Cardiovascular Disease and HIV: Pathophysiology, Treatment Considerations, and Nursing Implications

Justin M. Cournoyer, RN, BSN
Aven P. Garms, RN, BSN
Kimberly N. Thiessen, RN, BSN, CPEN
Margaret T. Bowers, RN, DNP, FNP-BC, CHFN
Melissa D. Johnson, PharmD, MSH, AAHIVE
Michael V. Relf, RN, PhD, AACRN, ACNS-BC, CNE

HIV infection has progressed from an acute, terminal disease to a chronic illness with cardiovascular disease as the leading cause of death among persons living with HIV. As persons living with HIV infection continue to become older, traditional risk factors for atherosclerosis compounded by the pathophysiological effects of HIV infection and antiretroviral therapy markedly increase the risk for cardiovascular disease. Further, persons living with HIV are also at high risk for cardiomyopathy. Critical care nurses must recognize the risk factors for cardiovascular disease and the pathophysiology and complex treatment options in order to manage care of these patients and facilitate multidisciplinary collaboration. Two case studies are used to highlight the treatment options and nursing considerations associated with cardiovascular disease among persons living with HIV. (Critical Care Nurse. 2016;36[5]:37-47)

Recent advances in the management of HIV infection have increased life expectancy among persons living with HIV. Because persons living with HIV are living longer, they are increasingly affected by health conditions associated with aging, such as cardiovascular disease. Among persons living with HIV, the leading cause of death is cardiovascular disease.1 HIV infection and antiretroviral therapy increase the risk for atherosclerotic heart disease and myocardial infarction by creating a proinflammatory, proatherogenic environment at the onset of HIV infection and throughout the life of the person living with HIV.2 In addition to atherosclerosis, persons living with HIV are also at increased risk for cardiomyopathy and congestive heart failure. Thus, critical care nurses must understand the risk factors, pathophysiology, and unique treatment options related to cardiovascular disease in persons living with HIV in order to provide optimal care. These nurses are responsible for facilitating communication between the interprofessional team members while managing complex drug regimens during a patient’s hospitalization and are essential in providing patient education in preparation for discharge from the hospital.
Epidemiological Perspectives

According to the Centers for Disease Control and Prevention, in the United States, 1.1 million persons are living with HIV infection. The median age of those infected is 45 to 49 years. Two groups disproportionately affected by HIV, males and African Americans, are also at higher risk for hypertension, diabetes, and mortality due to cardiovascular disease. 

Epidemiological evidence indicates that 387,324 African Americans and 658,002 males were living with HIV in 2010.

HIV infection and antiretroviral therapy increase the risk for cardiovascular disease and accelerate the progression of atherosclerosis. As a consequence of HIV infection, both atherogenesis and endothelial dysfunction are accelerated, increasing the risk for cardiovascular events. Risk factors associated with cardiovascular disease, such as diabetes, dyslipidemia, and hypertension, are more prevalent in persons living with HIV than in the general population. For example, diabetes is diagnosed in 14% of persons living with HIV but in only 8.3% of the general US population. Similarly, dyslipidemia is noticeably more prevalent in persons living with HIV (44.7%) than in noninfected persons (33.5%). Further, hypertension affects 36.5% of persons living with HIV compared with 31.0% of the general population. After multivariate remodeling for sociodemographic and physiological covariants, a multisite study of more than 27,000 individuals indicated that persons living with HIV are at a 50% higher risk for an acute myocardial infarction than persons who do not have HIV infection. Further, the risk for cardiovascular disease is 2 times higher among persons living with HIV and receiving antiretroviral therapy than among the general public. Persons living with HIV have a higher risk not only for cardiovascular disease but also for complications after acute cardiovascular episodes. Patients living with HIV return to the hospital for heart failure after an acute myocardial infarction at significantly higher rates (3.3%) than do similar patients without HIV infection (1.4%, P = .02).

Atherosclerotic Cardiovascular Disease and HIV Infection

If the HIV disease is well controlled with antiretroviral therapy, persons living with HIV have a life expectancy comparable to that of the general population. As survival has improved, the focus of care has shifted to management of chronic disease in which cardiovascular disease, hypertension, diabetes, and kidney disease are common comorbid conditions requiring care and treatment. In addition to traditional risk factors for cardiovascular disease such as hypertension, tobacco use, dyslipidemia, insulin resistance, genetics, and impaired glucose tolerance, compounding risk factors due to the direct effects of HIV and antiretroviral therapy must be considered.

In all populations, atherogenesis is an inflammation-mediated process. Among persons living with HIV, atherogenesis is accelerated because of a constant proinflammatory state that exists throughout the lifetime of the infected person, even during antiretroviral therapy. Infection with HIV induces inflammatory oxidative stress, stimulates the production of reactive oxygen species, and causes platelet dysfunction. This proinflammatory environment combined with increased levels of reactive oxygen species contributes to plaque formation and accelerates the progression of atherosclerotic disease. Further, reactive oxygen species not only oxidize more low-density lipoprotein but also directly damage the vessel walls, causing endothelial dysfunction.

Exemplar Case Study 1

The following is a case study to explore treatment of a person living with HIV who has cardiovascular disease.
Ronald is a 55-year-old African American man. He is 6 ft (1.8 m) tall, weighs 220 lb (99 kg), and has a body mass index of 29.8. HIV infection was diagnosed in 1990. Since 1994, he has been taking saquinavir with ritonavir, a boosted protease inhibitor regimen. Although saquinavir with ritonavir is not first-line treatment today, Ronald is still on the regimen because it produced virological suppression and he is able to maintain adherence. In 2004, his HIV nurse practitioner modified his antiretroviral therapy by adding tenofovir disoproxil fumarate and emtricitabine, both of which are nonnucleoside reverse transcriptase inhibitors.

In addition to his antiretroviral medications, Ronald currently takes 60 mg pravastatin daily for dyslipidemia. His current lipid profile includes elevated levels of low-density lipoproteins (140 mg/dL), low levels of high-density lipoproteins (35 mg/dL), and elevated levels of total cholesterol (230 mg/dL). (To convert milligrams per deciliter of the 3 types of cholesterol to millimoles per liter, multiply by 0.0259.) He also takes metoprolol succinate 100 mg daily for hypertension. He drinks socially (1-2 drinks a month) and does not use tobacco. He engages in aerobic exercise less than once per week and consumes a diet high in fat and sodium.

Ronald reported that he had been experiencing chest pain at rest. He was referred to an outpatient cardiovascular testing facility to undergo a stress test. During the stress test, ischemia was noted via anterior leads (ST elevation in leads V1-V3). The stress test was stopped, and a diagnostic catheterization with possible intervention was ordered. The cardiac catheterization showed that Ronald had a 90% proximal lesion of the left anterior descending coronary artery, a 75% lesion in the proximal right coronary artery, and a 75% lesion in the mid circumflex artery.

Discussion of Case Study 1

In addition to the impact of HIV infection on the cardiovascular system, antiretroviral therapy also plays a role in cardiovascular disease. Specifically, protease inhibitors, including Ronald’s saquinavir with ritonavir regimen, have been associated with severe premature coronary disease. Persons living with HIV who are receiving protease inhibitors are at increased short-term risk for death and have a marked long-term risk for myocardial infarction and the need for coronary revascularization. In addition, protease inhibitors induce hyperlipidemia and insulin resistance, which are associated with atherogenesis. The cardiovascular effects of antiretroviral therapy are presented in Table 1. Because dyslipidemia in persons living with HIV plays an important role in atherogenesis and the progression of coronary artery disease, treating dyslipidemia is critical in slowing its damaging effects.

As the critical care nurse and other members of the health care team partner with Ronald to facilitate lifestyle modifications, including weight loss, diet modification, and exercise, they also consider the most effective pharmacological methods for managing the dyslipidemia. The goal is to maintain the current antiretroviral therapy regimen while optimizing the dyslipidemia regimen. Current guidelines for the treatment of

<table>
<thead>
<tr>
<th>Class</th>
<th>Cardiac effect</th>
<th>Nursing implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonnucleoside reverse transcriptase inhibitor</td>
<td>Dyslipidemia22</td>
<td>Must titrate to lowest dose of rosuvastatin and atorvastatin22</td>
</tr>
<tr>
<td>atazanavir with ritonavir</td>
<td>Increased risk of cardiovascular events23</td>
<td>Must use highest dose of pravastatin22</td>
</tr>
<tr>
<td>Integrase strand transfer inhibitor</td>
<td>None known22</td>
<td>Observe patient’s cardiac monitor for rhythm changes</td>
</tr>
<tr>
<td>raltegravir</td>
<td>PR-interval prolongation22</td>
<td>Encourage diet and exercise to minimize additional risk</td>
</tr>
<tr>
<td>Protease inhibitor</td>
<td>QT-interval prolongation22</td>
<td>factors of cardiovascular events</td>
</tr>
<tr>
<td>atazanavir with ritonavir</td>
<td>Higher risk of myocardial infarction22</td>
<td></td>
</tr>
<tr>
<td>Dual nucleoside reverse transcriptase inhibitor</td>
<td>Increased risk of cardiovascular events22</td>
<td>Encourage diet and exercise to minimize additional risk</td>
</tr>
<tr>
<td>inhibitor pairs (abacavir, tenofovir disoproxil</td>
<td></td>
<td>factors of cardiovascular events</td>
</tr>
<tr>
<td>fumarate, emtricitabine)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Many persons living with HIV require higher doses of statins to manage dyslipidemia. For Ronald, even the maximum dose of pravastatin (80 mg) is associated with a small risk for rhabdomyolysis, a life-threatening condition involving acute muscle breakdown leading to kidney failure. The risks and benefits of various statins used in conjunction with antiretroviral therapy are summarized in Table 2.

As the cardiac catheterization results indicated, Ronald has marked multivessel coronary artery disease. Because of the lesions, Ronald’s health care team is considering whether to perform a percutaneous coronary intervention with stent placement or a coronary artery bypass graft (CABG). Figure 1 provides a schematic flowchart of decision making in such situations. In patients without HIV infection, drug-eluting stents are preferred because the drugs inhibit cellular growth around the stent and reduce restenosis and the need for future revascularizations. In addition, compared with bare-metal stents, drug-eluting stents are associated with better outcomes within the first year; after 1 year, the risks for death and repeat revascularization are the same for both types of stent. However, persons living with HIV are more likely than HIV-negative persons to require recurrent revascularization, which is thought to be linked to elevated levels of C-reactive protein.

If Ronald were to have a stent placed, he would have to take aspirin indefinitely along with a P2Y12 (platelet aggregation) inhibitor such as clopidogrel, prasugrel, or ticagrelor for 1 year. Many times, in order to avoid development of gastric ulcers due to aspirin or a P2Y12 inhibitor, omeprazole is recommended. However, proton pump inhibitors like omeprazole reduce the production of stomach acid and decrease the effectiveness of antiretroviral drugs by increasing the pH of the gastric contents to a level too alkaline for absorption of antiretroviral agents. In order to avoid this situation, histamine 

<table>
<thead>
<tr>
<th>Statin</th>
<th>Cardiac effect</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>No dose adjustment with saquinavir (however, need to use lowest dose with other protease inhibitors and highest dose with nonnucleoside reverse transcriptase inhibitors)</td>
<td>Rhabdomyolysis&lt;sup&gt;24&lt;/sup&gt; Less effective in decreasing levels of low-density lipoprotein when used with protease inhibitor ART&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>More effective in lowering levels of low-density lipoprotein compared with pravastatin because of bioavailability&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Interact with metabolism of ART drugs via cytochrome P450 pathway&lt;sup&gt;22,25&lt;/sup&gt; Always titrate to lowest possible dose&lt;sup&gt;22&lt;/sup&gt; Must monitor toxic effects of ART&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>More effective in lowering levels of low-density lipoprotein compared with pravastatin because of bioavailability&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Interact with metabolism of ART drugs via cytochrome P450 pathway&lt;sup&gt;22,25&lt;/sup&gt; Titrate to lowest possible dose (&lt;20 mg)&lt;sup&gt;22,25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Highest bioavailability Fewer data on interaction with ART</td>
<td>No dose adjustments recommended when used with ART</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Contraindicated with ART</td>
<td>Contraindicated with ART</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Contraindicated with ART</td>
<td>Contraindicated with ART</td>
</tr>
</tbody>
</table>

HIV-associated dyslipidemia include administration of statins and ezetimibe (a cholesterol absorption inhibitor) as the essential first-line treatment. Supplemental benefits have also been associated with the use of fenofibrate, fish oil, and niacin. For someone taking saquinavir, as Ronald does, the dose of pravastatin can be increased from 60 mg to 80 mg, the highest dose for maximum benefit without renal or hepatic adjustment required. Atorvastatin and rosuvastatin are statins that are also approved for use with HIV-associated dyslipidemia but have stricter dose adjustment considerations.

Pravastatin is preferred for 2 reasons. First, protease inhibitors are P450 CYP3A4 inhibitors. Because pravastatin is not involved in this metabolic pathway, toxic effects are less likely. Second, many persons living with HIV require higher doses of statins to manage dyslipidemia. For Ronald, even the maximum dose of pravastatin (80 mg) is associated with a small risk for rhabdomyolysis, a life-threatening condition involving acute muscle breakdown leading to kidney failure. The risks and benefits of various statins used in conjunction with antiretroviral therapy are summarized in Table 2.

As the cardiac catheterization results indicated, Ronald has marked multivessel coronary artery disease. Because of the lesions, Ronald’s health care team is considering whether to perform a percutaneous coronary intervention with stent placement or a coronary artery bypass graft (CABG). Figure 1 provides a schematic flowchart of decision making in such situations. In patients without HIV infection, drug-eluting stents are preferred because the drugs inhibit cellular growth around the stent and reduce restenosis and the need for future revascularizations. In addition, compared with bare-metal stents, drug-eluting stents are associated with better outcomes within the first year; after 1 year, the risks for death and repeat revascularization are the same for both types of stent. However, persons living with HIV are more likely than HIV-negative persons to require recurrent revascularization, which is thought to be linked to elevated levels of C-reactive protein.

If Ronald were to have a stent placed, he would have to take aspirin indefinitely along with a P2Y12 (platelet aggregation) inhibitor such as clopidogrel, prasugrel, or ticagrelor for 1 year. Many times, in order to avoid development of gastric ulcers due to aspirin or a P2Y12 inhibitor, omeprazole is recommended. However, proton pump inhibitors like omeprazole reduce the production of stomach acid and decrease the effectiveness of antiretroviral drugs by increasing the pH of the gastric contents to a level too alkaline for absorption of antiretroviral agents. In order to avoid this situation, histamine 

---

**Table 2** Risks and benefits of statins with antiretroviral therapy (ART)

<table>
<thead>
<tr>
<th>Statin</th>
<th>Cardiac effect</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>No dose adjustment with saquinavir (however, need to use lowest dose with other protease inhibitors and highest dose with nonnucleoside reverse transcriptase inhibitors)</td>
<td>Rhabdomyolysis&lt;sup&gt;24&lt;/sup&gt; Less effective in decreasing levels of low-density lipoprotein when used with protease inhibitor ART&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>More effective in lowering levels of low-density lipoprotein compared with pravastatin because of bioavailability&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Interact with metabolism of ART drugs via cytochrome P450 pathway&lt;sup&gt;22,25&lt;/sup&gt; Always titrate to lowest possible dose&lt;sup&gt;22&lt;/sup&gt; Must monitor toxic effects of ART&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>More effective in lowering levels of low-density lipoprotein compared with pravastatin because of bioavailability&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Interact with metabolism of ART drugs via cytochrome P450 pathway&lt;sup&gt;22,25&lt;/sup&gt; Titrate to lowest possible dose (&lt;20 mg)&lt;sup&gt;22,25&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Highest bioavailability Fewer data on interaction with ART</td>
<td>No dose adjustments recommended when used with ART</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Contraindicated with ART</td>
<td>Contraindicated with ART</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Contraindicated with ART</td>
<td>Contraindicated with ART</td>
</tr>
</tbody>
</table>
Coadministration recommendations for use with antiretroviral agents. Critical care nurses should know that antiretroviral agents should be administered 2 hours before or 10 hours after administration of histamine₂-receptor antagonists to optimize absorption of agents used in antiretroviral therapy.

Another option to manage Ronald’s multivessel disease is CABG. According to the American College of Cardiology/American Heart Association practice guideline, surgical intervention is favored over percutaneous coronary intervention for patients with multivessel coronary artery disease and has higher survival benefits for patients with proximal lesions of the left anterior descending coronary artery (Figure 1). In a study with stratification for HIV status of patients with multivessel coronary artery disease who had CABG, outcomes were similar for HIV-negative patients and patients living with HIV immediately postoperatively. These outcomes included similar rates of myocardial infarction, stroke, mediastinitis, and reintervention. However, long-term follow-up revealed that persons living with HIV had an increased need for repeat revascularizations. In Ronald’s case, the recommended procedure would be CABG.

**Contractility-Related Cardiovascular Disease and HIV Infection**

Ronald’s case is an example of disease progression and treatment in a person living with HIV who has dyslipidemia and coronary lesions. However, another cardiac problem experienced by persons living with HIV is HIV-induced cardiomyopathy, which occurs in 10% to 20% of persons living with HIV. Dilated cardiomyopathy is the most common clinical manifestation in those living with HIV. It is defined as an ejection fraction less
than 40% with increased left ventricular dimensions when adjustments are made for body surface area. The pathophysiological basis of cardiomyopathy among those living with HIV is linked to the actions of cytokines and autoantibodies. The presence of HIV in the myocardium is associated with an increase in cytokines and cardiomyocyte apoptosis (programmed cell death) through signaling via the receptors CCR3, CCR5, and CXCR4. These chemokine receptors are involved in different parts of the immune response and can signal for apoptosis of cells recognized as foreign when the immune cascade is triggered. Additionally, glycoprotein 120, part of the core envelope gene of HIV, may also induce cardiomyocyte apoptosis through a mitochondrially controlled pathway involving the activation of inflammatory cytokines. Further, tumor necrosis factor α may decrease inotropy by failing to induce intracellular calcium influx and inducing the production of nitric oxide synthase, resulting in left ventricular dysfunction.

Theories have linked HIV-induced cardiomyopathy with both encephalopathy and toxic drug effects. Persons living with HIV who have encephalopathy are more likely to die of congestive heart failure than are those without encephalopathy, suggesting a relationship between the two. In both conditions, reservoir cells in the myocardium and cerebral cortex hold on to HIV-1 on their surfaces long after antiretroviral therapy has lowered plasma viral load. This retention results in the chronic release of tumor necrosis factor α, interleukin-6, and endothelin-1, leading to progressive tissue damage, encephalopathy, and cardiomyopathy. Similarly, myocarditis can lead to the release of functional cytokines, including tumor necrosis factor α and interleukin-6, and nitric oxide synthase, leading to myocardial damage and dysfunction associated with cardiomyopathy. Figure 2 provides a synthesis of the discussed linkages between biomarkers, HIV, and the resulting pathophysiological changes.

**Exemplar Case Study 2**

The following case study describes clinical care management of Elmer, a 50-year-old man who has been living with HIV for 16 years. He has been prescribed antiretroviral therapy since his diagnosis, but his struggle to adhere to the therapy has necessitated several changes in the regimen. His current therapy is the preferred protease inhibitor–based regimen, which includes atazanavir with ritonovir, emtricitabine, and tenofovir disoproxil fumarate. Because of Elmer’s difficulty with adherence, this treatment is optimal because it requires once-a-day dosing with a small number of pills.

In addition to HIV infection, Elmer has a history of cocaine use. He began using cocaine when he was 23...
years old and relapsed 2 years ago. He currently snorts cocaine when available but often smokes or injects crack cocaine because crack cocaine is easily accessible and less costly than other forms of the drug. His injection drug use contributed to a previous diagnosis of infective endocarditis of the tricuspid valve.

Elmer now comes to the emergency department because of chest pain that is not relieved at rest. He has had marked dyspnea on exertion for the past 2 weeks. A blood test reveals nonelevated levels of troponin when he arrives in the department and at 6 and 9 hours later, ruling out myocardial infarction. A 12-lead electrocardiogram reveals an absence of discrete P waves and an irregular rhythm, suggesting atrial fibrillation. A diagnostic cardiac catheterization is performed and reveals nons ischemic cardiomyopathy attributed to a history of cocaine use and HIV infection. Results of a chemistry panel include creatinine level 1.9 mg/dL (to convert to micromoles per liter, multiply by 88.4) and urea nitrogen concentration 45 mg/dL (to convert to millimoles per liter, multiply by 0.357), suggestive of renal insufficiency. Elmer is admitted to the cardiac care unit after the cardiac catheterization. Shortly after admission to the unit, Elmer experiences an episode of atrial fibrillation with a rapid ventricular rate.

Discussion of Case Study 2

Managing Elmer’s care requires considering several competing priorities. His care team must focus on mitigating the risk for stroke due to atrial fibrillation, minimizing workload of the heart while maximizing cardiac output, and monitoring for drug interactions and toxic effects, all while maintaining his current antiretroviral therapy regimen.

The medical providers consider ibutilide, amiodarone, digoxin, and β-blockers to manage the atrial fibrillation. Amiodarone is an antiarrhythmic agent that can be used for rate control in atrial fibrillation when other agents are ineffective or cannot be administered. Unfortunately, amiodarone has a long half-life (mean, 58 days) and severe interactions with the medications used in antiretroviral therapy. Further, inhibition of metabolism via the cytochrome P450 pathway by antiretroviral agents (specifically, atazanavir and emtricitabine) leads to increased serum levels of amiodarone, resulting in the potential for hypotension, bradycardia, and more cardiac arrhythmias. Because of increased serum levels of amiodarone, the risks of toxic effects due to amiodarone outweigh the benefits of managing the atrial fibrillation with this drug. Further, because of previous nonadherence to medications that resulted in HIV genotypic resistance to some antiretroviral agents, Elmer must maintain his current antiretroviral therapy regimen because few other options for treating HIV infection exist. Therefore, amiodarone is not an appropriate treatment for atrial fibrillation for Elmer.

Digoxin is a possible antiarrhythmic alternative to amiodarone to treat the atrial fibrillation because it is not contraindicated with use of antiretroviral therapy. However, digoxin has a narrow therapeutic index and can interact with some antiretroviral medications, resulting in higher or lower levels of serum digoxin, depending on the specific antiretroviral therapy regimen. Therefore, serum digoxin levels must be closely monitored to stay within the therapeutic range (0.5-0.8 mg/dL). Additionally, dosing of digoxin along with Elmer’s antiretroviral medications is complicated by renal insufficiency and concern for toxic effects. Digoxin is 50% to 70% cleared by the kidneys, resulting in a significantly longer half-life in patients with renal problems. Elmer’s renal insufficiency and the effect of his antiretroviral drugs on serum levels of digoxin must be considered in the initial dosing and maintenance of digoxin. Because of the renal insufficiency, the digoxin loading dose would have to be decreased by one-half and the maintenance dose reduced to 125 μg once daily. Because serum levels of digoxin are unpredictable when administered to a patient receiving antiretroviral therapy and because renal insufficiency puts Elmer at high risk for toxic effects due to digoxin, this antiarrhythmic agent is also not an appropriate treatment for the atrial fibrillation.

The third option for treating the atrial fibrillation is a β-blocker. This class of medication has no listed interactions with antiretroviral drugs and could regulate the atrial fibrillation with the lowest chance of toxic effects. Although β-blockers are safe with Elmer’s antiretroviral therapy regimen, not all are safe because of the renal insufficiency. Some β-blockers such as metoprolol and...
Atenolol are primarily excreted through the kidneys.\textsuperscript{25} Therefore, the critical care nurse should work with the multidisciplinary team to ensure that a non–renally cleared β-blocker, such as carvedilol, is prescribed.\textsuperscript{25}

Because Elmer has cardiomyopathy, which is exacerbated by atrial fibrillation, he has a risk for embolic stroke that can be reduced by using anticoagulants such as dabigatran, warfarin, apixaban, or rivaroxaban (Table 3). Apixaban and rivaroxaban are newer medications, and their interactions with antiretroviral drugs are unknown, and so they would not be recommended for Elmer. Dabigatran is indicated to prevent stroke and systemic embolization in patients who have nonvalvular atrial fibrillation and at least 1 additional risk factor for stroke.\textsuperscript{30} Dabigatran is more effective than warfarin in the prevention of embolic stroke in patients with atrial fibrillation and requires markedly less monitoring than does warfarin because of more predictable serum levels.\textsuperscript{43} Thus, dabigatran may be most beneficial considering Elmer’s history of nonadherence to medications prescribed. However, safe dosing of dabigatran in patients with renal insufficiency is unclear. Because Elmer has an elevated ratio of urea nitrogen to creatinine, renal clearance is an important consideration.\textsuperscript{44} Dabigatran is excreted primarily through the kidneys, whereas warfarin is metabolized primarily through the cytochrome P450 pathway.\textsuperscript{25,44} Decreased renal clearance leading to toxic effects of dabigatran could result in bleeding complications, and although dabigatran does have more predictable serum levels than does warfarin, because no method of monitoring and no antidote for the former drug are available, the risk of toxic effects could outweigh the benefits in someone with compromised kidney function. Thus, although dabigatran is more effective in stroke prevention, warfarin is a better choice for Elmer because of the renal insufficiency.

## Conclusion

Critical care nurses who manage care for patients such as Ronald and Elmer must understand the complex pathophysiology of cardiovascular disease among persons living with HIV. Further, when administering medications, nurses must remember that protease inhibitors inhibit P450 CYP3A4, a situation that could result in toxic effects due to the drugs. Similarly, nurses must consider the effect of P2Y12 (platelet aggregation) inhibitors on the absorption of antiretroviral agents. Because high-level compliance with medications is essential in HIV treatment, unnecessary changes in an antiretroviral therapy regimen should be avoided. Overall, nurses play an important role in preventing interactions between antiretroviral agents and other medications, optimizing the effectiveness of antiretroviral therapy and preventing avoidable toxic effects.

As illustrated in both case studies, care of persons living with HIV involves considering competing priorities of care. Pharmacological considerations, in particular, require frequent reference to the compatibility of coadministered drugs, drug dosing information, and management of signs and symptoms. In case study 1, the factors influencing decision making for managing coronary artery disease in a person living with HIV are

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Less coagulation monitoring\textsuperscript{43}</td>
<td>Primary renal clearance\textsuperscript{25} Limited data on dosage for renal insufficiency \textsuperscript{25} Worse outcome: toxic effects of dabigatran and bleeding complications No antidote</td>
</tr>
<tr>
<td></td>
<td>No known interaction with antiretroviral therapy (ART)\textsuperscript{22}</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>Less renal clearance\textsuperscript{25}</td>
<td>Regular coagulation monitoring Unpredictable interaction with ART medications\textsuperscript{22} Metabolism via cytochrome P450 pathway\textsuperscript{25} Worst outcome: not effective and embolic stroke</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Less coagulation monitoring Less renal clearance</td>
<td>Limited data on interaction with ART medications Worse outcome: unfavorable interaction with ART medications</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Less coagulation monitoring</td>
<td>Limited data on interaction with ART medications Primarily renal clearance Worse outcome: unfavorable interaction with ART medications</td>
</tr>
</tbody>
</table>

### Table 3

Anticoagulant medications to prevent stroke associated with atrial fibrillation
examined. This case study illustrates the complex pharmacological management after a stent placement in a patient receiving antiretroviral therapy and factors that influence surgical intervention. In case study 2, complex issues in managing drug therapy options for a patient with atrial fibrillation are examined. Critical care nurses must understand the risk factors and pathophysiological changes to help provide patient education and collaborate with the other members of the interprofessional team. Further, nurses must consider the complex pharmacological issues between antiretroviral therapy and antilipemics, antiarrhythmics, and anticoagulants.

Financial Disclosures
None reported.

To learn more about caring for patients with HIV in the intensive care unit, read “Pharmacological Considerations in Human Immunodeficiency Virus–Infected Adults in the Intensive Care Unit” by DeFreitas et al in _Critical Care Nurse_, April 2013;33:46-56. Available at www.ccnonline.org.

References


HIV infection has progressed from an acute, terminal disease to a chronic illness with cardiovascular disease as the leading cause of death among persons living with HIV. As persons living with HIV infection continue to become older, traditional risk factors for atherosclerosis compounded by the pathophysiological effects of HIV infection and antiretroviral therapy markedly increase the risk for cardiovascular disease. Critical care nurses must recognize the risk factors for cardiovascular disease and the pathophysiology and complex treatment options in order to manage care of these patients and facilitate multidisciplinary collaboration.

- As a consequence of HIV infection, both atherogenesis and endothelial dysfunction are accelerated, increasing the risk for cardiovascular events.
- In all populations, atherogenesis is an inflammation-mediated process. Among persons living with HIV, atherogenesis is accelerated because of a constant proinflammatory state that exists throughout the lifetime of the infected person, even during antiretroviral therapy.
- Theories have linked HIV-induced cardiomyopathy with both encephalopathy and toxic drug effects.
- The Figure provides a synthesis of the discussed linkages between biomarkers, HIV, and the resulting pathophysiological changes.
- Because high-level compliance with medications is essential in HIV treatment, unnecessary changes in an antiretroviral therapy regimen should be avoided. Overall, nurses play an important role in preventing interactions between antiretroviral agents and other medications, optimizing the effectiveness of antiretroviral therapy and preventing avoidable toxic effects.

![Figure](Schematic illustration of HIV-induced atherogenesis and cardiovascular disease.)

Cardiovascular Disease and HIV: Pathophysiology, Treatment Considerations, and Nursing Implications
Justin M. Cournoyer, Aven P. Garms, Kimberly N. Thiessen, Margaret T. Bowers, Melissa D. Johnson and Michael V. Reif

Crit Care Nurse 2016;36 37-46 10.4037/ccn2016839
©2016 American Association of Critical-Care Nurses
Published online http://ccn.aacnjournals.org/

Personal use only. For copyright permission information:
http://ccn.aacnjournals.org/cgi/external_ref?link_type=PERMISSIONDIRECT

Subscription Information
http://ccn.aacnjournals.org/subscriptions/

Information for authors
http://ccn.aacnjournals.org/misc/ifora.xhtml

Submit a manuscript
http://www.editorialmanager.com/ccn

Email alerts
http://ccn.aacnjournals.org/subscriptions/etoc.xhtml