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Cardiovascular Risk Management for Patients with Rheumatoid Arthritis: A Case Report

Rachel Bethke

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Rachel M. Bethke

University of North Dakota

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Abstract

Extensive research has shown that people suffering with rheumatoid arthritis (RA) are at a substantially increased risk for morbidity and mortality from cardiovascular (CV) disease. Although this connection is widely accepted by rheumatology experts, primary care providers are often tasked with CV risk management of the RA patient and they may not be fully aware of the increased risk. The lack of clear clinical guidelines for CV management in this population has led to under diagnosis and under treatment of CV risk factors. The case presented in this report will follow Mr. Foster, a 59 year old man with RA and uncontrolled hypertension. Mr. Foster presented to the clinic with influenza like illness but an uncontrolled blood pressure was noted at the visit. The goal of this case report will be to define appropriate CV risk detection and management for Mr. Foster and best practices for management of CV risks in the setting of RA. A current literature review was performed using Pub Med, Clinical Key, and CINAHL search engines to ascertain the best evidence based practices for assessing and managing CV risk in RA patients. This report will not include discussion of lifestyle modifications or diabetes screening and management, but these topics should not be downplayed in the CV risk management of this population. This report will conclude with five CV risk management techniques for the primary care provider.

Keywords: rheumatoid arthritis, cardiovascular risks, hypertension

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Background

The case of Mr. Foster presented a treatment challenge in the management of rheumatoid arthritis (RA) and cardiovascular (CV) disease. He is a 59 year old man with RA and uncontrolled hypertension. He is currently prescribed Lisinopril by his primary care provider but reports that he almost exclusively sees his rheumatologist and rarely follows up with primary care. He reports that his rheumatologist doesn't tend to screen or counsel about hypertension, diabetes, or high cholesterol, but mainly focuses on RA symptoms and medications. Mr. Foster noted that his blood pressure always runs around 140/90 and he thought that was acceptable. Mr. Foster's situation raises the question of whether RA increases the risk of CV disease and how to best manage the increased risks in this population. Mr. Foster's situation also raises the issue that rheumatology specialists may not be appropriately managing or communicating this increased risk and the responsibility might fall to primary care providers.

According to Rempenault et al. (2017) patients with rheumatoid arthritis have an increased risk of CV disease when compared to the general population. A recent meta-analysis of 24 RA mortality studies found that patients with RA have a 50 percent increased risk of CV related death than those without RA (Dadoun et al., 2013). The increased risk of CV disease is primarily due to the chronic inflammation that accompanies RA as well as the traditional risk factors (Hansen, 2018). The inflammation associated with RA has been proven to lead to accelerated atherosclerosis (Hansen, 2018). Many studies have found that the risk of CV disease in RA is equivalent to the CV risks associated with diabetes mellitus (Bartels et al., 2016).

Despite the widespread knowledge that CV risks are increased in the RA patient, there are still gaps in care for this population and, compared to their peers, RA patients receive less

stringent management of lipids, hypertension, and diabetes mellitus (Bartels et al., 2016). According to Bartels et al. (2016) the disparities in care for this population could include gaps in RA knowledge by primary care providers. In one survey only 32 percent of primary care providers were aware of the increased CV risks in RA patients (Bartels et al., 2016). On the other side, rheumatology specialists were very aware of the increase CV risks but did not feel comfortable or have time to manage hypertension, diabetes, and hyperlipidemia in the specialty setting (Bartels et al., 2016). This lack of aggressive management on either side has led to preventative care gaps in this at-risk population (Bartels et al., 2016). To lend to this treatment challenge is the fact that CV risk management professional guidelines for the RA patient are vague and identifying at risk patients is not clearly outlined in current guidelines (Bartels et al., 2016). Appropriate CV risk identification and management in the RA patient is the purpose of this case report.

Case Report

Mr. Foster is a 59 year old man who presented to the clinic with complaints of fever, chills, headache, cough, sore throat, and body aches. The onset of his symptoms began five days ago, and the symptoms haven't worsened or improved since that time. He described his cough as a persistent dry "nagging" cough. The cough did tend to keep him up at night and he had to call in sick to work for the past 2 days due to lack of sleep. He reported his pain as generalized mild muscle aches but described his headache as "severe". Rest improved his symptoms slightly, and he had also been using ibuprofen to control fever and muscle aches with mild relief. He reported he had also been using over the counter cough syrup with little effect on his harsh cough. He denied recent sick contacts although he does work at a retail job and is around many different

people who present to the store every day. He presented to the clinic because his symptoms were not improving and they were affecting his productivity and keeping him out of work.

Mr. Foster's medical history includes the diagnosis of RA and hypertension. He follows with a rheumatologist for his RA and reported that his symptoms have been in excellent control. He denied surgical history. He also denied tobacco, alcohol, and drug use and abuse. He drinks approximately 1 cup of coffee per day. He is married with grown children who are all in good health.

Mr. Foster denied allergies. He is currently prescribed and taking Lisinopril 10 mg daily, Humira 40 mg injection every 2 weeks, Methotrexate 10 mg injection every week, and a daily multivitamin supplement. He reported taking his medications as prescribed with no obvious side effects.

The review of systems was negative except for the symptoms listed in his history of present illness. He reported the 5 day history of sore throat, runny nose, fever, headache, body aches, and cough. He denied shortness of breath, chest pain, swelling in legs, rashes and night sweats. He denied joint pain and swelling and reports that his RA is in excellent control on current medication regimen.

Vital signs included a heart rate of 90, respiratory rate of 30, temperature of 102.4, and blood pressure of 140/90. A repeat blood pressure later in the visit revealed a reading of 142/92. He stated that is blood pressure normally runs around 140 systolic. His primary care provider prescribed the Lisinopril but he reported that he doesn't follow up with his primary provider as much as he does his rheumatologist. He stated that his rheumatologist doesn't normally address his blood pressure, cholesterol, or other screenings but mostly concentrates on his RA symptoms

and medications. Mr. Foster could not remember the last time he had routine labs screening his cholesterol and for diabetes.

His physical exam was unremarkable besides rhinorrhea. Differential diagnoses included pneumonia, influenza, or viral upper respiratory infection. The patient did receive his flu shot this season but is on immunosuppressant medications for his RA. Mr. Foster was swabbed for influenza which came back positive. He was given a prescription for Tamiflu due to his chronic immunosuppression. He was advised to stay home and was instructed about supportive cares including adequate rest, nutrition, fluids, and completing the Tamiflu prescription. He was instructed to follow up if his symptoms were not improving in 48 hours or if he developed shortness of breath or chest pain. A chest x-ray would be completed if he is not improving to rule out concurrent pneumonia. Mr. Foster was also encouraged to set up a return visit in 2 weeks to address his uncontrolled hypertension and other CV risks. This leads to the question if CV risk management is different for the RA patient and how to best conduct his follow up visit. The literature review will address appropriate CV risk management for patients with RA in the primary care setting.

Literature Review

The aforementioned information necessitates aggressive and targeted CV risk management in patients with RA. This literature review will address the current literature and formulate an action plan for CV risk management in the primary care setting. One of the top recommendations found in a majority of the current literature is that lowering RA disease activity reduces CV risk (Barber et al., 2015). Barber et al. (2015) performed a systematic review of current guidelines on this topic and revealed that they all included recommendations for early treatment of RA to reduce symptoms, inflammation, and CV risk. The 2015/2016

guidelines from the European League Against Rheumatism (EULAR) agreed with this recommendation and went even further to say that RA patients should be treated with disease-modifying antirheumatic drugs (DMARDs) early in the disease course and long-term to reduce CV risk (Agca et al., 2017). Chodara, Wattiaux, and Bartels (2017) found that control of RA disease with a "treat to target" approach should be managed by a specialist of rheumatology for the best RA and CV outcomes. Mr. Foster is appropriately managed by a rheumatologist and is on methotrexate (a DMARD) and Humira (a Tumor Necrosis Factor (TNF) Inhibitor), he denies joint pain and reports his disease is "under control". Methotrexate is the frontline treatment for RA and has been found through a systematic literature review by Westlake et al. (2010) to reduce CV risks in RA patients by decreasing inflammation that may accelerate atherosclerosis. In fact, those never treated with methotrexate had increased risk of CV death by 70 percent compared to patients treated with the medication (Westlake et al., 2010). Westlake et al., (2010) also described that patients on methotrexate were found to have improved physical functioning and mobility which may increase exercise tolerance, decrease body mass, and had the opportunity to decrease CV risk through lifestyle modification.

Patients on DMARD therapy such as methotrexate are frequently able to decrease their use of other medications such as NSAIDS and glucocorticoids which can positively impact their CV risk (Westlake et al., 2010). NSAIDS have been proven to be associated with increased risk of CV mortality and events (Westlake et al., 2010). Glucocorticoids have also shown a negative impact on hypertension, dyslipidemia, and weight gain, increasing CV risk (Westlake et al., 2010). The PRECISION-ABPM study is a large double blind randomized trial of 444 patients that found ibuprofen was associated with a significant increase in systolic blood pressure compared to naproxen or celecoxib (Ruschitzka et al., 2017). The PRECISION-ABPM study

also found that ibuprofen increased blood pressure 3 mm Hg on average, increased new incidence of hypertension, and made already existing hypertension more difficult to manage (Ruschitzka et al., 2017). These findings are clinically relevant because it has been found that a decrease of systolic blood pressure by just 2 mm Hg can decrease risk or stroke by 10 percent and ischemia by 7 percent (Ruschitzka et al., 2017). According to a systematic review of RA guidelines Barber et al., (2015) found that five separate guidelines all addressed NSAIDS and the consensus was that they increased CV risk in the RA patient and should be avoided in known or high risk CV disease. If use cannot be avoided, consider using the lowest dose for the shortest period of time. Mr. Foster does use ibuprofen and he should be counseled on the increased risk this places him at for CV disease, especially with uncontrolled hypertension. NSAID counseling and monitoring is an essential factor of CV risk management in the RA patient.

CV risk assessment is a topic with many varying guidelines and expert opinions. All of the current guidelines advocate for some type of risk assessment because calculation of CV risk leads to early identification of risk factors so that intervention can begin (Chodara et al., 2017). Risk assessments developed for the general population such as the Framingham Risk Score (FRS) and the Reynolds Risk Score (RRS) do not take into account specific RA risks and therefore have been found to underestimate CV risk in the RA patient (Symmons, 2015). The FRS and RRS use values such as age, gender, smoking status, blood pressure, diabetes status, and lipid levels and then assign the patient a score to calculate the patients 10 year risk of CV events (Agca et al., 2017). A number of RA specific CV risk score calculators have been developed such as the Expanded Cardiovascular Risk Prediction Score for RA (ERS-RA), the EULAR 1.5 multiplier and the QRISK2 (Crowson et al., 2017). According to Crowson et al., (2017) after a validation analysis of patients from seven countries, the QRISK2, EULAR 1.5

multiplier and the ERS-RA algorithms did not more accurately predict CV risk than general risk calculators such as the FRS and RRS.

Because the evidence does not pinpoint the most effective CV risk calculator, most of the guidelines have leaned on expert opinion to make their final recommendations. The 2017 EULAR task force addresses the problem by recommending the application of a 1.5 multiplier to general population risk prediction models in order to estimate the increased risk of CV disease in all RA patients (Agca et al., 2017). The previous guidelines from EULAR limited the use of the multiplier only to those with RA whom met certain criteria, but when research results found it was still under-predicting CV risk, they amended the guideline in 2017 to include every patient with RA (Agca et al., 2017). The EULAR multiplier is also thought to be more user friendly and does not make a practitioner use a different risk assessment than they do for the general population (Agca et al., 2017). EULAR also amended this recommendation because studies have shown that CV risks are increased in every RA patient, even those newly diagnosed or in the early stages of the disease (Agca et al., 2017). The EULAR recommendations found that CV risk assessment should be completed within 1-2 years of disease onset and then, if the patient is at low-moderate risk, they should be reassessed at least once every 5 years (Agca et al, 2017). Quality indicators released by the Canadian Institutes of Health Research also concurred with this recommendation and advised screening at least once every 5 years if at low risk based on CV predictor score (Barber et al. 2015). The recent clinical update by Chodara et al., (2017) critically reviewed all of the current research from the past 5 years on this topic and also recommended the EULAR multiplier but they did address that there remains a need for a "validated, user-friendly estimation of CVD risk in patients with RA" (para. 6). In conclusion

until a RA specific CV risk calculator is available and validated as useful, most guidelines suggest the EULAR multiplier and CV risk calculators designed for the general population.

One of the major modifiable risk factors for CV disease is hypertension and the prevalence in RA patients has been found to be higher than the general population (Panoulas, John, & Kitas, 2008). Not only is the prevalence of hypertension increased but the management and control of hypertension in the RA population is less than adequate (Panoulas et al, 2008). The increased risk of hypertension in RA is multifactorial and is linked to inflammation, physical inactivity due to joint pain, and frequently used medications such as NSAIDS and corticosteroids (Pall, Szanto, & Farsang, 2013). NSAIDS and corticosteroids have also been found to inhibit the antihypertensive effects of medications, including diuretics, ACE/ARB, and beta blockers (Pall et al., 2013). There are currently no recommendations on which anti-hypertensives are preferred in RA patients and no evidence that treatment thresholds should vary from that of the general population (Agca et al., 2017). The current national guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) advise screening all adults yearly for hypertension, but rheumatology guidelines aim for a blood pressure screening at 80 percent of all visits (Barber et al., 2016). The ACC/AHA guidelines for hypertension management suggest that lifestyle modifications should be prescribed to all patients with elevated blood pressure, these include salt restriction, weight loss, The Dietary Approaches to Stop Hypertension (Dash) diet, exercise, and limited alcohol intake (Basile & Block, 2018). The ACC/AHA guidelines also suggest treating blood pressure over 140/90 in all adults when using in office readings, ambulatory or home monitoring blood pressure should be treated to a goal of 130/80. (Basile & Block, 2018). Patients with RA have a similar risk of CV disease as patients with diabetes, and the diabetes association also follows the 140/90 guidelines unless high risk or current CV

disease, then a target of 130/80 is more appropriate if the patient can tolerate the treatment without side effects (de Boer et al., 2017). The Joint National Committee (JNC 8) guidelines on HTN recommend treatment for a blood pressure >150/90 in adults >60 years or >140/90 in younger adults regardless of comorbidities such as diabetes or RA (Chodara et al., 2017). In Mr. Foster's case his hypertension is uncontrolled at levels over 140/90 and with his high CV risk with RA he might benefit from a blood pressure closer to 130/80 per ACC/AHA and ADA recommendations. Clinical trials have demonstrated 4 classes of medication that should be considered for initial hypertension treatment and they include thiazide diuretics, long acting calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin 2 receptor blockers (ARBs) (de Boer et al., 2017). Mr. Foster is currently on Lisinopril which is an appropriate first line therapy, but his blood pressure is uncontrolled so the dose should be increased or a second agent could be added (de Boer et al., 2017). Mr. Foster needs close follow up on his blood pressure at every office visit and adjustment in therapy as needed according to current guidelines.

Another CV risk factor that needs to be assessed at Mr. Foster's follow up visit is his lipid levels. Lipid levels are an integral piece of CV risk recognition and should ideally be measured when RA disease is stable and well controlled (Agca et al., 2017). Patients with active RA disease tend to have paradoxical lipid levels. Although their CV risk is increased, they tend to have lower total cholesterol (TC) and low density lipoprotein (LDL) levels compared to the general population (Agca et al., 2017). Patients with active disease tend to have higher triglyceride levels and low high-density lipoprotein (HDL) levels, therefore the TC/HDL ratio is a better predictor for CV risk outcomes in the RA population (Agca et al., 2017). Statins are the treatment of choice for dyslipidemia in the RA population, they have been found to reduce CV

risk and have anti-inflammatory effects (Saoulaidopoulos, Nikiphorou, Dimitroulas, & Kitas, 2018). The results of two trials, the TRACE (Trial of Atorvastatin for Primary Prevention of Cardiovascular Events in RA and the TARA (Trial of Atorvastatin in RA), on the statin effect in RA patients found decreased arthritis symptoms and lipid levels., The trials also found that patients who were taken off statin therapy suffered increased all-cause and CVD mortality (Chodara et al., 2017). None of the published guidelines for RA quantified how to treat patients with RA for hyperlipidemia differently than the general population. The CIHR recommended a lipid profile within 1-2 years of diagnosis and then at least once every 5 years if low risk (Barber et al. 2015). Treatment should be provided to moderate or high risk patients according to national guidelines (Barber et al., 2015). A systematic review of current guidelines by Barber et al., (2015) summarized that all current literature advised statin therapy as the first line treatment and screening and treatment should be based on current national guidelines.

Mr. Foster's follow up visit will focus solely on CV risk management. The fact that his RA is well controlled is a positive indicator of his CV risk. Mr. Foster should have an individualized risk assessment using the FRS and EULAR multiplier (or other general population CV risk calculator) and he should be appropriately treated for his uncontrolled hypertension. He will need to have lipid screening and blood glucose testing as well as height and weight completed for BMI. Mr. Foster will also benefit from counseling on minimizing NSAID use, healthy diet, exercise, and the fact that RA increases his CV risks. Future research should focus on RA specific CV recommendations, such as how to best ascertain CV risk and how to determine optimal thresholds for the use of statins and anti-hypertensives. The role of the multidisciplinary care team also needs to be researched as both rheumatology specialists and primary care providers are unsure of their role in CV risk management (Barber et al., 2015).

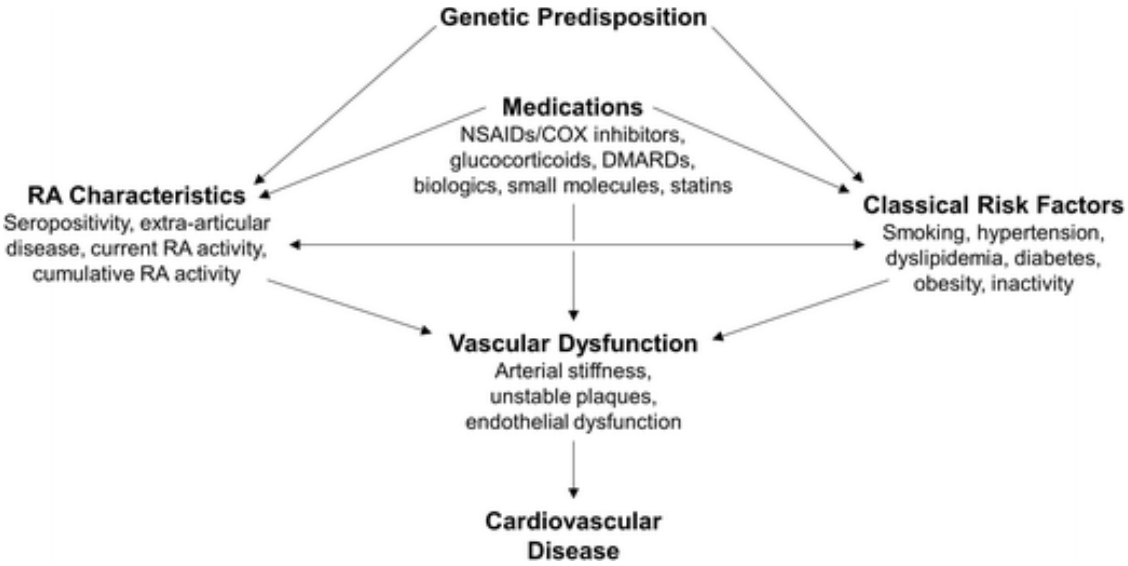
Learning Points

There are many overarching principles that should be applied to every person at risk for CV disease and they are not exclusive to RA patients. Although not addressed in the case report, RA patients should not be exempt from education regarding lifestyle modifications including the benefits of a healthy diet, regular exercise, and smoking cessation. Diabetes screening and treatment is also another important factor that was not addressed in this case report, but is included in most CV risk predictors such as the Framingham score. Figure 1.0 is an excellent resource for primary care providers because it points out the multifactorial risks of CV disease in the RA patient (Chodara et al., 2017). It is of upmost importance for primary care providers to recognize the higher risk for CV disease in patients with RA compared to the general population and apply the following recommendations in collaboration with a rheumatologist.

- RA patients benefit from rheumatology consult to have their disease and inflammation appropriately managed and adequately controlled in order to decrease their CV risks.
- NSAIDS and corticosteroids should be prescribed with caution especially for patients with known CV risk factors or CV disease.
- Comprehensive individual CVD risk assessment with risk calculation should be performed at least every 5 years or more frequently with major changes in anti-rheumatic therapy or high risk patient based on Framingham score (or other general population CV risk assessment) with a multiplier of 1.5.
- Screen for hypertension at every visit and treat elevated blood pressures according to JNC 8 and American Heart association guidelines.
- Screen with a lipid profile within 1-2 years of disease onset (preferably when RA is stable) and then at least once every 5 years if normal. Dyslipidemias should be treated

according to national guidelines and statins are the preferred treatment for patients with RA.

Figure 1.0



(Chodara et al., 2017)

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