REVIEW ARTICLE

The Surgeon and AIDS

Twenty Years Later

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Background: Since the first reports on indications and outcome for abdominal procedures in the HIV/AIDS patient were published 20 years ago, the epidemiology and presentation of surgical illness have changed remarkably with the advent of new antiviral regimens. A review of the now occasional, but still important, role of the surgeon in contemporary treatment of HIV/AIDS is presented.

Data Sources: Information was obtained by PubMed searches of medical journals, examination of reference lists, and Web resources.

Study Selection: Articles on operative indications, outcomes, precautions, source of transmission, and pathophysiology of HIV/AIDS were selected.

Data Extraction: Data was obtained from peer-reviewed articles and references.

Data Synthesis: The last 2 decades have seen a decrease in operative mortality from as high as 85% to approximately 15% with a corresponding improvement in morbidity. Surgical emergencies such as appendicitis occur in HIV patients with the same frequency as non-HIV patients and are treated with equivalent results. Concern about transmission of HIV in the operating room has lessened somewhat. Although still a hazard, the probability of HIV transmission with accidental exposure is low, with risks below 0.5% for percutaneous hollow-bore needles and less than 0.1% risk for mucus membrane exposure.

Conclusions: Improved surgical outcomes together with of accurate data on the modes and likelihood of accidental transmission of HIV to members of the surgery team have resulted in the treatment of HIV/AIDS patients becoming an accepted part of routine surgical practice.

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In June 1981 the Centers for Disease Control published a report of 5 patients with *Pneumocystis carinii* pneumonia.[1] A month later, an article published by the *New York Times* stated: "Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer [Kaposi sarcoma]. . . . The cause of the outbreak is unknown, and there is as yet no evidence of contagion." [2] These reports marked the beginning of public awareness of AIDS in the United States and the onset of the major epidemic in the last half of the twentieth century.

Public health education and community awareness, in conjunction with advances in antiretroviral therapy, have decreased the number of new AIDS cases from approximately 70 000 in 1995 to about 43 000 in 2002. The mortality rate has had a corresponding decrease from approximately 16 per 100 000 persons in 1995 to 5 per 100 000 persons in 2002.[3,4]

Twenty years since the first indications for abdominal operation in the AIDS patient were published, the epidemiology is now well understood and surgical involvement in the management of patients with AIDS has changed remarkably.[5-9] In concert with improved medical treatment, there has been a major decrease in the number of operations for AIDS-related surgical illness. At the same time the surgery curriculum has undergone change to ensure surgeons are knowledgeable with regard to their much reduced, although still important, role in contemporary treatment of AIDS.

PATHOPHYSIOLOGY OF HIV/AIDS

Infection with the HIV is responsible for the development of AIDS. As a bloodborne pathogen, HIV can be transmitted to the host directly, by a mucous membrane exposure to infected blood or body fluids, or by percutaneous instrumentation. Although the majority of new cases continue to be acquired through male-to-male sexual contact and intravenous drug use, an increase in HIV infection caused

by vertical transmission (mother to child) and heterosexual contact has been observed.[3]

Once introduced into the bloodstream, the virus attaches to receptors on the host's CD4 lymphocytes. After phagocytosis, the virus releases its RNA. Reverse transcriptase, a unique enzyme characteristic to the HIV virus, incites the cell to synthesize copies of DNA complementary to the viral RNA template (cDNA). The cDNA migrates into the nucleus of the infected cell and becomes a part of the chromosomal material of the host. Thus, the infected lymphocyte manufactures large numbers of new viral particles that, after lysis of the host cell, are released back into the bloodstream to infect the other CD4 lymphocytes. The systematic depletion of CD4 cells from greater than 500 cells/mm^3 to less than 200 cells/mm^3 eventually causes profound host immunosuppression.[10]

The Centers for Disease Control define 3 clinical categories of HIV infection.[10] During the first stages of the disease (category A) the patient may have nonspecific signs of acute viral infection such as fever, chills, and general malaise. Next, there is a period of asymptomatic disease that can vary from several months to decades. During this time the viral load is slowly increasing while CD4 cells are being depleted. Development of symptoms and regional adenopathy defines AIDS-related complex (category B).[11] Finally, the development of an AIDS-defining clinical condition (eg, Kaposi sarcoma) or a CD4 cell count of less than 200 signals the onset of clinical AIDS (category C).[10]

The clinical manifestations of AIDS may include complications of immunosuppression that require surgical management. Occasionally, the depressed host response can obscure the presentation of an otherwise non-HIV/AIDS–related surgical illnesses, resulting in a delayed or missed diagnosis and thus complicating management. At other times, the presence of HIV/AIDS distracts the clinician into believing the illness is part of the HIV/AIDS clinical spectrum, which can perhaps delay the diagnosis of a common non-HIV/AIDS–related illness. In certain patients a surgical illness unique to AIDS may be the first manifestation of the disease; earlier in the epidemic this infrequently had been the signal event for diagnosis of HIV infection.[6]

PRESENTATION OF THE ACUTE ABDOMEN

Abdominal pain necessitating medical evaluation is a complaint in 12% to 45% of patients with HIV infection.[12] Earlier studies in selected populations showed that 41% to 86% of cases of abdominal pain had HIV-related causes.[12-15] These reports noted that cytomegalovirus (CMV) gastroenteritis was the predominant cause of acute abdominal pain, followed by lymphomas, Kaposi sarcomas, and mycobacterial disease. Advances in highly active antiretroviral therapies, however, have produced a significant reduction in abdominal complications associated with opportunistic infections, particularly peritonitis secondary to atypical bacteria and fungi.[16] For example, Monkemuller et al[17] found that opportunistic infections in patients referred for endoscopy fell from 69% in the pre-antiviral era to 13% currently. Furthermore, 62% of patients taking protease inhibitors who had chronic diarrhea and who were referred for endoscopy responded to medical therapy, as opposed to 33% of historical controls.[18]

When assessing the acute abdomen in the HIV patient, the surgeon must consider illnesses common in non-HIV patient groups, such as appendicitis. A recent report emphasized that only 11% of HIV-positive patients with acute abdominal pain had a cause associated with HIV/AIDS. Of the 8% of HIV-positive patients who required surgery, only 1 patient (0.9%) had an opportunistic infection.[19] Hence, conditions such as appendicitis, diverticulitis, cholecystitis, pancreatitis, hepatitis, peptic ulcer disease, ischemic bowel disease, and symptomatic abdominal aortic aneurysm can be present in the HIV patient, unrelated to the immunocompromised state, and will occur with the same frequency as in non-HIV patients.[19,20]

Although the need for surgical intervention in the HIV/AIDS patient with abdominal complaints is low, the general surgeon will often be consulted owing to the lack of clarity in the interpretation of findings from the initial abdominal examination. Once consulted, the surgeon should determine whether the patient has a nonoperative condition mimicking surgical illness or a surgical emergency. Late diagnosis and delay of surgical exploration in HIV/AIDS patients have resulted in increased morbidity and mortality.[21] Emergency abdominal exploration by itself predisposes the AIDS patient to an increased mortality risk.[6-8] Indeed, laparotomies in the HIV/AIDS patient have been reported to have high mortality rates (57% to 86%) for emergent operations, while elective procedures carried a 43% mortality rate.[7,22] These poor outcomes have prompted suggestions that operative procedures in AIDS patients provide little benefit and that attention should be directed to early recognition.[8] However, with new antiviral therapy the operative mortality is 11% to 19% for emergency abdominal surgery and the risk-benefit analysis is more in favor of laparotomy.[21,23,24] When it is decided that the abdominal symptoms represent a surgical emergency, appropriate resuscitation is initiated to improve surgical outcome, such as nasogastric decompression, fluid replacement, antibiotic administration, transfusion of blood products, and (if not already under way) consultation for antiviral therapy.

CLINICAL ASSESSMENT OF THE ACUTE ABDOMEN

As with any assessment of the acute abdomen, the medical history will be a key component in evaluating the HIV/AIDS patient's symptoms. Although most patients today are aware of their HIV status, undiagnosed HIV-related illness can be discovered at the time of surgery.[6] A history of risk factors, including sexual practices and intravenous drug abuse, may be associated with an increased risk of HIV infection; however, the physician must keep in mind the rise in the infection rate in heterosexual patients. Hepatitis B (HBV) and C (HCV) viruses are common coinfections.[25] A detailed history of medications may give insight to diagnosis, since some antiviral medications are known to cause pancreatitis (didanosine) and kidney stones (indi-

var).[26,27] Many patients are well informed of their HIV status and can relate CD4 counts, which can assist in the determination of the degree of immunosuppression. This is important in calculating risks and benefits of surgery as well as the possibility of opportunistic infections, which may not present until CD4 counts are less than 200 cells/mm^3.[28] History of diarrhea, prior opportunistic infections, or neoplasms will also give insight to the nature of the diagnosis.[29]

Fever and nonspecific abdominal pain are common among patients with AIDS who do not have a surgical illness.[30] During the physical examination, oral candidiasis, generalized lymphadenopathy, and Kaposi skin lesions point to the stage of disease and degree of immunosuppression. Signs of peritoneal inflammation may be delayed or absent even in the face of a surgical emergency, and more than one pathologic process may be present in the immunocompromised patient.[29]

CD4 counts and viral loads in addition to the standard laboratory tests are useful in developing a prognosis in the AIDS patient. Postoperative CD4 counts of 200 cells/mm^3 or less are associated with a higher mortality rate.[28,31] However, obtaining these values from the laboratory within the time needed to develop a definitive management plan may be difficult. The number of CD4 cells is roughly 10% of the lymphocyte count.[32] Lymphocyte counts greater than 2000 cells/mm^3 are usually associated with a CD4 count higher than 200 cells/mm^3 and a total lymphocyte count less than 1000 is associated with a CD4 count less than 200 cells/mm^3.[33] Postoperative viral loads greater than 75 000 RNA copies/mL are associated with a higher complication and mortality rates.[24] Low white blood cell counts have similarly been associated with increased complications and mortality,[22,24] although this is not a uniform finding.[34,35] As with the seronegative patient, normal serum albumin levels in AIDS patients are correlated with a better outcome.[34]

Plain radiographs of the abdomen may delineate perforated bowel (extraluminal gas), or dilated loops of bowel associated with bowel obstruction. The low diagnostic yield of plain abdominal radiographs has led to use of abdominal computed tomographic (CT) scan almost routinely.[36] Pneumatosis intestinalis, readily revealed on CT scan, suggests bowel necrosis and impending perforation.[37] Intraperitoneal fluid collections characteristic of opportunistic infections may also only be discovered on CT scan. Fluid collections can be aspirated with the aid of CT scan or ultrasound for microbiologic testing and, if infected, can possibly be resolved with the use of image-guided percutaneous drainage. Ultrasound is most useful for investigation of suspected calculous disease of the hepatobiliary system such as cholecystitis, cholangitis, and pancreatitis.

SPECIFIC CONDITIONS

Appendicitis

Acute appendicitis in the patient with AIDS is often due to obstruction of the appendix by a fecalith or a lymphoid hyperplasia but can also be a result of acute CMV infection,[21,38] mycobacterial infection,[39,40] and Kaposi sarcoma.[41] Reports of appendicitis cases among AIDS patients indicate that 30% are caused by complications of AIDS-related conditions.[30] The clinical presentation of the patient who has HIV/AIDS with appendicitis is characteristic right lower quandrant pain, usually associated with a low to normal white blood cell count.[42] The postoperative morbidity is similar in patients who are HIV seropositive and those who are HIV seronegative.[42] Patients who have developed AIDS may have an opportunistic infection mimicking acute appendicitis that results in operation, which may result in an increased morbidity postoperatively.[31,42] For example, "typhlitis," an inflammation of the cecum, appendix, and/or ileum, can mimic appendicitis.[43] This infection originates from normal gut flora, and is often a result of profound immunosuppression (neutrophil counts less than 1000/mm^3) or the use of cytotoxic drugs during chemotherapy. Medical management with broad-spectrum intravenous antibiotics is the preferred management.[43] Therefore, in AIDS patients, CT scan or even laparoscopy should be considered prior to surgical intervention.[30,31]

In 1992, a San Francisco group reported an increased rate of perforation, gangrenous appendicitis, and initial appendiceal abscess among patients with AIDS.[30] Delay in diagnosis may be due to confusion when the patient has a normal or low white blood cell count (which is actually elevated over their chronically lower-than-normal white blood cell count), or when it is believed there is a medical cause of the abdominal pain.[44]

Bowel Perforation

The previously high incidence of bowel perforation secondary to CMV infections[6,7] and Kaposi sarcoma[45] has decreased with retroviral drug therapy. Perforations now are more likely due to lymphomas or disseminated mycobacterial disease.[19,46] Nevertheless, in patients with acute bowel perforation a high suspicion for underlying opportunistic infections is warranted. Acute bowel perforation also elevates the gravity of the prognosis because it signifies an advanced stage of HIV infection.[21,22,29]

The terminal ileum and colon are the most common sites for perforations secondary to CMV enterocolitis.[47] Proof that CMV is the cause of these perforations is confirmed by finding intranuclear inclusion bodies on biopsy specimens of perforation sites.[48] Surgical management of the site of perforation requires suture plication of gastroduodenal perforations, resection and anastomosis of small-bowel perforations, and colostomy for colonic perforations. Cytomegalovirus infection affects the arterioles of the gastrointestinal tract; therefore, perforations are ischemic lesions.[47] Long segments of intestine are involved; this may inhibit normal healing of bowel anastomoses, and is an indication for performing a diverting stoma in selected patients. Antiviral chemotherapy is initiated if not already established.

Bowel Obstruction

Bowel obstruction and intussusception secondary to Kaposi sarcoma, lymphoma, and opportunistic infections

in AIDS patients suggests multifocal disease or widespread dissemination. The intermediate prognosis is poor. The mean survival for disseminated and localized *Mycobacterium avium-intracellulare* is from 3 to 6 months and 11 months, respectively, and the median survival for lymphoma is 4 to 6 months.[49-51] It is generally agreed that surgery offers only palliation of the acute problem with little benefit in prolonging the course of the disease.[21,23,29,51] Small-bowel resection is performed with primary anastamoses, while colonic resections may require fecal diversion.[47] When operative treatment is not emergent, nonsurgical diagnosis of opportunistic infection by CT scan or ultrasound-guided needle biopsy of appropriate sites may be attempted.[23,29]

Toxic Megacolon

Toxic megacolon in the HIV-positive patient has been associated with CMV opportunistic infections or *Clostridium difficile* colitis. Multiple hospitalizations and frequent use of antibiotics and chemotherapeutic agents predisposes HIV/AIDS patients to *C difficile* infection.[52] Bowel perforation and megacolon is an indicator of advanced AIDS and carries a serious prognosis because of the likelihood of death due to peritonitis or other AIDS-related complications.[6] In one case series, emergency subtotal colectomy was associated with an extremely poor outcome and a mortality rate greater than 50%.[53] A conservative approach including colonoscopic decompression of the dilated colon and medical management was shown to have a more favorable short-term outcome.[53] However, Davidson et al[21] achieved a higher success rate for emergent colectomies with early operation, since patients were better able to withstand bowel resection when peritoneal contamination was less severe.

Hepatobiliary Disease

Chronic hepatitis B and C infections share common routes of transmission with HIV infection. Approximately 50% of HIV patients are infected concomitantly with either HBV or HCV which, if not controlled, often leads to cirrhosis.[25] Once clinical AIDS has evolved, opportunistic infections occur in the hepatobiliary tree. Hepatic opportunistic disease seen with CD4 counts less than 100 cells/mm^3 include CMV and fungal infections; *Cryptococcus neoformans, Histoplasma capsulatum, Candida albicans,* and *Coccidiodes immitis*.[54] *Mycobacterium avium-intracellulare* is seen in HIV-infected patients with severe immunosuppression and CD4 counts less than 50 cells/mm^3.[55,56] The characteristic multiple small hepatic abscesses may require liver biopsy for diagnosis. The liver is commonly involved in systemic disease that has disseminated lymphohematogenously. Diagnosis of the liver abnormalities often may be established through biopsy and culture of peripheral sites such as the blood, skin, gastrointestinal mucosa, lymph nodes, and bone marrow.[57] *Entamoeba histolytica* infections of the gastrointestinal tract may spread to the liver and form an abscess. Although this infection is not infrequent among the male homosexual population with AIDS, formation of a liver abscess is an unusual complication.[25]

Cholangiopathy, if not an adverse effect of medication, is a consequence of HIV infection because opportunistic pathogens infiltrate the hepatic parenchyma and cause obstruction of the biliary tree terminal branches. Mechanical obstruction of the bile ducts may be due to enlarged nodes at the porta hepatis. Common opportunistic infections include *Cryptosporidium* species, CMV, and *Microsporidia*.[55,57,58]

Inflammatory changes secondary to invasion of the ducts result in a sclerosing cholangitis that may be identified by thickened ducts seen on ultrasound. Endoscopic retrograde cholangiopancreatography is used to culture the bile or obtain biopsy samples and will guide the specific antimicrobial chemotherapy used for treatment.[57] Operative care for these patients has a limited role beyond diagnosis.

It is important to note that gallstone cholecystitis occurs with equal frequency in HIV-positive and HIV-negative patients, although acute acalculous cholecystitis occurs at a higher frequency in HIV/AIDS patients.[59] Cholecystectomy is typically required for the patient with acute cholecystitis, and is associated with favorable outcomes and a mean survival period of longer than 2 years even in immunosuppressed patients (CD4 count $<$200 cells/mm^3).[60]

Splenomegaly

Splenomegaly, a common physical examination and CT scan finding among patient with AIDS, is usually caused by CMV, *Mycobacterium tuberculosis*, *M avium-intracellulare*, *Pneumocystis carinii,* splenic abscess, lymphoma, or Kaposi sarcoma.[61-65] Some patients may have portal hypertension from severe liver disease, portal vein fibrosis or thrombosis.[61] Patients with an enlarged spleen commonly have left upper quadrant pain, and the spleen is tender to palpation. Splenectomy has been performed with good results for HIV-related immune thrombocytopenia and may be necessary because of spontaneous rupture of the enlarged spleen or rupture from incidental trauma or for relief of symptoms.[46,61,66] Rupture from splenic abscess may also cause bleeding and require operation.

Neoplasms

Kaposi sarcoma, once considered a neoplasm only of the skin but since found in the gastrointestinal tract, lung, liver, and even the heart of AIDS patients, was more common early in the AIDS epidemic.[29] However, a dramatic decline in Kaposi lesions was observed after introduction of the new antiviral regimens.[67] Non-Hodgkins lymphoma, usually an aggressive B-cell lymphoma, is commonly seen in the gastrointestinal tract.[68] Recently, an increasing number of colorectal adenocarcinomas have been diagnosed at an earlier age and more advanced stage in HIV-positive than in HIV-negative patients.[69]

The mean survival time for non-Hodgkins lymphoma has been reported to be from 4 to 29 months, and for adenocarcinoma 12 months, with similar survival times for Kaposi sarcoma.[30,51,69] Surgery in these patients is for the purpose of diagnosis of the disease (needle biopsy),

with palliative surgical intervention for complications secondary to bleeding, obstruction, or perforation of the gastrointestinal tract. Endoscopy and endoscopic ultrasound for visualization and staging should be the diagnostic procedures of choice with chemotherapy as the primary management of lymphoma.[70]

Vascular Disease

In case series of 28 patients with a mean age of 31 years, Marks and Kuskov[71] observed a causal association of HIV infection with vascular aneurysms and fibroproliferative aortoiliac occlusive disease. A rapid, focal, necrotizing arteriopathy with aneurysm or progressive granulomatous vasculitis with vascular occlusion was described. Due to their immunocompromised state, large-artery vasculitis with causative organisms such as *Salmonella* species, *Haemophilus influenza,* and *M tuberculosis* develops.[72] *Salmonella* species are known to have an affinity for atherosclerotic plaques. Adherence of the microbe to plaques in the distal aorta or iliac arteries results in invasive infection, pseudoaneurysm formation, and potential for rupture. A recent case series of 16 patients described a "large-artery vasculitis," which had a striking clinicopathologic overlap with Takayasu disease.[73] Surgical management of pseudoaneurysms before rupture is beneficial. Reconstruction of these patients after resection proceeds along guidelines for the management of any mycotic aneurysm infection, with excision of all infected tissue followed by an extraanatomic reconstruction. Surgical mortality is similar to that of non-HIV patients, and preoperative antiretroviral treatment may reduce the complication rate by increasing CD4 counts.[74]

The increasing life expectancy of HIV/AIDS patients demands reliable vascular access. As for non-HIV/AIDS patients, polyteteraflouroethylene grafts for hemodialysis are associated with a higher infection rate when compared with autogenous ateriovenous fistulas.[75] Gorski et al[76] confirmed a significant infection rate and recommended that prosthetic grafts be avoided if possible, especially if intravenous drug abuse is a risk factor.

Anorectal Disease

The immunosuppressed patient with AIDS is at an increased risk for abcesses, fistulas, fissure, human papillomavirus infection, and squamous carcinoma of the anus.[77-79] Condylomata acuminata can be very large and will commonly need to be surgically excised, followed by local topical therapy. Although some studies have reported an increase in wound complications and delayed healing times,[78,80] others have reported good surgical results.[81] Surgical management for these conditions is dependent on the extent of the abnormality.[80]

EPIDEMIOLOGY OF OCCUPATIONAL TRANSMISSION OF HIV

The average risk of HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% (95% confidence interval [CI] = 0.2%-0.5%).[82,83] After a mucous membrane exposure, it is approximately 0.09% (95% CI = 0.006%-0.5%).[82,83] Episodes of HIV transmission after nonintact skin exposure have been documented, and although the average risk for transmission by this route has not been precisely quantified, it is estimated to be less than the risk for mucous membrane exposures.[84,85] The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified but is probably considerably lower than for blood exposures.[86]

Epidemiologic and laboratory studies suggest that several factors affect the risk of HIV transmission after an occupational exposure. Risk with percutaneous exposure to HIV is found to be greater with exposure to a larger quantity of blood from a patient with HIV/AIDS, such as a device visibly contaminated with the patient's blood, a procedure that involves a needle being placed directly in a vein or artery, or a deep injury.[87]

The risk of transmission is increased with exposure to blood from a patient with terminal illness, possibly reflecting either the higher titer of HIV in blood late in the course of AIDS or other factors (eg, the presence of syncytia-inducing strains of HIV). Although a lower viral load (eg, <1500 RNA copies/mL) or one that is below the limits of detection probably indicates a lower titer exposure, it does not entirely rule out the possibility of transmission.[87]

RECOMMENDATIONS FOR POSTEXPOSURE PROPHYLAXIS

Recommendations for HIV postexposure prophylaxis include a basic 4-week regimen of 2 drugs.[88] Combinations of agents used for HIV exposures are zidovudine and lamivudine; lamivudine and stavudine; or didanosine and stavudine. An expanded regimen that includes the addition of a third drug is recommended for HIV exposures that pose an increased risk for transmission. When the virus is known or suspected to be resistant to one or more of the drugs considered for the prophylaxis regimen, the selection of drugs to which the patient's virus is unlikely to be resistant is recommended. In special circumstances (eg, delayed exposure report, unknown source person, pregnancy in the exposed person, resistance of the source virus to antiretroviral agents, or toxicity of the prophylaxis regimen) consultation with local experts and/or the National Clinicians' Post-Exposure Prophylaxis Hotline (1-888-448-4911) is advised.[88] Occupational exposures should be considered urgent medical conditions to ensure timely postexposure management and administration of hepatitis B immunoglobulin, hepatitis B vaccine, and/or antiretrovirals.

CONCLUSIONS

At the onset of the AIDS epidemic in 1984, pessimism was pervasive regarding operative treatment of the HIV/AIDS patient. Discouragingly poor surgical outcomes and concern about accidental exposure and infection with the virus dismayed surgeons. Current and accurate knowledge about the modes and degree of risk of transmission has lessened apprehension but not caution in the operating room. All surgical team members must routinely practice

safe techniques to avoid blood-borne viral infection. Antiviral advances have resulted in a major decline in opportunistic infection and, consequently, AIDS-related surgical emergencies are correspondingly rare. Operative outcomes are now favorable, approaching mortality and morbidity rates similar to patients without HIV infection. Surgical diseases unique to the AIDS patient still require operation for diagnostic, palliative or curative intent.

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