3 (0.4)	4.2 (0.4)	4.2 (0.7)	4.1(0.4)	0.006
Preop Hgb level, mean (SD)	14.3 (1.3)	12.9 (1.5)	12.6 (2.0)	12.4(2.6)	<0.001
Steroid use, *n* (%)	64 (27.0)	90 (26.4)	13 (32.5)	7 (35.0)	0.73
Steroid dose, *n* (%)					0.33
1–10 mg	25 (39.1)	34 (37.8)	10 (76.9)	4 (57.1)	
11–20 mg	26 (40.6)	36 (40.0)	2 (15.4)	3 (42.9)	
21–30 mg	7 (10.9)	8 (8.9)	0 (0)	0 (0)	
31–40 mg	6 (9.4)	12 (13.3)	1 (7.7)	0 (0)	
Biologics use, *n* (%)	11 (4.6)	26 (7.6)	3 (7.5)	2 (10.0)	0.48

(41.0±13.7 years), followed by groups 2, 3, and 4 (36.1± 11.0 years). Male to female ratio was the highest in group 1 (3.4:1), followed by group 4 (1.9:1), group 2 (0.8:1), and group 3 (0.6:1). There were statistically significant differences among the groups regarding age (p= 0.03) and gender (p< 0.001). The groups were similar with respect to ASA status, smoking history, and co-morbidities including diabetes mellitus, cardiac disease, hypertension, vascular, renal, liver, lung, and cerebrovascular diseases. Also, no differences in the rates of preoperative steroid use, steroid dose, and biologics use were observed. Regarding laboratory data, there were significant differences among the groups with respect to preoperative albumin (p=0.006) and Hgb levels (p<0.001). The mean albumin level was the highest in group 1 (4.3±0.4 g/dL) and the lowest in group 4 (4.1±0.4 g/dL).

Regarding intraoperative findings (Table 2), the groups were comparable with respect to the rate of individual surgeon, type of procedure, operative approach anastomotic technique, and operative time. The only significant intraoperative difference was operative blood loss (p<0.001). The mean operative blood loss was the highest in group 3 (296.3±209.2 mL) and the lowest in group 1 (201.2±140.9 mL).

The distribution of the postoperative complications with their unadjusted rates in each group is provided in Table 3. Overall, 162 patients (25.4 %) had postoperative infectious complications. SSIs were observed in 111 patients corresponding an overall rate of 17.4 %. Group 1 had the lowest SSI rates (overall SSI 12.7 % and organ/space SSI 5.5 %). The highest rate of overall SSI (37.5 %) and organ/space SSI (27.5 %) were observed in group 3. AL occurred in a total of 34 patients (5.6 %). The rate of AL was the lowest in group 1 (3.4 %) and the highest in group 4 (15.0 %) followed by group 3 (10.0 %). The rates of overall infectious

Table 2 Comparison of intraoperative characteristics among the study groups

Intraoperative characteristics	Study groups				*P* value
	Group 1 (Hgb≥10 non-transfused) *n*=237	Group 2 (Hgb≥7 and <10 non-transfused) *n*=341	Group 3 (Hgb≥7 and <10 transfused) *n*=40	Group 4 (Hgb<7 transfused) *n*=20	
Surgeon, *n* (%)					0.08
1	43 (18.1)	61 (17.9)	6 (15.0)	2 (10.0)	
2	18 (7.6)	49 (14.4)	7 (17.5)	5 (25.0)	
3	28 (11.8)	39 (11.4)	6 (15.0)	3 (15.0)	
4	37 (15.6)	25 (7.3)	3 (7.5)	0 (0)	
5	23 (9.7)	29 (8.5)	3 (7.5)	2 (10.0)	
6	20 (8.4)	23 (6.7)	3 (7.5)	1 (5.0)	
7	14 (5.9)	26 (7.6)	0 (0)	4 (20.0)	
8	16 (6.8)	19 (5.6)	4 (10.0)	0 (0)	
9	11 (4.6)	24 (7.0)	1 (2.5)	1 (5.0)	
10	12 (5.1)	12 (3.5)	1 (2.5)	1 (5.0)	
Other surgeons	15 (6.3)	34 (10.0)	6 (15.0)	1 (5.0)	
Operative procedure, *n* (%)					0.46
CP and IPAA	172 (72.6)	228 (66.9)	26 (65.0)	13 (65.0)	
TPC and IPAA	65 (27.4)	113 (33.1)	14 (35.0)	7 (35.0)	
Approach, *n* (%)					0.12
Laparoscopy	86 (36.3)	109 (32.0)	8 (20.0)	4 (20.0)	
Open	151 (63.7)	232 (68.0)	32 (80.0)	16 (80.0)	
Laparoscopic approach, *n* (%)					0.60
Straight laparoscopy	65 (75.6)	86 (78.9)	6 (75.0)	4 (100)	
Single incision	12 (14.0)	13 (11.9)	0 (0)	0 (0)	
Hand-assisted	5 (5.8)	4 (3.7)	2 (25.0)	0 (0)	
Robotic	4 (4.7)	6 (5.5)	0 (0)	0 (0)	
Anastomotic technique, *n* (%)					0.34
Double stapled	235 (99.2)	337 (98.8)	40 (100)	19 (95.0)	
Mucosectomy and hand-sewn	2 (0.84)	4 (1.2)	0 (0)	1 (5.0)	
Pouch type, *n* (%)					0.18
J-pouch	237 (100)	340 (99.7)	39 (97.5)	20 (100)	
S-pouch	0 (0)	1 (0.3)	1 (2.5)	0 (0)	
Op. time, min, mean (SD)	190.1 (69.1)	195.8 (71.9)	209.1 (73.4)	198.7 (67.7)	0.43
Op. blood loss, mL, mean (SD)	201.2 (140.9)	248.4 (161.4)	296.3 (209.2)	281.3 (175.2)	<0.001

CP completion proctectomy, *TPC* total proctocolectomy, *IPAA* ileal pouch-anal anastomosis

complications were 18.6, 26.7, 47.5, and 40 % in the groups 1, 2, 3 and 4, respectively.

In order to adjust for relevant covariates, the variables that were found to be statistically different among the four groups (age, gender, preoperative albumin and Hgb levels, and intraoperative blood loss) were entered in a multivariate logistic regression model. OR and 95 % confidence intervals were computed for the primary and secondary outcomes, comparing patients from each group to the control group (group 1). The results of multivariate analysis for the primary outcomes are presented in Table 4. Compared with group 1, group 4 was associated with the highest AL OR (OR=8.98), followed by group 2 (OR=3.67), and group 3 had the highest organ/space SSI OR (OR=8.53), followed by group 4 (OR=7.50). With respect to the secondary outcomes (Table 5), the largest odds ratio for overall SSIs occurred in group 4 (OR=6.11), followed by group 3 (OR=5.98), and the largest OR for overall infectious complications occurred in group 3 (OR=4.50), followed by group 4 (OR=3.69).

Compared to group 2, group 3 had higher rates of organ/space SSI (OR=4.34) and overall SSI (OR=2.81). No statistical differences were observed with respect to risk of AL and overall infectious complications between these two groups.

Table 3 Distribution of postoperative infectious complications

Postoperative complications	Study groups				Total n=638
	Group 1 (Hgb≥10 non-transfused) n=237	Group 2 (Hgb≥7 and <10 non-transfused) n=341	Group 3 (Hgb≥7 and <10 transfused) n=40	Group 4 (Hgb<7 transfused) n=20	
Overall SSI	30 (12.7)	59 (17.3)	15 (37.5)	7 (35.0)	111 (17.4)
Superficial	17 (7.2)	36 (10.6)	4 (10.0)	3 (15.0)	60 (9.4)
Deep	2 (0.8)	9 (2.6)	1 (2.5)	0 (0)	12 (1.9)
Organ/space	13 (5.5)	23 (6.7)	11 (27.5)	5 (25)	52 (8.2)
Anastomotic leak	8 (3.4)	21 (6.2)	4 (10.0)	3 (15.0)	36 (5.6)
Pouch leak	1 (0.4)	5 (1.5)	2 (5.0)	0 (0)	8 (1.3)
Fistula/sinus	5 (2.1)	11 (3.2)	3 (7.5)	2 (10.0)	21 (3.3)
UTI	8 (3.4)	23 (6.7)	4 (10.0)	0 (0)	35 (5.5)
Pneumonia	1 (0.4)	1 (0.3)	2 (5.0)	0 (0)	4 (0.6)
Sepsis	0 (0)	4 (1.2)	5 (12.5)	0 (0)	9 (1.4)
Other infections	5 (2.1)	13 (3.8)	0 (0)	0 (0)	18 (2.8)
Overall infectious complications	44 (18.6)	91 (26.7)	19 (47.5)	8 (40.0)	162 (25.4)
Mortality	0 (0)	0 (0)	1 (2.5)	0 (0)	1 (0.2)

SSI surgical site infection, *UTI* urinary tract infection

Discussion

In surgical practice, the oldest and most famous indication for blood transfusion is the "10/30" rule which suggests that Hgb should be maintained at or above 10 g/dL (liberal transfusion practice). This rule was first proposed by Adams and Lundy in 1942 and was based on the assumption that anemia is tolerated poorly and transfusions improve outcomes.[10] However, since the first description of the link between blood transfusion and postoperative infectious complications,[15] there has been a growing body of evidence which suggests that transfusion in the perioperative period is associated with higher rate of infectious complications.[2,5,6,16]

In light of such findings, the liberal transfusion practice has been challenged by a number of randomized studies using restrictive strategies. These studies included either cardiac, vascular, or orthopedic patients, and the authors concluded that compared to the liberal practice, the restrictive strategy does not adversely affect patient outcomes.[7,8,17] However, there is no published data to date on the impact of the lower transfusion threshold on postoperative infectious complications in colorectal surgery patients.

Table 4 Multivariable logistic regression analysis evaluating possible risk factors associated with anastomotic and organ/space SSIs

Risk factors	Anastomotic leak		Organ/space SSI	
	Odds ratio (95 % CI)	P value	Odds ratio (95 % CI)	P value
Group		0.04		0.001
2 vs 1	3.67 (1.29–10.39)	0.01	1.96 (0.81–4.73)	0.13
3 vs 1	4.86 (0.85–27.86)	0.08	8.53 (2.59–28.00)	0.0004
4 vs 1	8.98 (1.41–57.12)	0.02	7.50 (1.62–34.69)	0.001
3 vs 2	1.33 (0.28–6.32)	0.72	4.34 (1.58–11.93)	0.004
Age[a]	0.97 (0.94–1.00)	0.12	0.97 (0.94–1.00)	0.05
Gender (female vs male)	0.50 (0.19–1.30)	0.16	0.72 (0.33–1.58)	0.41
Preop alb level[b]	0.43 (0.18–1.04)	0.06	1.14 (0.51–2.56)	0.74
Preop Hgb level[c]	1.38 (1.04–1.81)	0.02	1.24 (0.99–1.57)	0.07
Operative blood loss[d]	0.99 (0.99–0.1)	0.02	0.99 (0.99–1.00)	0.47

[a] 1-year increase

[b] 1-mg/dL increase

[c] 1-g/dL increase

[d] 1-mL increase

Table 5 Multivariable logistic regression analysis evaluating possible risk factors associated with overall SSIs and overall infectious complications

Risk factors	Overall SSIs		Overall infectious complications	
	Odds ratio (95 % CI)	*P* value	Odds ratio (95 % CI)	*P* value
Group		0.0008		0.003
2 vs 1	2.13 (1.13–4.02)	0.02	2.38 (1.36–4.15)	0.002
3 vs 1	5.98 (2.29–15.59)	0.0003	4.50 (1.86–10.93)	0.0009
4 vs 1	6.11 (1.73–21.62)	0.005	3.69 (1.09–12.62)	0.04
3 vs 2	2.81 (1.24–6.39)	0.01	1.89 (0.88–4.07)	0.1
Age[a]	0.98 (0.96–0.99)	0.03	0.98 (0.96–0.99)	0.03
Gender (female vs male)	0.88 (0.50–1.54)	0.65	1.62 (0.99–2.62)	0.05
Preop albumin level[b]	0.72 (0.41–1.26)	0.24	0.71 (0.43–1.18)	0.19
Preop Hgb level[c]	1.26 (1.06–1.50)	0.008	1.28 (1.09–1.50)	0.002
Operative blood loss[d]	1 (0.99–1.00)	0.83	1.00 (0.99–1.00)	0.36

[a] 1-year increase

[b] 1-mg/dL increase

[c] 1-g/dL increase

[d] 1-mL increase

In our clinical practice, symptoms of anemia and/or signs of hemodynamic instability are the main indications for transfusion rather than Hgb level alone. In the absence of anemia-related symptoms and hemodynamic instability, as a general rule, transfusion is not administered if perioperative Hgb level is at least 10 g/dL. On the other hand, transfusion is almost always indicated when Hgb<7 g/dL. Of note, all the patients with a Hgb level less than 7 g/dL received transfusion in this study. Although there is variation in the Hgb threshold (7 to 9 g/dL), the approach of considering a Hgb threshold of 7 g/dL is supported by recent systematic reviews.[11,12] Considering groups 2 and 3 with a total of 381 patients in whom Hgb level ≥7 g/dL and <10 g/dL, we found that restrictive strategy was the preferred practice as the majority of the patients (group 2 with 341 patients, 90 %) did not receive transfusion in this population. Nevertheless, we still identified 40 patients who received transfusions (group 3), and in our opinion, these transfusions were unnecessary.

We studied a large number of patients (638) with UC undergoing IPAA to determine if restrictive transfusion strategy could reduce the postoperative infectious complications. As seen from the risk-adjusted group comparisons, our findings indicate that there was a trend toward a higher likelihood of AL and organ/space SSIs as Hgb level drops and patients received transfusions. This was also the case for our secondary outcomes, overall SSIs, and overall infectious complications.

The most notable finding was that, although no significant differences were detected between groups 3 and 2 with respect to the rates of AL and overall infectious complications, unnecessary transfusion (group 3) was associated with significantly higher likelihood of organ/space SSIs and overall SSIs as opposed to non-transfusion (group 2). These results support our contention that, compared to liberal transfusion strategy, restrictive strategy with a Hgb threshold level as low as 7 g/dL indeed results in less postoperative infections in UC patients undergoing RP/IPAA.

Considering perioperative characteristics, one might question that compared to group 2, group 3 with a higher incidence of diabetes mellitus, cardiac, vascular, liver and lung disease, preoperative lower albumin and Hgb levels, a higher percentage of steroid use and total proctocolectomy procedures, longer operative times, and more intraoperative blood loss should have already a higher infectious complication rate (Tables 1 and 2). However, univariable analysis showed no statistical differences among the four groups in terms of perioperative characteristics except age, gender, preoperative albumin and Hgb levels, and operative blood loss. Additionally, the statistically significant variables were adjusted in a multivariable analysis model. Thus, our analysis was as balanced as possible in terms of fair group comparisons.

We conducted this study in UC patients undergoing IPAA surgery since this population carries a higher risk of developing postoperative infections. These patients may have preexisting immunosuppression due to poor nutritional status and administration of immunosuppresants. Besides, surgical trauma caused by a major procedure like IPAA has a further depressive effect on the immune system.[6,18] As expected, these factors contributed to an overall infectious complication rate of 25 % and overall SSI rate of 17.4 % (superficial SSI=9.4 %, deep SSI=1.9 %, organ/space SSI=8.2 %) in this study. Similar rates were also reported by Uchino et al. in a study including 192 patients with UC undergoing IPAA surgery (overall SSI=14.1 %).[18] These rates are somewhat higher than those previously reported for other elective colorectal surgical procedures. In a prospective study of 2809 patients undergoing resection of the colon and rectum, Tang et al.

reported an overall SSI rate of 4.7 % (superficial SSI=3 %, organ/space SSI=2 %).[16]

The detrimental effects of transfusion are believed to be mediated by the immunosuppressive features of the transfused blood. The mechanism of this immunosuppression is not well understood, but it has been demonstrated that transfusion is associated with diminished cell-mediated immune response, decreased T helper to suppressor ratio, decreased natural killer cell activity, and decreased macrophage antigen presentation.[4,19] In addition to these, perioperative blood transfusion in patients with inflammatory bowel disease leads to depression of peripheral lymphocytes and T cells.[20]

Although the safety of blood products has improved, other transfusion risks still exist. These risks including transfusion reactions and transmission of pathogens (hepatitis B and C, HIV) have been largely reduced through advancements in blood banking. However, these risks are not likely to ever be completely eliminated.[21] Clearly, implementing a lower Hgb threshold could lead to lesser utilization of transfusion, reducing these risks.

There are several options which can be used to reduce transfusion-related infectious complications. It has been suggested that use of leukocyte-depleted blood may eliminate immunosuppression.[22] However, randomized trials have failed to confirm that leukocyte depletion reduces the risk of infectious complications.[23,24] Another option is autologous transfusion. This method is useful in patients with a normal Hgb; however, anemia is a common finding in UC patients undergoing surgery, restricting the use of this method in these patients. In addition, no difference in the risk of postoperative infection between recipients of allogeneic versus autologous blood transfusion is reported in a meta-analysis.[25] Lastly, preoperative management of anemia with erythropoietin or iron could be employed, but this may take a number of weeks before surgery.

This study has several limitations. First, there is a potential for selection bias due to its retrospective nature and non-randomized design. A prospective randomized trial would give a better idea on the role of restrictive transfusion strategy in the prevention of infectious complications. Second, the lack of association of the severity of disease with infectious complications is another limitation. Anemia could be a reflection of the severity of disease; therefore, transfusions might be commonly required in patients with severe disease. Third, there is no data on the units of red blood cells and amount of crystalloid solutions administered in this study. There is evidence from enhanced recovery after surgery (ERAS) protocols that these volumes are critical for good outcomes. Finally, the present data do not allow us to conclude on the safety of the restrictive transfusion threshold in patients with cardiac co-morbidity since these patients were excluded in this study. Nevertheless, a randomized trial showed that a lower transfusion threshold (Hgb 8 g/dL) does not adversely affect outcomes in patients undergoing coronary artery bypass graft surgery.[8]

In conclusion, data from this study support the hypothesis that blood transfusion increases the occurrence of infectious complications in UC patients undergoing IPAA surgery. Therefore, for hemodynamically stable surgical patients, we suggest considering transfusion at a Hgb of 7 g/dL, with the threshold based on the value established as safe in the reported clinical trials.

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Primary Discussant

James W. Fleshman, M.D. (Dallas, TX): I want to thank the authors for the opportunity to preview the manuscript and the SSAT for the opportunity to comment. Congratulations Dr. Gorgun on your presentation. The idea of withholding transfusion above the level of Hgb of 7 g/dL is sound for many reasons. The idea that infectious complications may directly result from unwarranted transfusion is difficult to prove. The group from Cleveland Clinic has given us some insights but, in my opinion, has not been able to prove their point, and as they admit in their discussion, a prospective trial with randomization, to eliminate differences in the study groups, may be needed to answer the question definitively.

The issues of disease severity and operative difficulty are indeed the reasons I have doubts that transfusion is the cause of the higher infection rate. Group 3 (transfused patients with Hgb 7 to 10) with a majority of women, low albumin and preoperative anemia, and higher blood loss intraoperatively also had a higher percentage of steroid use and a higher number of total proctocolectomy procedures. Operative times were longer, and these patients, who had a higher incidence of liver, lung, vascular, and cardiac disease, should be expected to have a higher infectious complication rate than group 2. These factors, I believe, should be considered cumulatively. I would refer you to Table 1.

The comparison of anastomotic leak and organ space infections seems to be more influenced by preoperative albumin and hemoglobin levels and operative blood loss (an indicator of operative difficulty).

I would like to ask the authors the following questions:

1. How many units of blood or cells were transfused and how much intraop and postop crystalloid was given? There is evidence from ERAS that lower volumes are critical to good outcomes.

2. How many patients were transfused because they were symptomatic from hypovolemia or poor oxygen delivery in group 3 and were any receiving pressure support?

3. Were emergency operations in patients with fulminant colitis and compromised colon on biologic immunosuppression included in the patient population and were they equally distributed amongst the groups?

Thank you again for the opportunity to review and comment.

Closing Discussant

Dr. Gorgun: Thank you, Dr. Fleshman for reviewing our manuscript and for your valuable comments. As you indicated, the idea of withholding blood transfusion above the level of a hemoglobin level 7 g/dL is certainly sound for many reasons; however, whether infectious complications directly result from unwarranted transfusion is difficult to prove. Our study aimed to answer this specific question in IBD patients after pouch surgery, and this theory was more strongly confirmed based on the results of our study. We designed the study and the analysis to be able to answer this question as objectively as possible. With no doubt, a prospective randomized study could answer this question in the ideal world accurately; however, needless to say conducting such a study would not be very easy.

Your point on group 3 (Hb level btw 7 and 10 and had blood transfusion) having higher risk factors as compared to group 2 is well taken. However, we know that female gender, higher in group 3, is a low risk factor for anastomotic leak and there was a clinically minimal meaningful difference in preoperative albumin and hemoglobin levels between the two groups. Regarding the all other factors, univariable analysis showed no statistical differences. Additionally, the covariates that were found to be statistically different among the groups were adjusted in the multivariable analysis. Thus, our analysis for group comparisons was as balanced as possible in terms of fair comparison.

Now, I would like to address your each question:

1. We did not extract data regarding the amount of blood transfusion and postoperative crystalloid solution administered. So, we do not have any specific answer to this question.

2. In group 3, no patient had any signs or symptoms due to hypovolemia. Rather, patients in group 3 were transfused solely based on the perioperative lowest hemoglobin level which was between 7 and 10 mg/dL. In addition, no patients in this group received pressure support. Hemodynamic instability was an exclusion criteria for group 3.

3. All the emergency operations due to factors such as fulminant colitis or compromised colon for any reason were excluded in all the groups.

Thank you again for your thorough review and comments.