Anorectal Surgery in Human Immunodeficiency Virus-Infected Patients

Clinical Outcome in Relation to Immune Status

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PURPOSE: Anorectal disease is commonly found in human immunodeficiency virus (HIV)-infected patients. The aim of this study was to determine the spectrum of anorectal disease, its surgical treatment, clinical outcome, and its relation to immune status. METHODS: Medical records of all HIV-infected patients with anorectal pathology that required surgical treatment from January 1984 to January 1994 were retrospectively reviewed. Patients were divided into five different groups: common anorectal pathology (hemorrhoids, polyps, Group A); condylomata acuminata (Group B); perianal sepsis (abscesses, fistulas, Group C); anorectal ulcers (Group D); malignancies (Group E). RESULTS: Eighty-three patients needed 204 surgical consultations (13 percent conservative, 87 percent operative) for 170 anorectal diseases. Fifty-one patients had multiple anorectal pathology. Operative intervention resulted in adequate wound healing and symptom relief in 59 percent of patients, adequate wound healing without relief of symptoms in 24 percent of patients, and disturbed wound healing in 17 percent of patients. Disturbed wound healing was related to type of anorectal disease ($P < 0.001$) and to preoperative $CD4^+$-lymphocyte counts ($P < 0.01$). Disturbed wound healing and most insufficient immune status were encountered in Groups C, D, and E. Within these groups low $CD4^+$-lymphocyte counts were a risk factor for disturbed wound healing ($P = 0.004$). Median postoperative survival was highest (4.7 years) in Group A, lowest (0.6 years) in Groups D and E, and related to type of anorectal disease ($P = 0.0001$). CONCLUSIONS: The spectrum of anorectal disease is complex. Type of anorectal disease is strongly related to immune status, wound healing, and postoperative survival. [Key words: Anorectum; HIV; Surgery; Wound healing; Immune status; Postoperative survival]

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As the number of acquired immunodeficiency syndrome (AIDS) cases continues to increase, surgeons will be involved in the management of human immunodeficiency virus (HIV)-infected patients more frequently. Patients are susceptible to a spectrum of diseases that may cause a variety of symptoms and complaints.[1–7] Diseases of the anorectum, the most common port of entry for HIV and other pathogens in homosexual men, are frequently (6–34 percent) encountered in patients with AIDS.[7–11] Intravenous drug abusers with AIDS have a considerably lower incidence (3 percent) of anorectal disease than male homosexuals.[8, 9]

Anorectal pathology in the HIV-infected male homosexual patient is diverse. It comprises common conditions such as hemorrhoids and polyps. Common venereal diseases associated with anoreceptive intercourse include gonorrhea, syphilis, and chlamydial infections.[10] Conditions recognized as being more prevalent and mostly more extensive in HIV-infected patients are condylomata acuminata and infections with herpes simplex virus, cytomegalovirus (CMV), *Mycobacterium avium intracellulare*, and *Candida albicans*.[10–12] In addition to these infectious diseases, HIV-infected patients are at increased risk for anorectal carcinoma, lymphoma, and Kaposi's sarcoma (KS).[10–12] The presumed poor wound healing and infaust prognosis of underlying disease tend to discourage surgeons from performing elective anorectal surgery in HIV-infected patients.[13–16] The aim of this study was to determine the spectrum of anorectal disease, its surgical treatment, and treatment results with special attention to immune status and postoperative prognosis.

PATIENTS AND METHODS

Medical records of all HIV-infected patients were reviewed, with special attention to anorectal pathology that required surgical treatment between January 1, 1984, and January 1, 1994. All records were studied

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in detail to identify age, sex, risk factors for HIV infection, immune status ($CD4^+$-lymphocyte counts), cultures and histology of anorectal lesions, type and results of treatment of anorectal lesions, and postoperative survival. According to the literature[11] patients were divided into five different groups with respect to type of anorectal lesion: common anorectal pathology (hemorrhoids, polyps; Group A), condylomata acuminata (Group B), perianal sepsis (abscesses, fistulas; Group C), anorectal ulceration (Group D), and anorectal malignancies (Group E).

Data from patients who had multiple diagnoses were tabulated separately for each diagnosis. Lesions were only included in the study if at the moment of treatment the patient was known to be HIV-seropositive. $CD4^+$-lymphocyte counts (normal value, 460-1450 $\times$ 10^6/liter), assessed within a maximum of six weeks before surgical treatment, were considered to be representative of the patient's immune status on the date of treatment.

Operative treatment was considered successful if relief of symptoms was achieved within four weeks after the operation. Wound healing was arbitrarily considered to be disturbed when infiltration and/or purulent discharge was encountered more than four weeks after the operation.

To test for differences between proportions, the chi-squared test with Yates' correction was used. Analysis of $CD4^+$-lymphocyte counts per group was performed by analysis of variance with repeated measurements, with patients as random effect component and type of anorectal disease as fixed effect (BMDP®, Statistical Software, Inc., Los Angeles, CA, 1992). To analyze the probability of disturbed wound healing, a logistic random effect model was used. As fixed effect the type of anorectal disease was used, and as random component the patient effect and the logarithm of the $CD4^+$-lymphocyte counts as covariate were used (Egret®, Statistics and Epidemiology Research Corporation, Seattle, WA, 1991). Postoperative survival time was calculated from the first operative intervention until death or end of study period. Postoperative survival curve was calculated by using the Kaplan-Meier method; comparisons were done with the log-rank test. *P* values of less than 0.05 were considered significant.

RESULTS

Clinical Data

Within the study period, 1,117 HIV-positive patients had been treated at the Academic Medical Centre of the University of Amsterdam. At the end of the study period, 748 of those patients (68 percent) had been defined as having AIDS. During the ten-year period a total of 355 patients (32 percent) were referred for general surgical consultation. Anorectal disease was the reason for surgical consultation in 83 patients (7.4 percent; mean age, 39 (range, 24–64) years). As for risk factors of HIV infection, 78 patients (94 percent) were homosexual/bisexual, 1 was an intravenous drug user (1 percent), and 1 was a hemophiliac (1 percent). These 83 patients (82 males, 1 female) needed 204 surgical consultations for 170 anorectal lesions. Fifty-one of these patients were found to have multiple anorectal pathology (Fig. 1).

Treatment (204) of the 170 lesions consisted of conservative measures in 13 percent (26) and operative interventions in 87 percent (178). Patients were seen at the outpatient department in regular intervals of two to six weeks until complete wound healing, relief of symptoms, and/or end stage of treatment was achieved. Follow-up period ranged from 2 to 42 (mean follow-up, 16) weeks. Number of diagnoses and number of procedures in patients in the different groups are summarized in Table 1.

Fourteen of 83 patients (17 percent) had hemorrhoids, and 9 patients (11 percent) had polyps of the anorectum (Group A). Ten patients were treated conservatively and 13 operatively by hemorrhoidectomy or polypectomy. Histologic examination of the polyps showed no malignancies.

Twenty-eight of 83 patients (34 percent) had diagnoses of condylomata acuminata and were treated either by diathermy or excision (Group B). These condylomata showed in general a more rapid and progressive growth than in non-HIV-infected patients. Malignancy was seen in the warts of eight patients (29 percent; squamous-cell carcinoma *in situ* in seven patients and invasive squamous-cell carcinoma in one patient).

Forty-six of 83 patients (55 percent) underwent surgical interventions for perianal sepsis (Group C). Six patients had serious septic complications or uncommon presentations of anorectal sepsis. Three of them had severe necrotizing gangrene for which multiple necrotectomies, construction of a stoma, and hyperbaric oxygen treatment were applied. Three other patients presented primarily with abscesses in the brain, liver, and mediastinum, respectively. Later, these abscesses turned out to be metastatic abscesses from an "asymptomatic" perianal fistula. Surgical treatment was not essentially different from that in

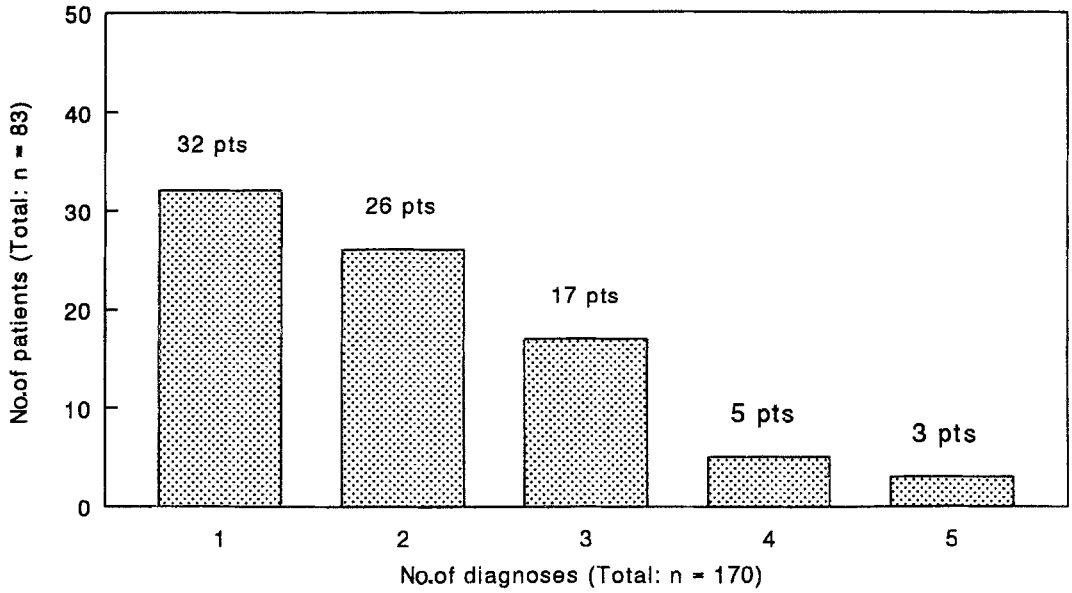

Figure 1. Number of patients (pts) in whom one or more diagnoses of anorectal disease were established.

Table 1.
Number of Diagnoses and Operative Procedures in Patients Suffering from Anorectal Disease that Needed Surgical Treatment

	Group A	Group B	Group C	Group D	Group E
No. (%) of patients*	23 (28)	28 (34)	46 (55)	27 (33)	14 (17)
No. of diagnoses	33	34	62	27	14
No. of operative procedures	17	34	84	33	10

Group A consisted of patients with common anorectal disease; Group B, condylomata acuminata; Group C, perianal sepsis; Group D, anorectal ulceration; Group E, malignancies.

* Patients who had multiple diagnoses were tabulated separately for each diagnosis.

non-HIV-infected patients and included incision and adequate drainage of abscesses, fistulotomy and lay-open procedures in case of fistula treatment. Sphincterotomies were avoided, because most patients previously suffered from diarrhea and incontinence.

A total of 27 of 83 patients (33 percent) underwent treatment for anorectal ulcers (Group D). In one of these patients an abdominoperineal rectum amputation was performed, because of perforation of the distal rectum. Twenty-six patients needed an operative procedure consisting of excision without (16 patients) or with (13 patients) mucosal advancement to resurface the defect. Three of these 26 patients underwent an excision combined with mucosal advancement after an unsuccessful excision only. Anorectal ulceration was related to herpes simplex virus infection in 30 percent (positive cultures) and to CMV infection in 29 percent of patients (cytonuclear inclusion bodies, typical for CMV infection, in the light-microscopy, confirmed by a specific immunoperoxidase staining).

Other than the 7 patients with malignant *in situ* transformation of condylomata acuminata, 1 patient with invasive carcinoma in the condylomata acuminata and 13 other patients (14; 17 percent) had anorectal invasive carcinoma (Group E). Histology of anorectal specimens revealed three Kaposi's sarcomas, one lymphoma, nine invasive squamous-cell carcinomas, and one transitional cell carcinoma. Patients with KS (3) or lymphoma (1) were treated routinely with chemotherapy. Treatment of patients with deeply infiltrating squamous-cell carcinoma ($\geq$T2, 4) consisted of a combination of chemotherapy (5-fluorouracil and mitomycin C) and radiotherapy.[17] Patients with T1 tumors not infiltrating the anal sphincter muscles (5) were excluded from the combination modality treatment and were treated by radical local excision. In one patient with a transitional-cell carcinoma, an abdominoperineal rectum amputation was performed because of extensive tumor growth into the presacral space in combination with a fistula complex.

Effectiveness of Surgery

Operative intervention resulted in adequate wound healing and symptomatic relief in 59 percent of patients (49 of 83 patients who underwent surgery). Adequate wound healing without relief of symptoms was found in 24 percent of patients (20 of 83 patients who underwent surgery), whereas disturbed wound healing was encountered in 17 percent of patients (14 of 83 patients who underwent surgery).

Symptoms of all patients in Groups A and B resolved within four weeks after operative treatment. In 37 patients (80 percent) in Group C, symptoms resolved. In Group D, excision of an anorectal ulcer was successful in 7 of the 16 patients (44 percent); symptom relief was achieved in 12 of 13 patients (92 percent) in whom surgical excision of an anorectal ulcer was combined with mucosal advancement. Excision combined with mucosal advancement appeared to be significantly better compared with the results of excision alone ($P = 0.02$). In Group E symptom relief was achieved in all but one patient (93 percent).

Disturbed Wound Healing and Immune Status

Of 178 operative procedures 125 (70 percent) preoperative $CD4^+$-lymphocyte counts were available. These data were used to analyze the relation between preoperative $CD4^+$-lymphocyte counts, wound healing, and type of anorectal disease.

In all patients with common anorectal pathology and/or condylomata acuminata, wound healing was adequate. Wound healing was disturbed in seven patients with perianal sepsis (7/46; 15 percent), in four patients with anorectal ulceration (4/27; 15 percent), and in three patients with malignancies (3/6; 50 percent). Disturbed wound healing was related to type of anorectal disease, *i.e.*, perianal sepsis, ulcers, and malignancies ($P < 0.001$). The mean and 95 percent confidence interval of preoperative $CD4^+$-lymphocyte counts of patients in the five different groups are shown in Figure 2. Patients with ulcers or malignancies (Groups D and E) had significantly lower $CD4^+$-lymphocyte counts compared with those having common pathology, condylomata, or perianal sepsis (Groups A, B, and C) ($P < 0.01$). Within Groups C, D, and E, low $CD4^+$-lymphocyte counts were a significant risk factor for disturbed wound healing; the lower the $CD4^+$-lymphocyte counts were, the higher the risk of disturbed wound healing was ($P = 0.004$).

Postoperative Survival Time

By the end of the study period, 53 of 83 patients (64 percent) had died. In-hospital mortality after operative treatment for anorectal disease was zero. Median postoperative survival time was highest (4.7 years) after surgery for common anal pathology and lowest (0.6 years) for ulcers and malignancies (Fig. 3). There

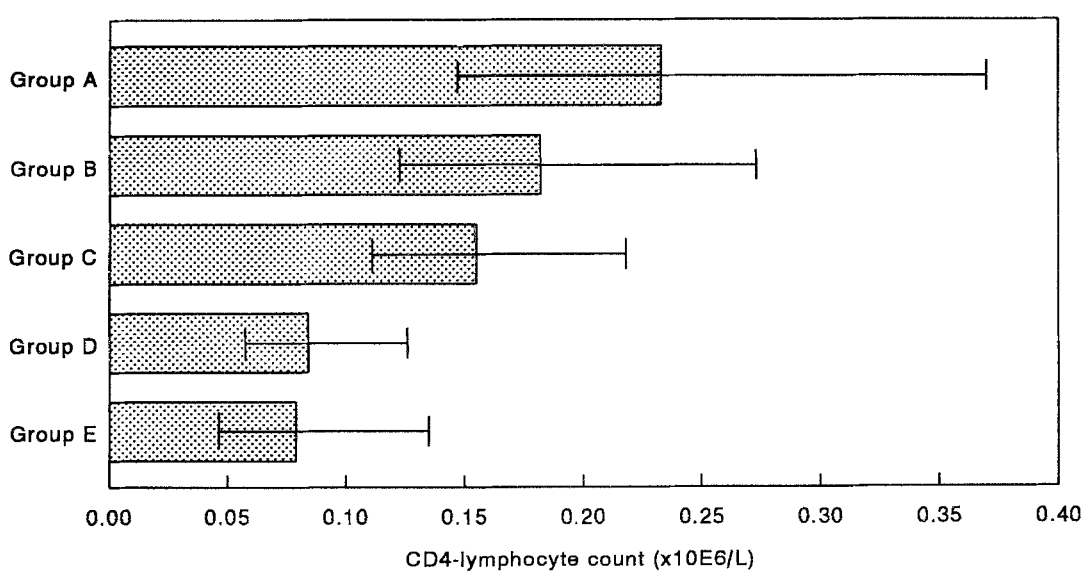

Figure 2. Mean and 95 percent confidence interval of preoperative $CD4^+$-lymphocyte counts of patients in the five different groups. Immune status is related to type of anorectal disease ($P < 0.01$). Group A consisted of patients with common anorectal disease; Group B, condylomata acuminata; Group C, perianal sepsis; Group D, anorectal ulceration; Group E, malignancies.

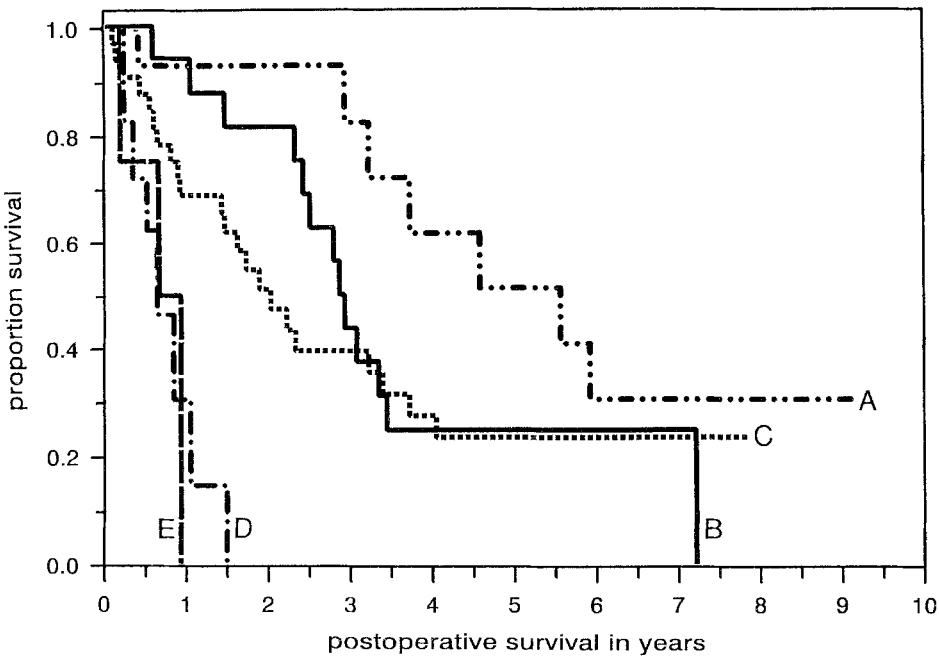

Figure 3. Kaplan-Meier postoperative survival curve of patients in the five different groups. Comparisons were done with the log-rank test. Median postoperative survival times for the different groups were 4.7 years (Group A), 2.7 years (Group B), 1.9 years (Group C), 0.6 years (Group D), and 0.7 years (Group E). Group A consisted of patients with common anorectal disease; Group B, condylomata acuminata; Group C, perianal sepsis; Group D, anorectal ulceration; Group E, malignancies.

is a highly significant trend that shows postoperative survival time decreases with type of anorectal disease ($P = 0.0001$). Causes of death of patients were not related to anorectal disease.

DISCUSSION

In the present study 24 percent of patients did not have relief of symptoms within four weeks after the operation. Disturbed wound healing more than four weeks after the operation was found in 17 percent of patients. Anorectal pathology was subdivided in five different types. Group A consisted of patients with common anorectal disease, Group B condylomata acuminata, Group C perianal sepsis, Group D anorectal ulceration, and Group E malignancies. The frequency distribution for the five different groups found in this study is in accordance with the literature (Table 1).[10, 11] Type of anorectal disease was related to disturbed wound healing, to preoperative $CD4^+$-lymphocyte counts, and to postoperative survival.

Surgeons tend to be discouraged from performing elective anorectal surgery in HIV-infected patients because of the presumed poor wound healing and dismal prognosis caused by the underlying disease.[13–16] This study attempts to determine whether it is justified that surgeons deal with anorectal pathology in a restrictive way.

Hemorrhoids and polyps (Group A) are not associated with HIV infection. Presentation and surgical treatment of these lesions in HIV-infected patients in our study group are not different from that in non-HIV-infected patients. Anal condylomata acuminata (Group B) are benign viral infections, which are related to specific human papilloma virus strains. Malignant transformation of condylomata into squamous-cell carcinoma *in situ* was seen in 25 percent of patients in this study, as has been reported in the literature in HIV-infected patients.[18, 19] Progression of *in situ* carcinoma to invasive squamous-cell carcinoma in condylomata acuminata occurred in one patient in this study and has only incidentally been reported in the literature,[9, 20] probably because of limited survival of HIV-infected patients. Data are conflicting as to whether there is an increase in the incidence of perianal sepsis (Group C) in HIV-infected patients.[9] What appears to be undisputed is that there is a different pattern of anorectal sepsis with rare and severe septic complications.[9] In the present series the incidence of serious septic complications and uncommon presentations of anorectal sepsis was

remarkably high (13 percent). Therapy-resistant and symptomatic ulcers (Group D) in HIV-infected patients are usually treated by excision only. Because of disappointing therapeutic results, it was decided to combine excision with mucosal advancement, which had a significantly better effect on patients' complaints.[21] Since the beginning of the AIDS epidemic, the incidence of anorectal malignancies (Group E), especially squamous-cell carcinoma, has increased. Treatment of patients with deeply infiltrating squamous-cell carcinoma (≥T2) is advised to consist of a combination of chemotherapy (5-fluorouracil and mitomycin C) and radiotherapy.[17] Patients with T1 tumors not infiltrating the anal sphincter muscles can be excluded from this combination treatment method and can be treated by radical local excision. Lymphoma and KS are primarily treated with chemotherapy and are, therefore, only incidentally seen by the surgeon.[22–27]

Effectiveness of Surgery and Disturbed Wound Healing

Symptomatic relief with adequate wound healing was seen in 59 percent of patients in the present study. This is in accordance with one other study in the literature.[10] Disturbed wound healing in HIV-infected patients has been reported to vary from 4 to 34 percent,[10, 11, 13, 14, 16] and in this study wound healing was disturbed in 17 percent of patients. Low rates of successful surgery and disturbed wound healing were mainly seen in patients with perianal sepsis, anorectal ulcers, or malignancies (Groups C, D, and E). Anorectal fistulas and abscesses (Group C) should be adequately drained to avoid metastatic abscesses and massive necrotizing gangrene, as was seen in 13 percent of our patients. Patients suffering from anorectal ulceration (Group D) are preferably treated by local excision combined with mucosal advancement.[20] Patients in Group E are not frequently seen by the surgeon, because they are mostly primarily treated nonoperatively. In this study, those patients who had been treated operatively, had disappointing treatment results (disturbed wound healing in 50 percent of patients).

Disturbed Wound Healing and Immune Status

In HIV-infected patients immune status can be quantified by $CD4^+$-lymphocyte counts. Data are conflicting as to whether preoperative $CD4^+$-lymphocyte counts can be related to wound healing disorders.[8, 10, 14, 16, 28] In the present study immune status was significantly more disturbed in patients with ulcers or malignancies compared with those having common pathology, condylomata, or perianal sepsis (Fig. 2). Moreover, low $CD4^+$-lymphocyte counts in patients with perianal sepsis, ulcers, or malignancies were a risk factor for development of disturbed wound healing within each of these groups. In patients with perianal sepsis, ulcers, or malignancies, it is advisable to determine the preoperative $CD4^+$-lymphocyte count to quantify the immune status of the patient and to estimate the risk of a wound-healing disorder. However, these data should be interpreted with caution because the present study is a retrospective analysis; the number of patients with disturbed wound healing was small, and the data on preoperative $CD4^+$-lymphocyte counts were incomplete (only available in 70 percent of cases).

Postoperative Survival Time

Postoperative survival time in HIV-infected patients with anorectal disease is reported to be short (0.7–1.3 years).[13, 14, 16] In this study survival time is also limited (0.6–4.7 years) but is not as poor as suggested in the literature. Postoperative survival time is related to type of anorectal lesion, *i.e.*, anorectal ulcers and malignancies (Fig. 3). This means that anorectal ulcers and malignancies present in a late stage of HIV disease, in which immune status is severely deteriorated. Survival time depends on evolution of the underlying HIV disease, rather than on anorectal pathology.

CONCLUSIONS

Results of operative treatment are dependent on type of anorectal disease. This may be because the type of anorectal disease is related to immune status, wound healing, and postoperative survival. In patients suffering from common anorectal pathology and condylomata acuminata results of operative treatment were relatively good. In patients with perianal sepsis major secondary complications were encountered. Adequate drainage of anorectal fistulas and abscesses should be performed to avoid metastatic abscesses and massive necrotizing gangrene. To achieve improvement of operative treatment in patients with anorectal ulceration, treatment should preferably consist of local excision combined with mucosal advancement.

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