

Surgical Site Infections in HIV-infected Patients: Results from an Italian Prospective Multicenter Observational Study

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Abstract

Background: The quality of life of the HIV-infected population in developed countries has substantially improved over the years. Accordingly, the clinical limitations in the surgical treatment of the HIV-infected patients are becoming fewer, and the number of HIV-infected patients undergoing surgical interventions of all types is increasing. However, available data on the incidence and risk factors for post-surgical complications, such as surgical site infections (SSI), in HIV-infected patients are still limited and often controversial. The aim of this study was to determine the incidence and the associated risk factors for SSI in HIV-infected patients.

Methods: A 1-year observational prospective multicenter surveillance study was conducted in 11 Italian Infectious Diseases Clinical Centers from which 305 consecutive HIV-infected patients undergoing different surgical procedures were enrolled. Postdischarge surveillance was conducted within 30 days after surgery. A number of variables were included in a multivariate analysis aimed at assessing potential risk factors for SSI, including body mass index, diabetes, Hepatitis C (HCV) and hepatitis B virus infection, lipodystrophy, HIV viral load, CD4 cell count and white blood cell count, preoperative hospital stay, National Nosocomial Infection Surveillance (NNIS) risk score, and any antimicrobial prophylaxis.

Results: SSI occurred in 29 of 305 (9.5%) patients, of which 17 (58.6%) SSI occurred during hospital stay, and 12 (41.4%) occurred during the postdischarge period. The SSI of the 29 patients were classified as superficial (21, 72.4%), deep (four, 13.8%), organ/space (one, 3.4%), and sepsis (three, 10.3%). Nearly 50% of the superficial and 50% of the deep SSI occurred during the postdischarge period. Organ/space infection and sepsis accounted for 13.7% of all SSI and were observed during the in-hospital stay. The multivariate analysis revealed that HCV co-infection was significantly associated to SSI occurrence. Total hospital stay was longer among patients with SSI than among those without SSI ($p = 0.041$).

Conclusion: Although 92.5% of our HIV-infected patients presented a NNIS score ≤ 1 , the SSI rate was twofold higher than that reported in Italian and European studies for the general population, with more severe clinical presentations. This is the first report of an association between HCV-HIV

co-infection and SSI occurrence. Additionally, the viro-immunological status of our patients was not related to SSI occurrence, which suggests the need for further research for other potential risk factors that may be implicated in the occurrence of SSI.

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Introduction

The quality of life and survival expectancy of HIV-infected patients have substantially improved [1, 2], and the clinical barriers towards surgical treatment of HIV-infected patients, which were once associated with poor surgical outcomes and to the surgeon's concern about accidental exposure with the HIV, are gradually disappearing [3]. Indeed, the number of HIV-infected patients undergoing "high-risk" surgical interventions, such as orthotopic liver transplantation (OLT), is increasing [4–6], although these patients do have a higher risk of mortality from infectious complications [6].

However, the body of literature currently available on the incidence and risk factors for surgical site infection (SSI) in HIV-infected patients is limited and controversial, and it remains to be established whether HIV-infected patients should be considered at higher risk for SSI occurrence. In addition, only few Italian studies have been conducted on SSI in HIV-infected patients [7]. Given this background, we conducted a prospective observational multicenter study on SSI in HIV-infected patients who were followed-up in Infectious Diseases Hospitals. The aim of our study was to determine the incidence of SSI and the associated risk factors in HIV-infected patients.

Methods

This was an observational prospective multicenter surveillance study conducted in 11 Italian Infectious Diseases Clinical Centers between December 2005 and December 2006 which enrolled 305 HIV-infected patients undergoing the following surgical procedures: caesarean sections, gastrointestinal, biliary, and hepatosplenic interventions, cervico-facial district, plastic, and dermatological interventions, cardiovascular interventions, lymphadenectomies, and orthopedic, genitourinary tract, and thoracic interventions.

A coordinating physician was assigned to each participating center to collect and manage the patient-specific demographic, clinical, and operation-specific data, including the Karnofsky Index [8], and the data on SSI occurrence, including sepsis related to SSI. The HIV-infected patients also submitted to postdischarge surveillance for the first 30 days following the operative procedure to enable the detection of SSI occurring after discharge.

SSI diagnosis was performed using the Centers for Diseases Control and Prevention (CDC) standardized criteria [9]. Sepsis was defined according to the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference [10]. In addition, the National Nosocomial Infection Surveillance (NNIS) risk index score was calculated according to CDC definition [11].

To assess potential risk factors for SSI, we first conducted a univariate analysis that included the following variables: gender, age, body mass index (BMI), diabetes, hepatitis C virus (HCV) infection, hepatitis B virus (HBV) infection, presence of lipodystrophy, HIV viral load, CD4 cell count and WBC at intervention time, preoperative hospital stay, which was stratified according to the median value for overall interventions, NNIS risk index score, and any preoperative antimicrobial prophylaxis. The HIV viral load and total hospital stay were categorized according to the median values of each variable. Univariate

analysis was performed using the χ^2 test, and the results were considered to be significant at $p < 0.05$.

Multivariate analysis was conducted using a backward stepwise elimination procedure, and the results were expressed in terms of odds ratio (OR) with their respective 95% confidence interval (CI).

Each participating institution received ethical approval from its respective Ethical Committee according to local regulations.

Results

Table 1 summarizes the main characteristics of the HIV-infected population enrolled in the study. SSI occurred in 29 of 305 (9.5%) patients; of these, 17 (58.6%) SSI occurred during hospital stay, and 12 (41.4%) occurred within 30 days after discharge.

Table 2 reports the classification of the 29 SSI according to the CDC's criteria and stratified both for in-hospital and postdischarge occurrence. Most of the SSI (72.4%)

Table 1
Characteristics of the HIV study population.

Total number of patients, n	305
Males/total, n	132 (43.3%)
Age, years, mean–median (range)	40.7–41 (19–74)
Body mass index, kg/m ² , mean–median (range)	23–22 (15–39)
Risk factor for HIV transmission, n	
Drug addiction	117 (38.4%)
Sexual (hetero–homosexual)	153 (50.2%)
Drug addiction and sexual	18 (5.9%)
Other ^a	17 (5.6%)
CDC group, n ^b	
A	126 (41.3%)
B	94 (30.8%)
C	85 (27.8%)
CD4+ cell, count nadir/mm ³ , mean–median (range)	233–192 (0–909)
Karnofsky index, mean–median (range)	91–100 (30–100)
HIV RNA, cp/ml, median (range) ^c	<50 (< 50 to > 500,000)
CD4+ cell, count/mm ³ , mean–median (range) ^c	413–375 (2–1,214)
White blood cell, count/mm ³ , mean–median (range) ^c	7,153–6,630 (1,000–23,300)
Diabetes, n	20 (6.5%)
HCVAb+ only, n	127 (41.6%)
HBsAg+ only, n	6 (2%)
HCV Ab+ and HBs Ag+, n	12 (3.9%)
ASA physical status, mean–median (range)	2–2 (1–5)
ARV number/total	253 (82.9%)
Lipodystrophy	53 (17.4%)

HCV Hepatitis C virus; HbsAg hepatitis B surface antigen; HCV Ab anti-HCV antibody; ASA American Society of Anesthesiologists; ARV antiretroviral therapy; ^a Vertical transmission, blood transfusion, unknown; ^b Centers for Disease Control and Prevention HIV group; ^c at intervention time

CDC classification of SSI	Total SSI (n = 29)	In-hospital SSI (n = 17; 58.6%)	Postdischarge SSI (n = 12; 41.4%)
Superficial	21 (72.4%)	11 (52.4%)	10 (47.6%)
Deep	4 (13.8%)	2 (50%)	2 (50%)
Organ/space	1 (3.4%)	1 (100%)	0
Sepsis	3 (10.3%)	3 (100%)	0

SSI Surgical site infections; CDC Centers for Diseases Control and Prevention

Type of intervention	Total, n	Median hospital stay (days)	Median NNIS risk score	Preoperative prophylaxis, n	Patients with SSI, n	Patients with postdischarge SSI, n ^a	Incidence of SSI (95% CI)
All	305	5	0	235 (77%)	29	12 (41.4%)	9.5% (6.1–13.0)
Caesarean section	101	5	0	98 (97%)	5	4 (80%)	5.0% (0.6–9.3)
Gastrointestinal, biliary and haepatosplenic ^b	59	9	1	47 (79.6%)	5	2 (40%)	8.5% (1.1–15.9)
Cervico-facial district ^c	28	4	0	16 (57.1%)	0	–	–
Plastic/dermatological	24	3	1	13 (54.2%)	3	0	12.5% (0–26.6)
Cardiovascular	22	9	1	16 (72.7%)	7	2 (28.6%)	31.8% (8.4–55.3)
Lymphadenectomy	22	8	0	5 (22.7%)	2	2 (100%)	9.1% (0–21.6)
Orthopedic	22	14	1	18 (81.8%)	4	1 (25%)	18.2% (0.5–35.9)
Genitourinary tract ^d	21	6	1	15 (71.4%)	3	1 (33.3%)	14.3% (0–30.4)
Thoracic	6	9	1	6 (100%)	0	–	–

NNIS National Nosocomial Infection Surveillance; CI confidence interval; ^a percentage refers to total number of SSI for the specific type of intervention; ^b includes ten interventions performed laparoscopically, for which the NNIS index score was modified by subtracting 1 point; ^c includes otorhinolaryngoiatric surgery (n = 9), odontoiatric procedures (n = 7), neurosurgery (n = 5), maxillo-facial (n = 3), ophthalmic (n = 1), and thyroid (n = 3) surgery; ^d includes nephrological (n = 5), andrological (n = 4) surgery, and other gynecological procedures except cesarean sections (n = 12)

were superficial. Nearly 50% of the superficial and 50% of the deep SSI occurred during the postdischarge period. Organ/space infection and sepsis accounted for 13.7% of all SSI and were observed during the in-hospital stay.

As reported in table 3, the highest SSI incidence rates were observed in cardiovascular (31.8%; 95% CI 8.4–55.3), orthopedic (18.2%; 95% CI 0.5–35.9), genitourinary tract (14.3%; 95% CI 0–30.4), and plastic and dermatological (12.5%; 95% CI 0–26.6) interventions. Lymphadenectomies and gastrointestinal interventions had lower and similar SSI incidence rates (9.1; 95% CI 0–21.6, and 8.5%; 95% CI 1.1–15.9, respectively). The lowest SSI rates were observed in cesarean, thoracic, and cervico-facial district interventions, with most of the SSI following lymphadenectomies and cesarean sections occurring in the postdischarge period (100% and 80%, respectively). These two latter interventions had also the lowest NNIS index score (= 0).

In the univariate analysis, age ≥ 45 years and HCV co-infection were significantly associated with SSI ($p = 0.036$, and $p = 0.008$, respectively), and the NNIS risk index score was close to significance ($p < 0.054$). Viro-

immunological status (CD4 cell count and HIV viral load) was not significant for SSI occurrence. In the multivariate analysis, only HCV infection remained significantly associated with SSI (Table 4).

Finally, total hospital stay was significantly associated to SSI (SSI rate = 15.1% among patients with total hospital stay > 5 days vs 4.8% for those with total hospital stay ≤ 5 days; OR 3.1 [95% CI 1.3–7.4]; $p = 0.041$).

Discussion

There are very few published studies dealing with SSI in HIV-infected patients, and most of the information that is available refers to selected surgical procedures [12–21].

In our prospective observational study, we collected data on different surgical procedures and found an overall SSI rate of 9.5%, which is nearly twofold higher than that reported in other Italian [7, 22–24] and European studies [22, 25] for the general population. However, because the SSI rate depends on the operative procedure, differences in the SSI rate between various populations could also be a result of the different distribution of the surgical procedures. The proportion of deep SSI detected during the

Characteristics	Total, n (%)	SSI infection, n (%)	Odds ratio (95% CI)	MLR-OR ^a (95% CI)
Gender				
Male	132	16 (12.1)	1	
Female	173	13 (7.5)	0.6 (0.3–1.3)	
Age (years)				
<45	210	15 (7.1)	1	1
≥45	95	14 (14.7)	2.2 (1.0–4.9)	2.0 (0.9–4.5)
HCV infection				
No	166	9 (5.4)	1	1
Yes	139	20 (14.4)	2.9 (1.3–6.7)	2.7 (1.2–6.3)
HIV viral load				
Undetectable	185	15 (8.1)	1	
Detectable	120	14 (11.6)	1.5 (0.7–3.2)	
CD4 cell count (/mm ³)				
≥200	230	20 (8.7)	1	
<200	75	9 (12.0)	1.4 (0.6–3.3)	
WBC number pre-intervention (/mm ³)				
≥4,000	258	22 (8.5)	1	
<4,000	47	7 (14.9)	1.9 (0.8–4.7)	
Preoperative hospital stay				
0–1	236	22 (9.3)	1	
>1	69	7 (10.1)	1.1 (0.5–2.7)	
NNIS risk index score				
0	157	10 (6.4)	1	
1–3	148	19 (13.0)	2.2 (1.0–4.8)	
Body mass index				
Underweight	38	4 (10.5)	1.4 (0.4–4.3)	
Normal	200	16 (8.0)	1	
Overweight	47	6 (12.8)	1.7 (0.6–4.6)	
Obesity	20	3 (15.0)	2.0 (0.5–7.7)	
Diabetes				
No	285	25 (8.8)	1	
Yes	20	4 (20.0)	2.6 (0.8–8.4)	
HBV infection				
No	286	28 (9.8)	1	
Yes	19	1 (5.3)	0.5 (0.1–4.0)	
Lipodistrophy				
No	252	21 (8.4)	1	
Yes	53	8 (15.1)	2.0 (0.8–4.7)	
Perioperative prophylaxis				
No	69	9 (13.0)	1	
Yes	236	21 (8.9)	0.7 (0.3–1.8)	

OR Odds ratio; MLR-OR multiple logistic regression odds ratio; ^a backward stepwise elimination procedure

postdischarge period in our study is higher than that generally reported for the general population [7, 25], which further underlines the importance of postdischarge surveillance for the HIV-infected patients. Another interesting finding in our HIV-infected population is the relatively high proportion of sepsis, i.e., three of 29 (10.3%) patients with SSI. Although we did not perform a case-control study, these findings suggest that SSI occur more frequently and are more severe in the population of HIV-infected patients than in the general population.

When SSI were analyzed according to the type of intervention, the highest rate was observed in cardiovascular surgery (7/22, 31.8%). However, these results should be considered carefully as few studies are available on HIV-infected patients in this clinical setting [16, 17], and other these studies report lower SSI rates (range 8–10%) [16, 17]. A possible explanation for the high rate of superficial SSI in cardiovascular interventions could be the close and careful follow-up to which the HIV-infected patient is submitted, particularly during the perioperative period. Another

explanation could also be the skin and mucosal microbial colonization rate of the HIV-infected population [26]. A high SSI rate was also observed for orthopedic surgery (18.2%; 4/22). In the literature, the SSI rate in HIV patients undergoing orthopedic surgery ranges from 16.7% in orthopedic trauma patients [27], to 71.4% [18, 19] in patients with open reduction of fractures. For cesarean sections, we found a 4.9% (5/101) SSI rate, which is lower than that reported in previous studies (range 6–29.2%) [14, 15]. In our study, cesarean sections were all elective since almost all of the HIV-infected pregnant women were regularly followed-up at each participating center, which could explain the lower SSI rate we found.

In terms of risk factors for SSI in HIV-infected patients, we found that HCV infection was the only risk factor independently associated with SSI occurrence (Table 4). The role of HCV infection in the HIV-infected population is of increasing interest since co-infection has been found to be significantly associated to AIDS progression and hepatitis/liver-related death [28–30]. To our knowledge, the association between HCV infection/liver disease and SSI has not yet been investigated. Unfortunately, and this represents a limitation of our study, we did not take into account the stage of liver disease of our HIV/HCV co-infected population.

Another interesting finding of our study was that the CD4+ cell count and the HIV viral load were not associated to SSI occurrence, although there is published data indicating an association between viro-immunological status and SSI occurrence (particularly for patients with low CD4+ cell counts) [12, 13].

Finally, we found that SSI was significantly associated with increased total hospital stay, thus representing also a considerable problem in terms of hospital costs.

The main limitation of our study is the lack of a control group among HIV-negative patients, primarily due to organizational difficulties related to the multicenter design of the study and to the fact that not all of the Infectious Diseases Centers participating in the study were able to obtain matching controls from surgical wards. Moreover, we did not stratify by clinic due to the limited number of interventions performed by each single clinic of the center.

Conclusion

Although 92.5% of our HIV-infected patients presented a NNIS score ≤ 1 , the SSI rate among our HIV patient population was twofold higher than that reported in Italian and European studies for the general population, with more severe clinical presentations. Moreover, we observed for the first time an association between HCV–HIV co-infection and SSI occurrence. Additionally, we found that the viro-immunological status of our patients was not related to SSI occurrence, which suggests the need to continue the search for other potential risk factors that may be implicated in the occurrence of SSI.

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