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Radical prostatectomy in patients infected with human immunodeficiency virus

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Abstract

OBJECTIVE—To present the complications and early outcomes in a small series of men infected with human immunodeficiency virus (HIV) and treated with radical prostatectomy (RP) for prostate cancer, and to review reports on surgery in HIV-positive patients.

PATIENTS AND METHODS—During 2002–2005, seven men infected with HIV underwent RP at our institution. For the five patients whose HIV status was known before surgery, we retrospectively examined preoperative variables, including HIV-specific data (clinical category, CD4 + lymphocyte count, viral load, duration of HIV diagnosis, and opportunistic infections), and the complications and early outcomes after RP.

RESULTS—Before RP all the patients were in the Center for Disease Control clinical category A (asymptomatic HIV infection). The CD4+ counts before RP ranged from 269–870 cells/μL and viral loads ranged from <50–18 700 copies/mL. Three patients were on highly active anti-retroviral therapy (HAART) at the time of surgery. After RP, two patients had incisional wound infections, including one requiring re-hospitalization for intravenous antibiotics. During the follow-up (median 26 months) none of the patients progressed to acquired immunodeficiency syndrome or developed biochemical recurrence of prostate cancer. One healthcare worker was exposed to contaminated urine and placed on prophylactic therapy, but has not sero-converted.

CONCLUSION—The risk of peri-operative complications in HIV-positive patients can be minimized by carefully selecting the patient and procedure, and by measuring routine and HIV-specific preoperative variables. The two infectious complications in this series were in patients with less favourable preoperative factors, i.e. the lowest CD4+ count and the highest viral load. Further experience is needed to determine whether the risk of surgical infections is higher in this cohort. However, our results are consistent with reports from other surgical specialties that surgery in asymptomatic HIV-positive patients is safe and effective.

Keywords

prostate cancer; radical prostatectomy; human immunodeficiency virus; HIV

INTRODUCTION

An estimated 1 million people in the USA are infected with HIV [1]; as approximately 75% of all HIV-infected patients are men, a significant number of HIV-infected patients are at risk of developing prostate cancer, the most common malignancy in men. With their life-expectancy

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CONFLICT OF INTEREST

None declared.

increased by the use of highly active anti-retroviral therapy (HAART), increasingly many HIV-positive men will be diagnosed with clinically relevant prostate cancer [2,3].

Data on the treatment of prostate cancer in HIV-infected patients are extremely limited. With only scattered case reports and case series, there are currently no studies, to our knowledge, discussing the outcomes of HIV-positive men undergoing radical prostatectomy (RP) for the treatment of prostate cancer. We present a small series, reporting the peri-operative complications and early outcomes in HIV-infected men undergoing RP for the treatment of prostate cancer. We also review reports on surgery in HIV-infected patients.

PATIENTS AND METHODS

Between December 2002 and August 2005, 1124 RPs were performed for the treatment of prostate cancer at Memorial Sloan-Kettering Cancer Center. After obtaining approval of the institutional review board, we retrospectively reviewed these patients to identify HIV-infected men who underwent RP for prostate cancer. Only patients who were diagnosed with an HIV infection before surgery were included in this study.

Before RP, the oncological variables obtained were the PSA level, Gleason grade and clinical stage; HIV-specific variables were the CD4+ lymphocyte count, viral load, history of opportunistic infections, and Centers for Disease Control (CDC) clinical and CD4+ T-lymphocyte categories [4]. The CDC clinical categories range from A (asymptomatic seropositivity) to C (AIDS diagnosis). The CD4+ T-lymphocyte category is defined by CD4 + lymphocyte counts, which for categories 1–3, respectively, are >500, 200–499 and <200 cells/ μ L. Peri-operative complications and the outcomes soon after RP were reviewed.

RESULTS

Seven HIV-infected men had RP during the period under review; two were diagnosed at the time of surgery or shortly afterwards, and were excluded from the study as preoperative HIV-specific data were not available. The study group thus comprised the five remaining patients; their characteristics are described in Table 1. The age range was 45–59 years, the PSA level 4.1–30.8 ng/mL, and the biopsy Gleason sum 6 or 7. Three patients were clinical stage T1c and two were clinical stage T2a. HIV-specific findings before RP included a viral load of <50–18 700 copies/mL and a CD4+ lymphocyte count of 269–870 cells/ μ L. These lymphocyte counts placed two of the patients into CD4+ Tlymphocyte category 2 and the remaining three into category 1. All five patients were clinical category A. None of the patients had any opportunistic infections before or after RP. Three of the five patients were on HAART at the time of surgery. The median (range) follow-up was 26 (11–32) months.

After RP two of the five patients had wound infections, including one requiring rehospitalization for i.v. antibiotics. No patients progressed to AIDS during the study period. Although one patient had a positive lymph node and extracapsular extension on pathological review, none had biochemical recurrence during the limited follow-up.

There were no blood exposures to any healthcare workers during this period. One healthcare worker was exposed to contaminated urine and was placed on prophylactic therapy; this worker has not sero-converted during the 6 months since exposure.

DISCUSSION

With the development of HAART therapy in the mid-1990s, the morbidity and mortality associated with HIV infections have significantly decreased [2]. HIV is now considered a chronic condition rather than a rapidly progressive, fatal disease [5]. This transition has

changed the treatment of concomitant diseases in HIV-positive patients. With data clearly showing that HIV-positive patients can live well over a decade with few or no sequelae from their disease, many asymptomatic HIV-positive patients now undergo elective screening and treatment for illnesses unrelated to HIV [6-8].

This phenomenon has also carried over to urological diseases. As the overall survival of HIV-infected men increases, the number of HIV-positive men aged >50 years will increase, which is expected to result in a concomitant increase in the incidence of prostate cancer in HIV-positive men [9]. This idea is supported by the results of prostate cancer screening in a cohort of HIV-positive men aged >35 years [3]. On multivariate analysis, increasing age ($P = 0.005$) and duration of HIV infection ($P = 0.047$) were significant risk factors for developing prostate cancer. Furthermore, the rate of prostate cancer among HIV-positive men aged 60–70 years was 20.5 times greater than among age-matched men in the general population ($P < 0.001$).

As many HIV-positive men on HAART will probably have a normal or near-normal life-expectancy, some of these men will develop prostate cancers which are clinically relevant. Consequently, increasingly many urologists will be called upon not only to diagnose prostate cancer in these patients, but also to treat them.

There are now several case studies reporting prostate cancer in HIV-infected men [10-12]. None of these reports, including the most recent study by Levinson *et al.* [12], specifically addresses the use of RP in a series of HIV-infected men. To our knowledge, the present series is the first to report peri-operative complications and outcomes in a preliminary series of HIV-infected men undergoing RP for prostate cancer.

There are few clinical data on elective surgery in HIV-positive patients available in other surgical subspecialties. Due to high complication rates in early series of AIDS-related surgery, there has been much hesitation in performing both elective and emergency procedures in HIV-positive patients [13-15]. Furthermore, unknown responses to treatment and the occupational risks to the surgical team have influenced physicians to treat HIV-infected patients with treatment strategies other than surgery.

The existing reports on complications in HIV-positive patients are often conflicting, and based mainly on small retrospective studies and series such as the present. The heterogeneity of patients with HIV and the large variety in the type of surgical procedures make it difficult to reach firm conclusions about outcomes and complication rates in these patients. Despite the shortcomings of the current data, several variables have been suggested as factors which may influence the complication rates in these patients after surgery. These include: (i) the CD4+ T-lymphocyte category; (ii) the clinical category of the HIV infection; (iii) the type of operative procedure; and (iv) the serum albumin level before surgery.

Among preoperative laboratory variables the CD4+ count and albumin level appear to have clinical relevance for stratifying risk in HIV-infected patients. The CD4+ lymphocyte count consistently correlates with HIV-related immune dysfunction and disease progression, and provides information needed to guide the medical management of people infected with HIV [18,19]. The CDC defines three CD4+ Tlymphocyte categories based on the patient's CD4+ lymphocyte count. Several of the larger and more recent studies have shown a significant increase in the morbidity and mortality associated with CD4+ counts of <200 cells/ μ L (category 3) [14,20-22]. Grubert *et al.* [22] retrospectively compared 235 patients with HIV undergoing obstetric and gynaecological procedures with 235 HIV-negative patients matched for procedure and age. They found that patients with CD4+ counts of <200 cells/ μ L, especially those undergoing abdominal procedures, had a three to four times greater risk of complications. These findings were supported by Lin *et al.* [21], who reviewed abdominal aortic surgery in

48 HIV-seropositive patients. They also showed a significant increase in overall operative morbidity in patients with CD4 counts of <200 cells/ μ L ($P = 0.041$).

However, the true prognostic significance of CD4+ lymphocyte counts remains debatable because of studies that have failed to reproduce these findings [23,24]. In a blinded, prospective study by Harrison *et al.* [24], there was a difference in the incidence of postoperative wound infections based on CD4+ lymphocyte counts. In the present series, all the patients had CD4+ lymphocyte counts of >250 cells/ μ L; two were in lymphocyte category 2 before surgery, one of whom developed a deep wound infection requiring re-hospitalization and i.v. antibiotics. Although this might have been coincidental, this patient had the lowest CD4+ lymphocyte count before RP, at only 269 cells/ μ L, despite receiving HAART. Currently, the predictive value of CD4+ lymphocyte counts remains unclear. Therefore, it seems most prudent to properly identify and optimize the immune status of CD4+-deficient patients before any elective surgery.

Serum albumin level also appears to have prognostic significance for the mortality and morbidity of HIV-infected patients. A low albumin level reflects a poor nutritional status and a declining overall state of health of the patient, which might not be clinically evident at the time of surgery. The significance of albumin levels of <3.5 g/dL in HIV-positive patients was examined in several series in both operative and non-operative settings [21,25]. These studies showed that hypoalbuminaemia is not only associated with greater morbidity but is also a better predictor of death than CD4+ lymphocyte counts [21,25].

At the time of the present study we were not routinely examining preoperative albumin levels. All of the present patients were well-nourished and clinically in excellent health. As they were all classified as clinical category A, they were unlikely to have a low serum albumin level. Nevertheless, based on the ease and availability of this test, and the significant risks associated with low albumin levels, we recommend it for all HIV-positive patients being evaluated for major urological surgery.

Another variable that might be useful in stratifying the risk of HIV-infected patients is the CDC clinical category. This staging system recognises the complete clinical continuum of HIV infections and allows physicians to categorize their patients. Because several studies have noted an increase in infection rates among symptomatic HIV-positive patients, the clinical categories might be useful for predicting complications after surgery in HIV-infected patients [16,17]. However, the utility of the clinical categories in predicting complications after surgery remains to be assessed, as it has not been confirmed in a prospective study.

Along with preoperative variables, the type of operative procedure might have a significant influence on the complication rates after surgery in HIV-positive patients. Several reports examined the incidence of complications in HIV-positive patients undergoing major abdominal procedures [14,21,22]. As previously noted, Grubert *et al.* [22] matched 265 HIV-positive patients with 265 HIV-negative patients according to age and procedure. The HIV-positive patients had a statistically higher complication rate in both abdominal and intra-uterine operations ($P < 0.001$). By contrast, complication rates were similar in minor operations, such as breast, cervical, or endoscopic procedures [22]. In reports on general and orthopaedic surgery, HIV-seropositivity also does not appear to influence the complication rates of minor or non-abdominal, elective procedures [7,26,27]. However, this differs in the setting of traumatic, emergency cases; in a large series of 476 patients with trauma, the wound infection rate was significantly higher in asymptomatic HIV-infected patients than in uninfected patients [28].

Based on these data, many of the elective endoscopic and minor urological procedures would probably be unaffected by the patient's HIV status, unless the patient was symptomatic or

significantly malnourished or immunocompromised. However, in more involved procedures such as RP or radical cystectomy, the significance of HIV positivity remains unclear. In the present series there were no major complications and no patient required a re-operation. However, two patients developed wound infections after RP, including one who required re-hospitalization. Although this rate of infection might seem high, there were too few patients to make any reasonable comment on the incidence of wound infections in HIV-positive patients. Considering all factors, we think that patients in CD4+ T-lymphocyte category 1 and clinical category A will likely tolerate RP well and should therefore be given the option to undergo this procedure as long as the patient has had an adequate assessment beforehand and is given peri-operative antibiotics.

The assessment in these patients before RP should include the variables used in sero-negative patients, along with HIV-specific variables such as CD4+ count, viral load and albumin level. Although not discussed here, the viral load and the history of opportunistic infections might also play a role in the preoperative evaluation of these patients. Both of these factors are intimately related to CD4+ lymphocyte counts and the overall immune status of these patients, and both affect the overall survival of HIV-positive patients [29].

In terms of risks to the physician, universal precautions should obviously be taken in all patients, not only those who are HIV-positive. Surgery in patients with a known blood-borne pathogen such as HIV or hepatitis should prompt surgeons to take special care in the handling and usage of sharp instruments. When universal precautions are followed, the risk of transmission remains low [30]. Nevertheless, some authors think that laparoscopic or robotic prostatectomy might have an important role in treating prostate cancer in HIV-positive patients, while minimizing the risk to the surgeon [12].

In the present series there were no instances of blood exposure to any healthcare workers, but one had ocular exposure to infected urine. Although the documented risk of transmission is <0.09% [30], the worker was placed on prophylactic therapy and had not sero-converted 6 months after the exposure.

In conclusion, like all specialists, urologists will be called upon more frequently in the future to evaluate and treat HIV-positive patients, not only for prostate cancer, but for all urological diseases. Urologists will be asked to understand the inherent risks involved in treating such patients and know how to minimize these risks for both the patient and themselves. In this early case series, we found that despite risks in this group of patients, RP can be safe and cause minimal morbidity in properly selected HIV-positive patients. The assessment of HIV-positive patients before surgery should include CD4+ counts, viral load, albumin levels, and clinical staging. More patients and a longer follow-up will be required to understand the significance of HIV sero-positivity in patients undergoing RP for the treatment of localized prostate cancer.

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Abbreviations

RP, radical prostatectomy; HAART, highly active antiretroviral therapy; CDC, Centers for Disease Control.

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The patients' characteristics

Characteristic	Patient				
	1	2	3	4	5
Age at surgery, years	57	49	50	45	59
Follow-up, months	11	32	27	26	19
Preoperative variables					
PSA, ng/mL	30.8	4.1	8.3	5.6	7.5
Biopsy Gleason grade	3 + 4	3 + 3	3 + 4	3 + 4	3 + 4
Clinical stage	T2a	T1c	T1c	T2a	T1c
Duration of HIV diagnosis, years	6	13	2	N/A	14
Viral load, copies/mL*	<50	<50	3600	18 700	<50
HIV clinical category	A	A	A	A	A
CD4+ count, cells/ μ L	858	269	410	680	870
CD4+T-lymphocyte category*	1	2	2	1	1
HAART	Yes	Yes	No	No	Yes
Pathological findings					
Stage	pT3a	pT2b	pT2b	pT2b	pT2b
RP Gleason grade	3 + 4	3 + 3	3 + 4	3 + 3	3 + 4
Surgical margin status	-ve	-ve	-ve	-ve	-ve
Lymph node status	+ve	-ve	-ve	-ve	-ve
Postoperative variables (at last follow-up)					
PSA, ng/mL	<0.1	<0.1	<0.1	<0.1	<0.1
Viral load, copies/mL*	<50	<50	2400	19 600	<50
HIV clinical category	A	A	A	A	A
CD4+ count, cells/ μ L	388	300	510	387	700
CD4+T-lymphocyte category*	2	2	1	2	1
Complications	None	Deep wound infection	None	Superficial wound inf.; lymphocele	None

* 1993 revised classification system for HIV infection expanded surveillance case definition for AIDS among adolescents and adults [4].