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HIV infection and poor renal outcomes following noncardiac surgery

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Background/aim: The relevance of HIV infection in perioperative renal risk stratification remains unclear. This research sought to investigate the impact of HIV infection, as well as other established preoperative risk factors for poor perioperative renal outcome (PPRO), in a population of 565,225 adult noncardiac surgery patients whose data were obtained from the 2009–2011 California State Inpatient Database.

Materials and methods: HIV status, established preoperative risk factors, and the study outcome (PPRO) were determined with the Clinical Classification Software codes recorded for each patient. Data were analyzed using univariate (Mann–Whitney U test, chi-square, and Fisher's exact test) and multivariate (binary logistic regression) statistical methods.

Results: The established preoperative risk factors were independently associated with PPRO. HIV infection was not an independent risk factor for PPRO in this study (odds ratio: 1.573, 95% confidence interval: 0.998–2.480; P = 0.051). Patients with HIV infection tended to have a higher burden of certain established preoperative risk factors for PPRO than patients without HIV infection.

Conclusion: HIV-infected patients should be thoroughly screened for established preoperative risk factors and carefully managed during the perioperative period to reduce their risk of PPRO.

Key words: HIV, noncardiac surgery, renal outcomes

1. Introduction

Renal dysfunction in nonsurgical, hospitalized HIV-infected patients is associated with significant morbidity and mortality. For instance, Lopes et al. found an almost 70% higher risk of long-term mortality in HIV-infected patients with acute kidney injury in comparison to HIV-infected patients without acute kidney injury (1). The prevalence of poor perioperative renal outcome (PPRO) in the hospitalized HIV-infected population has been estimated between 1.3% and 2.0% (2,3). It is unclear whether HIV infection is an independent risk factor for PPRO following noncardiac surgical procedures. The purpose of this study was to determine whether HIV infection is an independent risk factor for PPRO in patients undergoing noncardiac surgery when established preoperative risk factors are accounted for. We did not include cardiac surgery patients in this research for two reasons. First, renal dysfunction following cardiac surgery has been extensively studied (4). Second, the pathophysiology of renal dysfunction in noncardiac surgery patients is distinct from that observed in cardiac surgery patients (4) and therefore warrants investigation through a separate research study.

2. Materials and methods

This study was a subanalysis of data obtained for 565,225 adult patients (≥18 years old) undergoing various noncardiac surgery procedures (Table 1). Their data were obtained from the 2009–2011 California State Inpatient Database (SID). All data recorded in the SID are deidentified and publically available. The use of the data for this study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa. Clinical Classification Software (CCS) codes proposed by the Healthcare Cost and Utilization Project (Table 2) and the "present on admission" field in the SID were used to identify diagnoses of HIV infection and several established preoperative comorbid risk factors for PPRO (5,6). The CCS codes are predefined groupings of the International Classification of Disease, 9th edition (ICD-9) codes, proposed by the Healthcare Cost and Utilization Project, and are listed in Table 2. Surgical procedures were stratified according to procedural risk (Table 1).

Data related to patient age, sex, and emergent hospital admission were extracted from the SID for this study. The study outcome, PPRO, was defined as any of the following diagnoses that were not present on admission to hospital:

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Table 1. Proportion of patients included in the study population stratified by surgical procedure.

Surgical procedure	n (% of study population)
Above-knee amputation	4184 (0.7)
Below-knee amputation	11,735 (2.1)
Carotid endarterectomy	19,711 (3.5)
Colectomy[a]	32,621 (5.8)
Cystectomy[a]	2558 (0.5)
Gastrectomy[a]	13,475 (2.4)
Hip arthroplasty	100,677 (17.8)
Knee arthroplasty	138,895 (24.6)
Laparoscopic cholecystectomy	109,529 (19.4)
Lower extremity peripheral bypass surgery	9344 (1.7)
Nephrectomy[a]	11,448 (2.0)
Open abdominal aortic aneurysm repair[a]	3610 (0.6)
Open cholecystectomy[a]	13,632 (2.4)
Pancreatic resection[a]	2682 (0.5)
Spinal fusion	91,124 (16.1)
Total	565,225 (100.0)

[a]Defined as a high-risk surgical procedure in this study.

nephritis/nephrosis/renal sclerosis, acute and unspecified renal failure, or renal failure. In order to simplify the process of identifying patients in the SID who suffered from PPRO, CCS discharge diagnosis codes were used (Table 2), specifically CCS codes 156 (nephritis/nephrosis/renal sclerosis), 157 (acute and unspecified renal failure), and 158 (renal failure). The corresponding ICD-9 codes for PPRO are shown in Table 2. For the statistical analysis, age data were not found to be normally distributed and were subsequently analyzed with an independent Mann–Whitney U test. Data related to sex, race, admission route, and comorbidity were dichotomized and analyzed with Pearson's chi-square test or Fisher's exact test as appropriate. Independent predictors of PPRO were identified with a binary logistic regression model. $P < 0.05$ was considered statistically significant. Data were analyzed with SPSS 22.0 (IBM Corp., Armonk, NY, USA).

3. Results

The characteristics of the study population are presented in Table 3. Fourteen percent of surgical procedures were categorized as high-risk surgeries (Table 1). Approximately 59% of the study population was female. The median patient age was 64.0 (interquartile range: 52.0–74.0) years. Almost 29% of patients were admitted as emergent cases. Hypertension (56.0%), diabetes (22.5%), and peripheral vascular disease (8.1%) were the most prevalent comorbidities. HIV infection was present in 0.1% of noncardiac surgery patients.

The incidence of PPRO in this study was 2.21% (95% confidence interval: 2.17–2.25). Crude associations were observed between all patient clinical characteristics and PPRO, with the exception of HIV infection ($P = 0.344$, Table 3). In this study, all the established preoperative clinical risk factors for PPRO in the studies of Kheterpal et al. (5,6) were found to be independent predictors of PPRO (Table 4). HIV infection was not identified as an independent predictor of PPRO following noncardiac surgery (Table 4; odds ratio: 1.573, 95% confidence interval: 0.998–2.480; $P = 0.051$).

A subanalysis was performed to identify any potential differences in the burden of established preoperative risk factors for PPRO between the HIV-infected and HIV-uninfected groups (Z-test for two population proportions; Table 5). There was a higher prevalence of liver disease, renal disease, emergent admission, and male sex in the HIV-infected patient group when compared to the HIV-uninfected group. In addition, the HIV-infected patient group was younger than the HIV-uninfected patient group (Mann–Whitney U test; Table 5). Diabetes, hypertension, and congestive heart failure were more common in the HIV-uninfected group. Peripheral vascular disease and chronic

Table 2. CCS and ICD-9 codes used to identify comorbidities and study outcome.

Comorbidity/study outcome	CCS code(s)	ICD-9 code/s
HIV	5	042 0420 0421 0422 0429 0430 0431 0432 0433 0439 0440 0449 07953 27910 27919 79571 7958 V08
Diabetes	49, 50	24900 25000 25001 7902 79021 79022 79029 7915 7916 V4585 V5391 V6546 24901 24910 24911 24920 24921 24930 24931 24940 24941 24950 24951 24960 24961 24970 24971 24980 24981 24990 24991 25002 25003 25010 25011 25012 25013 25020 25021 25022 25023 25030 25031 25032 25033 25040 25041 25042 25043 25050 25051 25052 25053 25060 25061 25062 25063 25070 25071 25072 25073 25080 25081 25082 25083 25090 25091 25092 25093
Hypertension	98, 99	4011 4019 4010 40200 40201 40210 40211 40290 40291 4030 40300 40301 4031 40310 40311 4039 40390 40391 4040 40400 40401 40402 40403 4041 40410 40411 40412 40413 4049 40490 40491 40492 40493 40501 40509 40511 40519 40591 40599 4372
Congestive heart failure	108	39891 4280 4281 42820 42821 42822 42823 42830 42831 42832 42833 42840 42841 42842 42843 4289
Peripheral vascular disease	114, 115, 116, 117	4400 4401 4402 44020 44021 44022 44023 44029 4404 4408 4409 4439 5570 5571 5579 4410 44100 44101 44102 44103 4411 4412 4413 4414 4415 4416 4417 4419 4420 4421 4422 4423 44281 44282 44283 44284 44289 4429 44321 44322 44323 44324 44329 44770 44771 44772 44773 4440 44401 44409 4441 44421 44422 44481 44489 4449 44501 44502 44581 44589 4430 4431 44381 44382 44389 4460 4461 4462 44620 44621 44629 4463 4464 4465 4466 4467 4470 4471 4472 4473 4474 4475 4476 4478 4479 4480 4481 4489 4580 4581 4588 4589 4590 45989 4599 7859 79430 79431 79439 7962 V125 V1250 V1253 V1254 V1259 V151 V421 V432 V4321 V4322 V434 V717
Chronic obstructive pulmonary disease	127	490 4910 4911 4912 49120 49121 49122 4918 4919 4920 4928 494 4940 4941 496
Renal disease	156, 157, 158	5800 5804 58081 58089 5809 5810 5811 5812 5813 58181 58189 5819 5820 5821 5822 5824 58281 58289 5829 5830 5831 5832 5834 5836 5837 58381 58389 5839 587 5845 5846 5847 5848 5849 586 585 5851 5852 5853 5854 5855 5856 5859 7925 V420 V451 V4511 V4512 V560 V561 V562 V5631 V5632 V568
Liver disease	151	570 5715 5716 5718 5719 5720 5721 5722 5723 5724 5728 5730 5734 5735 5738 5739 7824 7891 7895 78959 7904 7905 7948 V427
PPRO (Study outcome)	***	***

***Same as the "renal disease" variable, except diagnosis listed as not present on admission to hospital.

obstructive pulmonary disease were more prevalent in the HIV-infected patient group when compared to the HIV-uninfected patient group, although this difference was not statistically significant (Table 5). Additionally, median renal risk index scores (6) were calculated for the HIV-infected (median score: 2.0, interquartile range: 2.0–4.0) and HIV-uninfected groups (median score: 2.0, interquartile range: 1.0–4.0). There was no statistically significant difference in median renal risk index scores between the two groups (Mann–Whitney U test; Table 5).

4. Discussion

All the established preoperative risk factors for PPRO in noncardiac surgery patients identified in the studies of Kheterpal et al. (5,6) were found to be independently associated with a higher risk of PPRO in this study.

Table 3. Characteristics of the study population expressed as a frequency (%).

Characteristic	All patients (n = 565,225)	Patients with PPRO (n = 12,500)	Patients without PPRO (n = 552,725)	P-value
Median age in years (interquartile range)	64.0 (52.0-74.0)	73.0 (63.0–82.0)	64.0 (52.0–74.0)	<0.001
Male sex	233,676 (41.3)	7153 (57.2)	226,523 (41.0)	<0.001
Emergent admission	162,979 (28.8)	5662 (45.3)	157,317 (28.5)	<0.001
High-risk procedure	80,026 (14.2)	4831 (38.6)	75,195 (13.6)	<0.001
HIV infection	734 (0.1)	20 (0.2)	714 (0.1)	0.344
Diabetes	127,003 (22.5)	4903 (39.2)	122,100 (22.1)	<0.001
Hypertension	316,348 (56.0)	9581 (76.6)	306,767 (55.5)	<0.001
Congestive heart failure	23,854 (4.2)	2414 (19.3)	21,440 (3.9)	<0.001
Peripheral vascular disease	45,740 (8.1)	2732 (21.9)	43,008 (7.8)	<0.001
Chronic obstructive pulmonary disease	37,502 (6.6)	1863 (14.9)	35,639 (6.4)	<0.001
Renal disease	49,349 (8.7)	4845 (38.8)	44,504 (8.1)	<0.001
Liver disease	20,225 (3.6)	793 (6.3)	19,432 (3.5)	<0.001

Table 4. Characteristics independently associated/not independently associated with PPRO in noncardiac surgery patients.

Characteristic	Odds ratio (95% confidence interval)	P-value
Age (per 1 year increase)	1.031 (1.029–1.032)	<0.001
Male sex	1.557 (1.500–1.616)	<0.001
Emergent admission	1.460 (1.405–1.517)	<0.001
High-risk procedure	3.463 (3.332–3.600)	<0.001
HIV infection	1.573 (0.998–2.480)	0.051
Diabetes	1.289 (1.239–1.342)	<0.001
Hypertension	1.311 (1.252–1.373)	<0.001
Congestive heart failure	1.992 (1.890–2.099)	<0.001
Peripheral vascular disease	1.333 (1.271–1.398)	<0.001
Chronic obstructive pulmonary disease	1.279 (1.211–1.350)	<0.001
Renal disease	3.203 (3.068–3.345)	<0.001
Liver disease	1.258 (1.163–1.361)	<0.001

However, HIV infection was not independently associated with a higher risk of PPRO. There is a potential explanation for this finding. Although we do not present data on antiretroviral therapy use, it is likely that as with the nonsurgical HIV-infected American population (7), HIV infection was well controlled through management with antiretroviral therapy in our study population of surgical patients. In medically treated HIV populations, antiretroviral therapy is noted to reduce the risk of patient morbidity and mortality. The positive impact of antiretroviral therapy on patient outcomes would no doubt extend to perioperative settings. Indeed, a case-control study by King et al. reported a reduction in 30-day postoperative mortality in HIV-infected patients receiving antiretroviral therapy versus HIV-infected patients who did not receive treatment (8). Furthermore, CD4 counts are higher in HIV-infected patients who receive antiretroviral therapy versus HIV-infected patients who do not receive treatment. Moreover, King et al. reported that the mortality risk associated with HIV infection and

Table 5. Prevalence of established preoperative risk factors for PPRO in HIV-infected and HIV-uninfected patients expressed as proportions of each population.

Preoperative risk factor	HIV-infected population	HIV-uninfected population	P-value
Median age (interquartile range)	51.0 (46.0–58.0)	64.0 (52.0–74.0)	<0.001
Male sex	0.903	0.413	<0.001
Emergent admission	0.349	0.288	<0.001
High-risk procedure	0.149	0.142	0.589
Diabetes	0.166	0.225	<0.001
Hypertension	0.405	0.560	<0.001
Congestive heart failure	0.025	0.042	0.017
Peripheral vascular disease	0.084	0.081	0.726
Chronic obstructive pulmonary disease	0.066	0.069	0.728
Renal disease	0.135	0.066	<0.001
Liver disease	0.106	0.036	<0.001
Median perioperative renal risk index score (interquartile range)	2.0 (2.0–4.0)	2.0 (1.0–4.0)	0.076

a CD4 cell count of >200/μL was equivalent to that of an uninfected patient aged >16 years, whereas the mortality risk in a patient with a CD4 cell count of >50/μL was equivalent to that of an uninfected patient aged >47 years (8). It is therefore possible that adequate management of HIV infection in our study population resulted in no overall difference in the levels of risk for PPRO observed between HIV-infected and HIV-uninfected patients. The mechanism likely to be responsible for this observation is the improvement or maintenance of an acceptable CD4 count in patients who received antiretroviral therapy.

A subanalysis found a higher prevalence of several established risk factors for PPRO in the HIV-infected patient group when compared with the HIV-uninfected patient group. However, this did not translate into a higher risk for PPRO in patients with HIV. When the renal risk index of Kheterpal et al. was applied to the data, the median risk scores in HIV-infected and HIV-uninfected patient groups were not statistically different. Therefore, whereas the prevalence of certain renal risk factors might be higher in the HIV-infected population, this is negated by the higher prevalence of the remaining risk factors in the HIV-uninfected group. This highlights potential differences in the importance of perioperative renal risk factors between HIV-infected and HIV-uninfected noncardiac surgery patients and requires further investigation.

There were limitations to this study. The SID did not contain data that could be used to calculate body mass index, which is one of the established preoperative risk factors for PPRO. Therefore, this study was unable to investigate the impact of this variable on the incidence of PPRO. In addition, only in-hospital renal outcomes are reported for the study population, as postdischarge outcomes were not recorded in the SID. The SID did not contain data related to CD4 counts and antiretroviral therapy use; therefore, it was not possible to investigate these variables in the subanalysis. Finally, the SID data represent the US population and cannot be generalized to other parts of the world, since there may be significant differences among healthcare systems, treatment approaches, and patient characteristics. Prospectively designed research, conducted in several regions around the world, is required to overcome the limitations reported in this study.

In conclusion, the findings of this study suggest that although HIV infection might not be an independent risk factor for PPRO in the setting of noncardiac surgery, patients with HIV infection carry many preoperative risk factors for PPRO. Therefore, HIV-infected patients should be thoroughly screened for established preoperative risk factors and carefully managed during the perioperative period to reduce their risk of PPRO.

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