Diverticulitis in immunosuppressed patients: A fatal outcome requiring a new approach?

Andreas Brandl, MD
Theresa Kratzer, MD
Reinhold Kafka-Ritsch, MD, PhD
Eva Braunwarth, MD
Christian Denecke, MD, PhD
Sascha Weiss, MD
Georgi Atanasov, MD
Robert Sucher, MD, PhD
Matthias Biebl, MD, PhD
Felix Aigner, MD, PhD
Johann Pratschke, MD, PhD
Robert Öllinger, MD, PhD

Accepted for publication Mar. 29, 2016

Correspondence to:
A. Brandl
Department of Visceral, Transplant and Thoracic Surgery
Medical University Innsbruck
Anichstraße 35, 6020 Innsbruck, Austria
Andreas.Brandl@charite.de

DOI: 10.1503/cjs.012915

Background: Diagnosis and treatment of diverticulitis in immunosuppressed patients are more challenging than in immunocompetent patients, as maintenance immunosuppressive therapies may mask symptoms or impair the patient's ability to counteract the local and systemic infective sequelae of diverticulitis. The purpose of this study was to compare the in-hospital mortality and morbidity due to diverticulitis in immunosuppressed and immunocompetent patients and identify risk factors for lethal outcomes.

Methods: This retrospective study included consecutive in-patients who received treatment for colonic diverticulitis at our institution between April 2008 and April 2014. Patients were divided into immunocompetent and immunosuppressed groups. Primary end points were mortality and morbidity during treatment. Risk factors for death were evaluated.

Results: Of the 227 patients included, 15 (6.6%) were on immunosuppressive therapy for solid organ transplantation, autoimmune disease, or cerebral metastasis. Thirteen of them experienced colonic perforation and showed higher morbidity (p = 0.039). Immunosuppressed patients showed longer stays in hospital (27.6 v. 14.5 d, p = 0.016) and in the intensive care unit (9.8 v. 1.1 d, p < 0.001), a higher rate of emergency operations (66% v. 29.2%, p = 0.004), and higher in-hospital mortality (20% v. 4.7%, p = 0.045). Age, perforated diverticulitis with diffuse peritonitis, emergency operation, C-reactive protein > 20 mg/dL, and immunosuppressive therapy were significant predictors of death. Age (hazard ratio [HR] 2.57, p = 0.008) and emergency operation (HR 3.03, p = 0.003) remained significant after multivariate analysis.

Conclusion: Morbidity and mortality due to sigmoid diverticulitis is significantly higher in immunosuppressed patients. Early diagnosis and treatment considering elective sigmoid resection for patients with former episodes of diverticulitis who are wait-listed for transplant is crucial to prevent death.

Contexte : Le diagnostic et le traitement des diverticulites sont plus délicats chez les patients immunosupprimés que chez les patients immunocompétents, étant donné que les thérapies immunosuppressives d'entretien peuvent masquer les symptômes ou réduire la capacité du patient à lutter contre les infections locales ou systémiques pouvant découler de la diverticulite. La présente étude avait pour but de comparer les taux de mortalité et de morbidité en milieu hospitalier associés à la diverticulite chez des patients immunosupprimés et immunocompétents et de cerner les facteurs de risque de décès.

Méthodes : Cette étude rétrospective portait sur des patients traités consécutivement pour une diverticulite du côlon hospitalisés dans notre établissement entre avril 2008 et avril 2014. Les patients ont été divisés en 2 groupes : immunocompétents et immunosupprimés. Les résultats primaires à l'étude étaient la mortalité et la morbidité pendant le traitement, et nous avons évalué les facteurs de risque de décès.

Résultats : Parmi les 227 patients retenus, 15 (6,6 %) suivaient une thérapie immunosuppressive en raison d'une greffe d'organe plein, d'une maladie auto-immune ou de métastases cérébrales. Parmi eux, 13 ont subi une perforation du côlon et présentaient un taux de morbidité supérieur (p = 0,039). Les patients immunosupprimés sont restés plus longtemps à l'hôpital (27,6 j c. 14,5 j, p = 0,016) et à l'unité de soins intensifs (9,8 j c. 1,1 j, p < 0,001), et présentaient des taux supérieurs d'intervention d'urgence (66 % c. 29,2 %, p = 0,004) et de mortalité pendant l'hospitalisation (20 % c. 4,7 %, p = 0,045). L'âge, une diverticulite perforée avec péritonite diffuse, une opération d'urgence, un résultat de protéine C réactive > 20 mg/dL et une thérapie immunosuppressive étaient des prédicteurs de décès significatifs. L'âge (rapport de risque [RR] 2,57, p = 0,008) et une opération d'urgence (RR 3,03, p = 0,003) sont demeurés significatifs après l'exécution d'une analyse multivariée.

Conclusion : Les taux de morbidité et de mortalité attribuables à une diverticulite du sigmoïde sont significativement plus élevés chez les patients immunosupprimés que chez les autres patients. Afin de prévenir les décès, il est essentiel de diagnostiquer et de traiter rapidement, possiblement par résection du sigmoïde, les patients ayant déjà souffert de diverticulite qui sont sur une liste d'attente pour une greffe.

Sigmoid diverticulitis is a frequent disease in Western countries, and its incidence is rising.[1] Treatment depends on the severity of the disease, which can vary from slightly symptomatic diverticulosis to perforated diverticulitis with fecal peritonitis.

Indications for solid organ and bone marrow transplantation continue to expand, and the number of patients receiving maintenance immunosuppressive therapy for this or other indications, such as autoimmune diseases or cancer, is increasing. Nonetheless, no specific clinical management indications for sigmoid diverticulitis in this subpopulation have yet been found nor have special treatment strategies for these patients been established. In our experience, diagnosis and treatment of diverticulitis in immunosuppressed (IS) patients are more challenging than in immunocompetent (IC) patients, as maintenance immunosuppressive therapies may on one hand mask symptoms and on the other impair the patient's ability to counteract the local and systemic infective sequelae of diverticulitis. The incidence of free peritoneal perforation or complicated disease is increasing in IS patients compared with IC patients.[2,3] Since a number of studies have shown high mortality associated with diverticulitis in IS patients, particularly in transplant recipients,[4–6] clinicians have been inclined to offer elective surgery after a single episode of uncomplicated disease.[7] A recently published study showed similar morbidity and mortality in elective surgery of the colon in kidney transplant recipients,[8] which supports the idea of preventive elective surgery for this high-risk group.

The aim of our study was to investigate morbidity and mortality in IS patients and to evaluate potential risk factors for lethal disease in these patients.

Methods

We performed a retrospective study of consecutive patients who received inpatient treatment for colonic diverticulitis in our department between April 2008 and April 2014.

Demographic data, grade of diverticulitis (Hansen/Stock or Hinchey classification),[9,10] diagnostic methods, antibiotic treatment, change of antibiotic treatment, interventional and operative treatment, maximum C-reactive protein (CRP), number of episodes, immunosuppressive therapy, immunosuppression at admission, reason for immunosuppression, days in the intensive care unit (ICU) and days in hospital, complications (surgical, pulmonary, gastrointestinal, cardiovascular, allergic, urinary tract infection, renal failure, neurologic) and death during hospital stay were assessed by retrospective chart analysis. Smoking habits and number of diverticulitis episodes were assessed at admission by the front-line clinician.

The study population was divided in 2 groups: IS patients undergoing immunosuppressive therapy and IC patients without immunosuppressive medication. Kidney transplant recipients with nonfunctioning grafts and who were not receiving immunosuppression were considered IC patients.

Inclusion and exclusion criteria

All adult patients who received inpatient treatment for diverticulitis of grade 1–3 (Hansen/Stock classification) of the sigmoid colon at our department were included. We excluded patients with asymptomatic diverticulosis and patients younger than 18 years.

Diagnosis and treatment of diverticulitis

The diagnosis of sigmoid diverticulitis was based on abdominopelvic computed tomography (CT) scan, ultrasound or contrast radiography. The indications for surgery in the emergency, early elective and elective surgery groups were consistent with established international guidelines.[7,11] An emergency operation was defined as surgery immediately after admission, early elective surgery was defined as surgery within 1 week after admission, and elective surgery was defined as a scheduled admission with programmed surgical resection.

Patients who had diffuse peritonitis or who were deemed to have extensive intraoperative contamination underwent damage control procedures with resection of the perforated colonic segment, open abdomen treatment with insertion of an abdominal vacuum sponge system followed by a second look operation 48 hours later, depending on whether an anastomosis or a colostomy would be performed.[12]

Primary end point

The primary end point was in-hospital mortality and morbidity during treatment. Furthermore, potential and known risk factors for death in all patients were analyzed.

Statistical analysis

We report categorical variables as frequencies (%) and quantitative variables as means ± standard deviation. We compared IC and IS patients with respect to categorical

variables using the Fisher exact test or the Pearson χ^2 test, while comparisons with respect to quantitative variables were performed using the Wilcoxon rank sum test. We considered results to be significant at $p < 0.05$. Logistic regression analysis was performed using the forward conditional method to test for intervariable relations. Factors that yielded a $p < 0.05$ in univariate analysis were assessed in the logistic regression model using the forward method. Statistical analyses were performed using SPSS software version 22.0 (SPSS, IBM Corp.).

Results

In total, 227 patients received inpatient treatment for diverticulitis during the observation period: 15 IS and 212 IC. The diagnosis of sigmoid diverticulitis was based on abdominopelvic CT scan in 80.6% of the patients, on ultrasound in 8.8%, and on contrast radiography in 9.2%. Fifteen (6.6%) patients were under immunosuppressive medication at the time of hospital admission or after solid organ transplantation. Five patients were treated by oral corticosteroids for vasculitis ($n = 2$), systemic lupus erythematosus ($n = 1$), myelitis of unknown origin ($n = 1$), or cerebral and hepatic metastasis of non–small cell lung cancer ($n = 1$).

All 10 of the transplant recipients were maintained on immunosuppressive therapy perioperatively. Immunosuppressive regimens varied to some degree according to the transplanted organ. Kidney transplant recipients received tacrolimus or cyclosporine, with or without mycophenolate mofetil and steroids. One liver transplant recipient was treated with maintenance tacrolimus only. Four lung transplant recipients received cyclosporin with or without mycophenolate mofetil or azathioprine with or without prednisone.

Table 1. Patient demographics and parameters comparing immunosuppressed with immunocompetent patients

Characteristic	Group; no. (%) or mean ± SD		*p* value	Characteristic	Group; no. (%) or mean ± SD		*p* value
	IS (n = 15)	IC (n = 212)			IS (n = 15)	IC (n = 212)	
Male sex	10 (6.7)	97 (45.8)	0.18	Maximum CRP, mg/dL	22.9 ± 10.6	17.8 ± 11.7	0.11
Age, yr	63.4 ± 12.2	62.1 ± 15.5	0.75	Therapy			
Smoker	1 (6.7)	55 (25.9)	0.12	Nonoperative	5 (33.3)	113 (53.3)	0.18
Comorbidities				Interventional (drain)	0	2 (0.9)	1.0
Diabetes	3 (20.0)	20 (9.4)	0.18	Operative	10 (66.7)	97 (45.8)	0.18
COPD	0	12 (5.7)	0.43	Elective	0	21 (9.9)	0.37
Hypertension	5 (33.3)	90 (42.5)	0.34	Urgent	0	14 (6.6)	0.61
CHD	0	29 (13.7)	0.12	Emergency	10 (66.7)	62 (29.2)	0.004
Renal insufficiency	3 (20.0)	20 (9.5)	0.19	Abdominal vacuum therapy	6 (40.0)	46 (21.7)	0.12
Obesity	2 (13.3)	22 (10.4)	0.49	Discharge with anus praeter	4 (26.7)	25 (16.5)	0.24
Grade of diverticulitis (Hansen/Stock)			0.039	Antibiotic switch	3 (20.0)	50 (23.6)	0.75
I	1 (6.7)	64 (30.2)		Complications*			
IIa	1 (6.7)	9 (4.2)		Surgical	4 (26.7)	26 (12.3)	0.11
IIb	7 (46.7)	74 (34.9)		Pulmonary	5 (33.3)	10 (4.7)	< 0.001
IIc	6 (40.0)	41 (19.3)		Cardiovascular	2 (13.3)	7 (3.3)	0.05
III	0	24 (11.3)		Gastrointestinal	1 (6.7)	4 (1.9)	0.22
Diagnostic tool			0.17	Allergic	0	2 (0.9)	0.71
Radiography	1 (6.7)	2 (0.9)		Urinary tract infection	0	5 (2.4)	0.55
Ultrasound	0	20 (9.4)		Renal failure	2 (13.3)	3 (1.4)	0.002
CT scan	14 (93.3)	169 (79.7)		Neurologic	0	3 (1.4)	0.64
Contrast radiography	0	18 (8.5)		Stay in ICU, d	9.8 ± 16.4	1.2 ± 4.2	< 0.001
Colonoscopy	0	2 (0.9)		Return to solid food, d	6.2 ± 7.5	6.1 ± 6.4	0.96
MRI scan	0	1 (0.5)		Discharge, d	27.6 ± 23.5	14.5 ± 19.9	0.016
No. of episodes			0.32	Death in hospital, no.	3 (20.0)	10 (4.7)	0.045
1	14 (93.3)	158 (76.7)					
2	1 (6.7)	19 (9.2)					
3	0	22 (10.7)					
4	0	4 (1.9)					
5	0	3 (1.5)					

CHD = congestive heart disease; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CT = computed tomography; IC = immunocompetent; ICU = intensive care unit; IS = immunosuppressed; MRI = magnetic resonance imaging; SD = standard deviation.

*Multiple complications possible per patient.

Patient, therapeutic, and diagnostic characteristics are shown in Table 1. Baseline patient characteristics and comorbidities did not differ between IS and IC patients.

Morbidity and mortality

A higher rate of complicated diverticulitis (i.e., Hansen/Stock ≥ 2b or Hinchey ≥ 2, $p = 0.039$) and consequentially a higher rate of emergency operations (66.7% v. 29.2%, $p = 0.004$) were observed in IS patients than in IC patients. This resulted in a dramatically longer stay in the ICU (9.8 ± 16.4 d v. 1.2 ± 4.2 d, $p < 0.001$) and a significantly longer hospital stay (27.6 ± 23.5 d v. 14.5 ± 19.9 d, $p = 0.016$). Examining the complication rate during the hospital stay, IS patients experienced pulmonary complications (33.3% v. 4.7%, $p < 0.001$) and renal failure (13.3% v. 1.4%, $p = 0.002$) more frequently than IC patients, whereas urinary tract infections ($p = 0.55$) and surgical ($p = 0.11$), cardiovascular ($p = 0.05$), gastrointestinal ($p = 0.22$), allergic ($p = 0.71$) and neurologic ($p = 0.64$) complications occurred equally in the groups. Four (26.7%) IS patients were discharged with an anus praeter compared with 25 (16.5%) patients in the IC group ($p = 0.24$). Hospital mortality was increased in IS (20%) compared with IC patients (4.7%; $p = 0.045$). A comparison of Hansen/Stock and Hinchey diverticulitis classifications is shown in Table 2.

Risk factors

Univariate analysis of potential risk factors associated with in-hospital mortality was statistically significant for age ($p = 0.008$), perforated diverticulitis with diffuse peritonitis ($p = 0.007$), emergency operation ($p = 0.001$), CRP > 20 mg/dL ($p = 0.049$) and immunosuppression ($p = 0.049$; Table 3).

Linear regression analysis revealed age (OR 2.57, $p = 0.008$) and emergency operation (OR 3.03, $p = 0.003$) as significant parameters.

Outcome of IS patients

Patient characteristics, therapy, and outcome of IS patients are shown in Table 4. Sigmoid perforation developed in 1 patient during the same hospital stay in which lung transplantation was carried out. He died of sepsis as a consequence of anastomotic leakage 2 weeks after transfer to a rehabilitation hospital. Two of the 3 IS patients who died in hospital died during their first episode of diverticulitis. Two of the 5 IS patients treated with anastomosis (40%)

Table 2. Comparison between Hansen/Stock and Hinchey classification

Hansen and Stock		Hinchey	
0	Diverticulosis	—	
I	Acute uncomplicated diverticulitis	—	
II	Acute complicated diverticulitis	—	
a	Phlegmon, peridiverticulitis	I	Pericolic abscess or phlegmon
b	Abscess, sealed perforation	II	Pelvic, intraabdominal or retroperitoneal abscess
c	Free perforation	III	Generalized purulent peritonitis
—		IV	Generalized fecal peritonitis
III	Chronic recurrent diverticulitis	—	

Table 3. Univariate and multivariate analysis of factors associated with death in hospital

	Univariate; no. (%) or mean ± SD			Multivariate	
Factor	All	Death	*p* value	OR (95% CI)	*p* value
Age, yr	62.2 ± 15.3	73.8 ± 10.5	0.008	2.57 (0.001 to 0.004)	0.008
Male sex	107 (47.1)	7 (6.5)	0.41	0.63 (–0.042 to 0.081)	0.95
Diabetes	23 (10.1)	1 (4.3)	0.61	–0.45 (–0.123 to 0.077)	0.77
COPD	12 (5.3)	0	0.48	–0.87 (–0.189 to 0.073)	0.74
Hypertension	95 (41.9)	5 (5.3)	0.52	0.67 (–0.040 to 0.082)	0.92
Renal insufficiency	23 (10.2)	2 (8.7)	0.39	0.19 (–0.093 to 0.112)	0.74
CHD	29 (12.8)	1 (3.4)	0.48	–0.14 (–0.106 to 0.092)	0.64
Obesity	24 (10.6)	1 (4.2)	0.59	–0.36 (–0.117 to 0.081)	0.49
Immunosuppression	15 (6.6)	3 (20.0)	0.045	1.85 (–0.007 to 0.232)	0.14
Solid organ transplant	10 (4.4)	2 (20.0)	0.11	–0.01 (–0.252 to 0.252)	0.95
Emergency operation	72 (31.7)	10 (13.9)	0.001	3.03 (0.035 to 0.163)	0.003
Hansen/Stock > 2b	47 (20.7)	7 (14.9)	0.007	1.51 (–0.017 to 0.128)	0.18
CRP > 20 mg/dL	95 (41.9)	9 (9.5)	0.049	–0.12 (–0.085 to 0.075)	0.88

CHD = congestive heart disease; CI = confidence interval; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; OR = odds ratio; SD = standard deviation.

Table 4. Descriptive data, therapy and outcome of immunosuppressed patients

Patient	Age, yr	Organ Tx	Years after Tx	Hansen/ Stock	Operative therapy	Damage control	No. episodes	IS therapy	Underlying disease	Complication	Days in ICU	Discharge day	Death in hospital
1	87	—	—	IIc	1) Sigmoid resection 2) Descendostomy	Yes	1	Methylprednisolone	Arteritis temporalis	Pneumonia	2	14	No
2	53	—	—	IIb	Hartmann procedure	No	1	Methylprednisolone	Myelitis unknown origin	Wound infection	0	42	No
3	42		—	IIb	—	—	1	Methylprednisolone	SLE	—	0	9	No
4	79	—	—	IIc	1) Sigmoid resection 2) Colorectostomy	Yes	1	Methylprednisolone	Cerebral vasculitis	—	1	14	No
5	72	—	—	IIb	—	—	2	Dexamethasone	NSCLC cerebral, hepatic metastasis	—	0	4	Yes
6	71	Kidney	4	IIb	1) Sigmoid resection 2) Colorectostomy, loop ileostomy	Yes	1	Tacrolimus, MMF, prednisolone	Kidney transplant	Sepsis, pleural effusion	4	87	Yes
7	47	Kidney	13–18	IIb	—	—	1	Tacrolimus, MMF, prednisolone	Kidney transplant	Acute renal failure	0	7	No
8	55	Kidney	9	IIb	Laparotomy, drainage	No	1	Cyclosporine, prednisolone	Kidney transplant	Forrest Ia bleeding stomach	10	34	No
9	76	Kidney	0.5	IIc	1) Lavage, suture 2) Sigmoid resection colorectostomy	Yes	1	Cyclosporine, MMF, prednisolone	Kidney transplant	—	35	35	No
10	55	Kidney	18	IIc	1) Sigmoid resection 2) Descendorectos-tomy	Yes	1	Hydrocortisone	Kidney transplant	Anastomotic leakage	39	57	No
11	58	Kidney	23–30	IIa	—	—	1	Cyclosporine, prednisolone	Kidney transplant	—	0	6	No
12	67	Liver	11	I	—	—	1	Tacrolimus	Liver transplant	—	0	4	No
13	62	Lung	2	IIc	Hartmann procedure	No	1	Cyclosporin	Lung transplant	—	5	22	No
14	60	Lung	0.1	IIb	1) Sigmoid resection, descendorectostomy 2) Hartmann procedure	No	1	Cyclosporin, azathioprine, methylprednisolone	Lung transplant	Anastomotic leakage	1	38	No*
15	64	Lung	0.6	IIc	1) Sigmoid resection 2) Descendorectos-tomy	No	1	Cyclosporin, MMF	Lung transplant	Pneumonia	41	41	Yes

ICU = intensive care unit; IS = immunosuppression; MMF = mycophenolate mofetil; NSCLC = non–small cell lung cancer; SLE = systemic lupus erythematosus; Tx = transplant.

*Patient died 2 weeks after transfer to rehabilitation hospital.

experienced an anastomotic leakage after colorectostomy compared with 9 of 97 IC patients treated with anastomosis (9.3%, $p = 0.031$) and were treated with colostomy.

Discussion

Immuniosuppressed patients show an increased incidence of diverticulitis (1%) compared with the general population (0.02%).[13] Studies have shown that among patients with diverticulosis diagnosed before transplantation, about 16% of cases developed under immunosuppression.[14]

We show that not only is the incidence of diverticulitis in these patients increased, the severity of the disease is also much higher than in the non-IS population, and the consequences are life threatening. Immunosuppression and steroid intake are known risk factors for perforated diverticulitis.[15,16]

Given the fatal outcome of diverticulitis in IS patients, there is a need to reconsider a strategy to reduce mortality. First, it is crucial to establish the correct diagnosis as soon as possible. Most common symptoms, such as abdominal pain, abdominal tenderness and leukocytosis with or without fever, should immediately lead to a CT scan to distinguish complicated from uncomplicated diverticular disease. A CT scan is the tool that best directs treatment during the initial acute episode of diverticulitis and is less subject to operator interpretation than an ultrasound.[17] Early diagnosis guides prompt therapy and is the most important variable at disease onset, particularly for IS patients.

Second, the question arises whether elective surgical resection of the sigmoid colon should be recommended in high-risk IS patients. Our findings are consistent with data published by others,[1,18] thus we suggest that the guidelines and recent recommendations for the treatment of complicated diverticulosis[11,19] should specify that recurrent and chronic diverticulitis be indications for elective sigmoid resection and should not be applied for patients under immunosuppression regimes.

In these patients, diverticulosis per se may be the indication for elective surgery, considering that emergency operations occur in 80%–90% at the first episode.[20] This thesis is underlined by several other studies, which have shown that complicated diverticulitis most commonly occurred during the first episode rather than during recurrent episodes.[21–23] Therefore, the aim in IS patients is to avoid diverticulitis. Smoking and obesity are known to increase the incidence of diverticulitis and complicated diverticulitis[24–27]; in contrast physical activity prevents diverticulitis and reduces the risk of complicated diverticulitis.[28,29] The effects of nutrition habits on diverticulitis are controversial.[30–32] In contrast to lifestyle changes, operative therapies for diverticulitis seem effective because they are independent of patients' compliance. Several studies have shown that a "prophylactic" sigmoid resection can prevent future episodes of diverticulitis and emergency colostomy.[7,33] However, no such data are available for IS patients. The question that remains unanswered is whether or not to perform a sigmoidectomy, given that the rate of recurrent hospitalizations for patients with diverticulitis after nonoperative management (4%–13%)[34] is comparable to the rate in those who have had a colectomy (5%–11%).[19] Certainly, the risk for anastomotic leakage must be counterbalanced by the benefits of lowering the risk of diverticulitis. Reshef and colleagues[35] showed in a case-matched comparison that there was similar morbidity (29%) and mortality (0%) in IS kidney transplant recipients ($n = 14$) and the IC control group. A 1%–3% risk of anastomotic failures requiring "rescue colostomy" persists in elective surgery.[36,37] In contrast, in terms of comparable risks in elective surgery, Krysa and colleagues[38] showed that emergency colorectal surgery in patients who received renal replacement therapy resulted in an 81% overall complication rate, mortality of 26% and a substantial anastomotic leakage rate of 71% for primary anastomosis. Our study confirms the increased anastomotic leakage rate after emergency operations and suggests performing a protective loop ileostomy in case of colorectostomy.

Thus, we suggest that elective surgery should be carried out before the development of diverticulitis and probably before immunosuppression; however, this may not be feasible in patients wait listed for liver transplantation, as cirrhosis and portal hypertension are associated with a higher risk (up to 53%) of anastomotic leakage and postoperative mortality mainly due to postoperative infections.[39,40] There is a lack of data on liver transplant recipients and diverticulitis, which suggests that this condition is rare and could be explained by the relatively low and often steroid-free immunosuppression necessary in these patients compared with recipients of other solid organ transplants.

In patients wait listed for renal transplantation the perioperative risk in those underoing colorectal surgery is elevated. Stewart and colleagues[41] showed in a large nationwide in-patient sample database that kidney transplant recipients experienced significantly fewer complications and had lower morbidity and mortality after colorectal surgery than patients with end-stage renal disease. Interestingly, Halabi and colleagues[42] showed that the risk of anastomotic leakage in kidney transplant recipients in elective colorectal surgery was equal to that of the general population, whereas acute renal failure, wound complications, and mortality were higher. Summing up published data, the best time point to carry out elective colorectal surgery is after kidney transplantation, but before diverticulitis.

For those patients wait listed for lung or heart transplantation, the perioperative risk should likewise be assessed carefully. The incidence of acute diverticulitis in heart transplant patients is described to be between 1.4% and 4.2%.[2,43] A comparable, but slightly lower incidence of 0.7%–1.4% has been reported for lung transplant recipients.[44] Diverticulitis in lung transplant recipients occurs

early, most likely in the first 2 years after transplantation, due to high levels of immunosuppression.[45] These results could be confirmed by our study.

For patients requiring immunosuppression for non-transplant reasons, similarly, the best time point for elective resection should be determined depending on the intensity of immunosuppression.

Several authors have proposed screening for diverticular disease in patients as part of the pretransplant evaluation process,[46–49] though McCune and colleagues[50] showed that pretransplantation colonic screening of patients older than 50 years was ineffective in predicting post-transplantation colonic complications.

Limitations

Our study was limited by its retrospective design and by the small group of IS patients (n = 15) in a total of 227 patients. Thus, a multivariate analysis of potential risk factors for in-hospital mortality in this small cohort was not conclusive. Furthermore, we were not able to draw a conclusion regarding the type and adjustment of immunosuppressive medication affecting morbidity and mortality due to diverticulitis in these patients given the small sample size.

Comparing the results of the multivariate analysis with the findings of previously published studies, we confirmed age is an independent risk factor for death.[51,52] Emergency operation increases the risk of death by more than 3 times in patients with colonic resection[53–56] and is performed in patients with perforated diverticulitis and peritonitis only.

Conclusion

Based on our findings and previously published results, it is difficult to make general recommendations on screening and treatment of diverticular disease in IS patients. Our study confirms the fatal outcome of diverticulitis in IS patients and underlines the importance of early diagnosis, including CT scan, and therapy given that in many cases the first episode of diverticulitis can be lethal.

Common guidelines for IC patients may not apply for IS patients, and the decision for elective sigmoid resection to prevent fatal outcomes due to sigmoid diverticulitis must be made individually based on additional risk factors and on an ideal time point for intervention.

Affiliations: From the Department of Visceral, Transplant and Thoracic Surgery, Medical University, Innsbruck, Austria (Brandl, Kratzer, Kafka-Ritsch, Braunwarth, Weiss); the Department of General, Visceral, Vascular and Thoracic Surgery, Charité Campus Mitte, Berlin, Germany (Brandl, Atanasov, Pratschke); and the Department of General, Visceral and Transplant Surgery, Charité Campus Virchow-Klinikum, Berlin, Germany (Denecke, Sucher, Biebl, Aigner, Pratschke, Öllinger).

Competing interests: None declared.

Contributors: A. Brandl, R. Kafka-Ritsch, J. Pratshke and R. Öllinger designed the study. A. Brandl, T. Kratzer, A. Braunwarth, S. Weiss, M. Biebl and F. Aigner acquired the data, which A. Brandl, T. Kratzer, R. Kafka-Ritsch, C. Denecke, S. Weiss, G. Atanasov, R. Sucher, M. Biebl and F. Aigner analyzed. A. Brandl wrote the article, which all authors reviewed and approved for publication.

References

1. Etzioni DA, Mack TM, Beart RW Jr, et al. Diverticulitis in the United States: 1998-2005: changing patterns of disease and treatment. *Ann Surg* 2009;249:210-7.
2. Detry O, Defraigne JO, Meurisse M, et al. Acute diverticulitis in heart transplant recipients. *Transpl Int* 1996;9:376-9.
3. Remzi FH. Colonic complications of organ transplantation. *Transplant Proc* 2002;34:2119-21.
4. Bardaxoglou E, Maddern G, Ruso L, et al. Gastrointestinal surgical emergencies following kidney transplantation. *Transpl Int* 1993; 6:148-52.
5. Catena F, Ansaloni L, Gazzotti F, et al. Gastrointestinal perforations following kidney transplantation. *Transplant Proc* 2008;40:1895-6.
6. Meyers WC, Harris N, Stein S, et al. Alimentary tract complications after renal transplantation. *Ann Surg* 1979;190:535-42.
7. Rafferty J, Shellito P, Hyman NH, et al. Practice parameters for sigmoid diverticulitis. *Dis Colon Rectum* 2006;49:939-44.
8. Scotti A, Santangelo M, Federico S, et al. Complicated diverticulitis in kidney transplanted patients: analysis of 717 cases. *Transplant Proc* 2014;46:2247-50.
9. Hansen O, Graupe F, Stock W. Prognostic factors in perforating diverticulitis of the large intestine. *Chirurg* 1998;69:443-9.
10. Hinchey EJ, Schaal PG, Richards GK. Treatment of perforated diverticular disease of the colon. *Adv Surg* 1978;12:85-109.
11. Fozard JB, Armitage NC, Schofield JB, et al. ACPGBI position statement on elective resection for diverticulitis. *Colorectal Dis* 2011;13 (Suppl 3):1-11.
12. Perathoner A, Klaus A, Muhlmann G, et al. Damage control with abdominal vacuum therapy (VAC) to manage perforated diverticulitis with advanced generalized peritonitis–a proof of concept. *Int J Colorectal Dis* 2010;25:767-74.
13. Qasabian RA, Meagher AP, Lee R, et al. Severe diverticulitis after heart, lung, and heart-lung transplantation. *J Heart Lung Transplant* 2004;23:845-9.
14. Hwang SS, Cannom RR, Abbas MA, et al. Diverticulitis in transplant patients and patients on chronic corticosteroid therapy: a systematic review. *Dis Colon Rectum* 2010;53:1699-707.
15. Chapman J, Davies M, Wolff B, et al. Complicated diverticulitis: Is it time to rethink the rules? *Arch Surg* 2005;242:576-581.
16. Von Rahden BH, Kircher S, Thiery S, et al. Association of steroid use with complicated sigmoid diverticulitis: potential role of activated CD68+/CD163+ macrophages. *Langenbecks Arch Surg* 2011;396: 759-68.
17. Ambrosetti P. Value of CT for acute left-colonic diverticulitis: the surgeon's view. *Dig Dis* 2012;30:51-5.
18. Salem L, Anaya DA, Roberts KE, et al. Hartmann's colectomy and reversal in diverticulitis: a population-level assessment. *Dis Colon Rectum* 2005;48:988-95.
19. Morris AM, Regenbogen SE, Hardiman KM, et al. Sigmoid diverticulitis: a systematic review. *JAMA* 2014;311:287-97.
20. Simianu VV, Flum DR. Rethinking elective colectomy for diverticulitis: a strategic approach to population health. *World J Gastroenterol* 2014;20:16609-14.
21. Issa N, Dreznik Z, Dueck DS, et al. Emergency surgery for complicated acute diverticulitis. *Colorectal Dis* 2009;11:198-202.
22. Pittet O, Kotzampassakis N, Schmidt S, et al. Recurrent left colonic diverticulitis episodes: More severe than the initial diverticulitis? *World J Surg* 2009;33:547-52.
23. Ritz JP, Lehmann KS, Frericks B, et al. Outcome of patients with acute sigmoid diverticulitis: multivariate analysis of risk factors for free perforation. *Surgery* 2011;149:606-13.

24. Dobbins C, Defontgalland D, Duthie G, et al. The relationship of obesity to the complications of diverticular disease. *Colorectal Dis* 2006;8:37-40.
25. Hjern F, Wolk A, Hakansson N. Obesity, physical inactivity, and colonic diverticular disease requiring hospitalization in women: a prospective cohort study. *Am J Gastroenterol* 2012;107:296-302.
26. Hjern F, Wolk A, Hakansson N. Smoking and the risk of diverticular disease in women. *Br J Surg* 2011;98:997-1002.
27. Rosemar A, Angeras U, Rosengren A. Body mass index and diverticular disease: a 28-year follow-up study in men. *Dis Colon Rectum* 2008;51:450-5.
28. Williams PT. Incident diverticular disease is inversely related to vigorous physical activity. *Med Sci Sports Exerc* 2009;41:1042-7.
29. Strate LL, Liu YL, Aldoori WH, et al. Physical activity decreases diverticular complications. *Am J Gastroenterol* 2009;104:1221-30.
30. Crowe FL, Appleby PN, Allen NE, et al. Diet and risk of diverticular disease in Oxford cohort of European Prospective Investigation into Cancer and Nutrition (EPIC): prospective study of British vegetarians and non-vegetarians. *BMJ* 2011;343:d4131.
31. Peery AF, Barrett PR, Park D, et al. A high-fiber diet does not protect against asymptomatic diverticulosis. *Gastroenterology* 2012;142:266-272.
32. Strate LL, Liu YL, Syngal S, et al. Nut, corn, and popcorn consumption and the incidence of diverticular disease. *JAMA* 2008;300:907-14.
33. Wong WD, Wexner SD, Lowry A, et al. Practice parameters for the treatment of sigmoid diverticulitis–supporting documentation. The Standards Task Force. The American Society of Colon and Rectal Surgeons. *Dis Colon Rectum* 2000;43:290-7.
34. Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. *Arch Surg* 2005;140:681-5.
35. Reshef A, Stocchi L, Kiran RP, et al. Case-matched comparison of perioperative outcomes after surgical treatment of sigmoid diverticulitis in solid organ transplant recipients versus immunocompetent patients. *Colorectal Dis* 2012;14:1546-52.
36. Andersen JC, Bundgaard L, Elbrond H, et al. Danish national guidelines for treatment of diverticular disease. *Dan Med J* 2012;59:C4453.
37. Collins D, Winter DC. Elective resection for diverticular disease: an evidence-based review. *World J Surg* 2008;32:2429-33.
38. Krysa J, Patel V, Taylor J, et al. Outcome of patients on renal replacement therapy after colorectal surgery. *Dis Colon Rectum* 2008;51:961-5.
39. Meunier K, Mucci S, Quentin V, et al. Colorectal surgery in cirrhotic patients: assessment of operative morbidity and mortality. *Dis Colon Rectum* 2008;51:1225-31.
40. Paolino J, Steinhagen RM. Colorectal surgery in cirrhotic patients. *ScientificWorld Journal* 2014;?:239293.
41. Stewart DB, Hollenbeak C, Boltz M. Renal transplant status in patients undergoing colorectal surgery: Is immunosuppression safer than kidney disease? *Surgery* 2012;152:537-547.
42. Halabi WJ, Jafari MD, Nguyen VQ, et al. Colorectal surgery in kidney transplant recipients: a decade of trends and outcomes in the United States. *Am Surg* 2013;79:1026-33.
43. Paul S, Escareno CE, Clancy K, et al. Gastrointestinal complications after lung transplantation. *J Heart Lung Transplant* 2009;28:475-9.
44. Maurer JR. The spectrum of colonic complications in a lung transplant population. *Ann Transplant* 2000;5:54-7.
45. Larson ES, Khalil HA, Lin AY, et al. Diverticulitis occurs early after lung transplantation. *J Surg Res* 2014;190:667-71.
46. Beaver TM, Fullerton DA, Zamora MR, et al. Colon perforation after lung transplantation. *Ann Thorac Surg* 1996;62:839-43.
47. Dominguez Fernández E, Albrecht KH, Heemann U, et al. Prevalence of diverticulosis and incidence of bowel perforation after kidney transplantation in patients with polycystic kidney disease. *Transpl Int* 1998; 11:28-31.
48. Fenton JJ, Cicale MJ. Sigmoid diverticular perforation complicating lung transplantation. *J Heart Lung Transplant* 1997;16:681-5.
49. Sawyerr OI, Garvin PJ, Codd JE, et al. Colorectal complications of renal allograft transplantation. *Arch Surg* 1978;113:84-6.
50. McCune TR, Nylander WA, Van Buren DH, et al. Colonic screening prior to renal transplantation and its impact on post-transplant colonic complications. *Clin Transplant* 1992;6:91-6.
51. Lidsky ME, Thacker JK, Lagoo-Deenadayalan SA, et al. Advanced age is an independent predictor for increased morbidity and mortality after emergent surgery for diverticulitis. *Surgery* 2012;152: 465-72.
52. Pisanu A, Reccia I, Deplano D, et al. Factors predicting in-hospital mortality of patients with diffuse peritonitis from perforated colonic diverticulitis. *Ann Ital Chir* 2012;83:319-24.
53. Masoomi H, Kang CY, Chen A, et al. Predictive factors of in-hospital mortality in colon and rectal surgery. *J Am Coll Surg* 2012;215: 255-61.
54. Jacobs DO. Clinical practice. Diverticulitis. *N Engl J Med* 2007;357: 2057-66.
55. Nagorney DM, Adson MA, Pemberton JH. Sigmoid diverticulitis with perforation and generalized peritonitis. *Dis Colon Rectum* 1985; 28:71-5.
56. McGillicuddy EA, Schuster KM, Davis KA, et al. Factors predicting morbidity and mortality in emergency colorectal procedures in elderly patients. *Arch Surg* 2009;144:1157-62.