Rheumatoid Arthritis and Heart Disease: Why You're at Increased Risk

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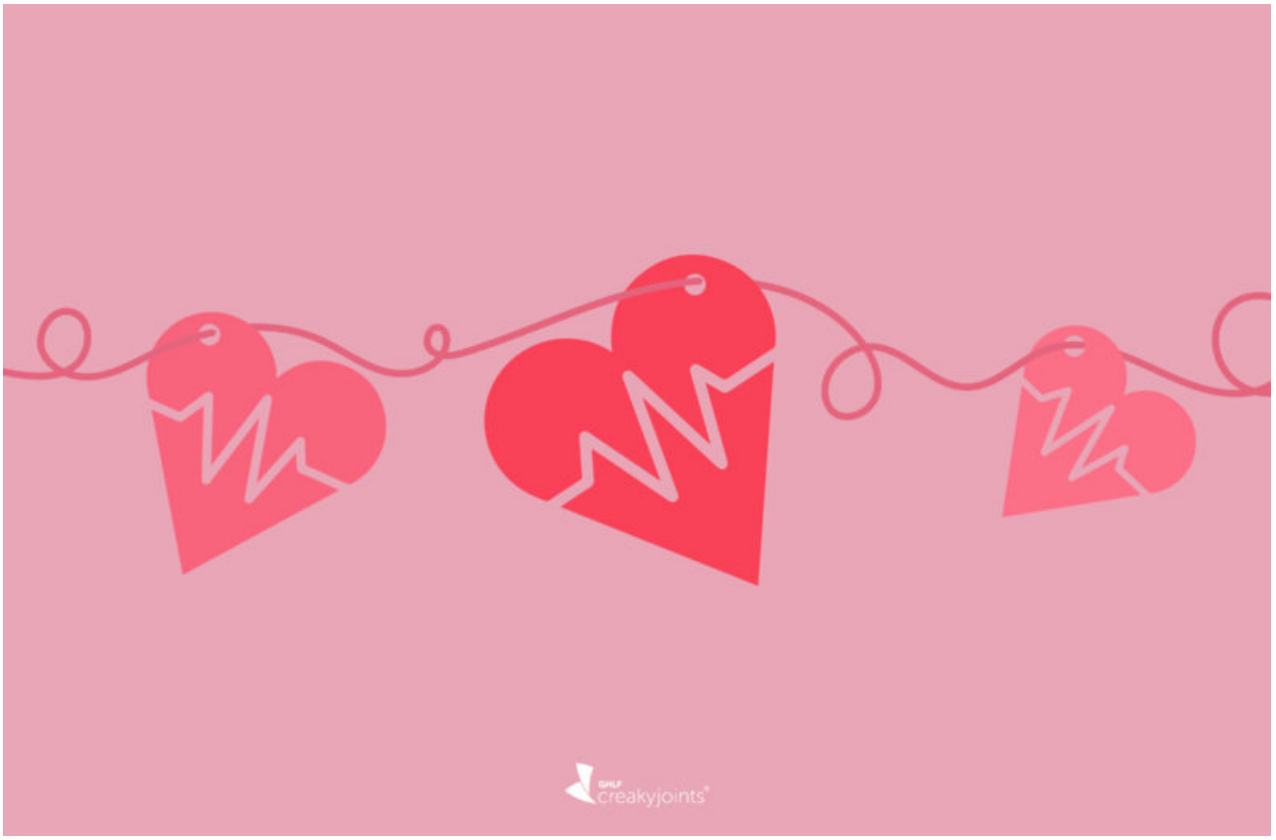
People with rheumatoid arthritis have nearly a 50 percent greater risk of developing cardiovascular disease. Knowing the different factors that can affect your heart disease risk is the first step in lowering it.

Check out A Patient's Guide to Understanding Rheumatoid Arthritis and Heart Disease (https://awareness.creakyjoints.org/ra-heart-health/) *for more information on this topic.*



(https://creakyjoints.org/wp-content/uploads/2021/03/0321_Heart_Health_Logo-1024x683.jpg)

For people with rheumatoid arthritis (RA), swollen and painful joints are often the most obvious and challenging symptoms. Even if you sometimes develop random fevers, fatigue, or other RA symptoms (http://creakyjoints.org/symptoms/rheumatoid-arthritis-symptoms/), you still likely think of RA as a "joint" condition.

But the truth is that this inflammatory disease can do far more than just damage your joints, especially if it is not well-controlled. Rheumatoid arthritis causes inflammation throughout your body, which can impact many different organs and systems.

In particular, rheumatoid arthritis-related inflammation can impact the heart and blood vessels, raising the risk of cardiovascular disease (CVD) in RA patients.

Numerous studies have examined the connection between RA and cardiovascular disease, and the findings can sound alarming. According to an analysis of several earlier studies, RA patients have, on average, nearly a 50 percent higher risk of developing CVD (https://pubmed.ncbi.nlm.nih.gov/22425941/) compared to the general population. They also have a 50 percent greater chance of dying (https://pubmed.ncbi.nlm.nih.gov/19035419/) from it — making heart disease one of the leading causes of death for people with RA.

What's more, many people with rheumatoid arthritis are not aware of this link between RA and their heart.

According to a review of research published in the journal *Arthritis Research & Therapy* (https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-019-1817-y) in 2019, anywhere from 73 percent to 97 percent of RA patients are not aware that merely having RA increased their risk of heart disease. "Misperceptions about [heart disease] were common, and the majority of subjects misestimated their actual CVD risk," the authors wrote.

In a recent survey of CreakyJoints members with rheumatoid arthritis (http://creakyjoints.org/comorbid-conditions/rheumatoid-arthritis-heart-disease-infographic), only 26 percent said they had ever been given information about RA and cardiovascular risk. A majority (60 percent) said they were never told that they personally have a higher heart disease risk because of RA.

While this information is certainly scary, the news isn't all bad.

In recent years, "there's been a great revolution in terms of new drugs [for RA] and we know a lot more about how to target the biggest cardiac risk factors," says George A. Karpouzas, MD (https://lundquist.org/george-karpouzas-md-facr), Professor of Medicine at the David Geffen School of Medicine at UCLA and Chief of Rheumatology at Harbor UCLA Medical Center in Los Angeles. "Our relationships with patients have also changed. Patients are considered equal partners in decision making; we actively commission their participation in their own care, and when patients feel empowered, they become motivated."

All of these factors put you in the driver's seat when it comes to managing your RA and related cardiovascular risks. By educating yourself and taking action, you can tip the odds of staying healthy in your favor.

In fact, in the CreakyJoints survey, while 53 percent of respondents said knowing about this link made them feel worried, 38 percent said they felt empowered to make changes in order to be healthier.

Step one: Learn more about how and why RA impacts your cardiovascular system.

Types of Cardiovascular Problems in Rheumatoid Arthritis

Rheumatoid arthritis can affect your risk of many types of cardiovascular issues, including:

Heart attack

People with RA are twice as likely (https://www.clevelandheartlab.com/blog/the-cardiac-risks-of-rheumatoid-arthritis/) as those without it to experience a heart attack. A heart attack occurs when a piece of plaque (fatty deposit in your arteries) breaks off, forms a clot, and blocks blood flow to the heart.

Stroke

Sometimes called a brain attack, a stroke occurs when blood supply to the brain is cut off, most often due to a blood clot. People with RA may be 60 to 100 percent more likely (https://www.ahajournals.org/doi/full/10.1161/strokeaha.115.012052#:~:text=Risk%20of%20any%20stroke%20is,relative%20to%20the%20general%20population.) to have a stroke compared to those without RA.

Pulmonary embolism

This is a blood clot in your lungs, and it can be fatal. People with RA are significantly more likely than others to develop a pulmonary embolism, but those with high levels of rheumatoid arthritis disease activity (http://creakyjoints.org/comorbid-conditions/high-disease-activity-rheumatoid-arthritis-blood-clot-risk/) are at greatest risk.

Coronary artery disease

The most common type of heart disease (https://www.cdc.gov/heartdisease/coronary_ad.htm), coronary artery disease occurs when the arteries leading to your heart become clogged with too much plaque (made of cholesterol and other substances). If a piece of plaque breaks off, it can form a clot, block blood flow to the heart, and cause a heart attack. Studies have found that people with RA have a 1.5 to twofold increased risk (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3890244/#:~:text=Patients%20with%20RA%20have%20a,by%20diabetes%20mellitus%20(3).) of coronary artery disease compared to the general population.

Heart failure

Heart failure is a chronic condition that occurs when the heart isn't strong enough to pump effectively, which makes you feel weak. Everyday activities can become challenging. Having RA makes you twice as likely (https://pubmed.ncbi.nlm.nih.gov/15692992/) as others to develop heart failure.

Atrial fibrillation

A type of irregular and usually rapid heartbeat, atrial fibrillation puts you at risk for having a stroke. People with RA are 60 percent more likely (https://www.the-rheumatologist.org/article/study-shows-rheumatoid-arthritis-linked-to-atrial-fibrillation/#:~:text=It%20is%20well%20known%20by,fibrillation%20than%20those%20without%20RA) than the general population to have this condition.

Reasons Rheumatoid Arthritis Raises the Risk of Heart Problems

1. Inflammation harms your heart and vessels

Rheumatoid arthritis is, at its core, an inflammatory disorder. Your immune system mistakenly identifies healthy tissue around your joints as an invader and attacks it. That attack causes inflammation and the pain, swelling, and warmth that go along with it. But the inflammation, unfortunately, isn't just limited to your joints. It can circulate throughout your entire body and damage other tissues, including those in your blood vessels and heart.

Inflammation irritates blood vessels (https://www.hopkinsmedicine.org/health/wellness-and-prevention/fight-inflammation-to-help-prevent-heart-disease#:~:text=%E2%80%9CFor%20short%2Dterm%20conditions%2C,of%20heart%20attacks%20and%20strokes.%E2%80%9D) throughout your body. It makes plaque more likely to form and also makes plaque less stable. This means that it is more apt to break off, form a clot, and block an artery that leads to your brain (causing a stroke) or your heart (causing a heart attack). It also makes you more prone to blood clots in the deep veins of your legs (deep vein thrombosis), which can travel to your lungs and cause a pulmonary embolism.

Additionally, inflammation causes LDL ("bad") cholesterol to oxidize, or become chemically changed. "Oxidized LDL can more easily slip under the lining of coronary vessels and get trapped there, where it causes even more inflammation, says Dr. Karpouzas.

This is more likely to occur in RA patients with high disease activity (https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-020-02307-8) than it is among those whose disease is in remission.

One reason people with RA have so much inflammation is that they have elevated levels of inflammatory cytokines (proteins), such as TNF alpha, says Namrata Singh, MD (https://rheumatology.uw.edu/faculty/namrata-singh-md-msci-facp), Assistant Professor of Rheumatology at the University of Washington in Seattle. These proteins "induce a pro-inflammatory, pro-thrombotic, and pro-coagulant state," which means they not only drive inflammation but they also make blood stickier so dangerous clots — including those that cause heart attacks and strokes — are more likely to form.

C-reactive protein (CRP), an inflammatory marker that is often elevated in RA patients, is also an important factor. "Higher levels of CRP are highly associated with greater incidence of myocardial infarction," aka heart attacks, says rheumatologist Iris Navarro-Millan, MD (https://www.hss.edu/physicians_navarro-millan-iris.asp), Assistant Professor of Medicine at Weill Cornell Medical College and Assistant Attending Physician at Hospital for Special Surgery in New York City.

2. HDL ("good") cholesterol doesn't do its job as well

"Bad" LDL (low-density lipoprotein) is the type of cholesterol (blood fat) that raises your risk of heart disease and stroke by forming plaque in your arteries. "Good" HDL (high-density lipoprotein) cholesterol is supposed to scoop up LDL and shuttle it to the liver so it can get flushed out of the body.

But research suggests that HDL might not be as beneficial as it is in people without RA.

At UCLA, rheumatologist Christina Charles-Schoeman, MD (https://www.uclahealth.org/christina-charles-schoeman), and her colleagues were among the first to identify the association between RA and "dysfunctional" HDL (https://europepmc.org/article/med/19790070) that doesn't do a good job of clearing LDL from your vessels.

"In particular, higher RA disease activity was associated with alteration in the protein composition of HDL and impairment of its function," she says.

Her group also found that a protein related to HDL, called PON1 (https://pubmed.ncbi.nlm.nih.gov/23917967/), was less active in RA patients, and that this shift "was associated with higher levels of inflammation and cardiovascular risk in RA patients" as evidenced by the plaque visible on carotid artery ultrasounds.

3. Traditional heart disease risk factors get magnified

Heart disease risk factors are health conditions or lifestyle issues that can raise your risk for developing cardiovascular disease. These common ones are also "highly prevalent" among patients with RA, according to a literature review (https://bmcrheumatol.biomedcentral.com/articles/10.1186/s41927-018-0014-y) co-authored by Dr. Navarro-Millan.

- High blood pressure
- High lipids (LDL cholesterol and triglycerides, another type of blood fat)
- Smoking
- Obesity
- Diabetes
- Sedentary behavior

In some cases, RA patients are even more apt to have these risk factors. Smoking, for instance, is more common among RA patients than it is among those without the disease. Physical activity rates also tend to be lower in people with rheumatoid arthritis. Some RA patients may have too much pain to exercise, but other may not realize that physical activity is recommended and beneficial for their joints as well as their cardiovascular health.

If you have any of the traditional risk factors for cardiovascular disease and then you add RA on top of it, your risk can become magnified. "The interaction of these risk factors with inflammation from RA causes them to super synergize," says Dr. Karpouzas.

4. Rheumatoid arthritis medications can affect heart disease risk

Rheumatoid arthritis is typically treated with different medications to control pain and inflammation. Some of these drugs can also affect heart disease risk, so it's important for you to be aware of these connections and discuss them with your rheumatologist.

Corticosteroids

Corticosteroids like prednisone are the biggest offenders, so consider their impact on heart health just one more reason to avoid them or use as low a dose as necessary to keep your RA in check.

Steroids can raise levels of lipids like LDL cholesterol and triglycerides, says rheumatologist Christie Bartels, MD (https://www.medicine.wisc.edu/people-search/people/staff/658), Associate Professor at the University of Wisconsin in Madison. "They can also make your blood pressure higher, make your blood sugar higher, and cause changes in systemic inflammatory responses."

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs, which include medications like ibuprofen (Advil) and naproxen (Aleve) and prescription versions, are another class of medication that you ought to be cautious about.

Although NSAIDs are, by definition, anti-inflammatory, most of them inhibit certain enzymes (https://www.uspharmacist.com/article/cardiovascular-risk-associated-with-nsaids-and-cox2-inhibitors) (COX-1 and COX-2) that may, in turn, raise the risk of cardiovascular events. That said, a meta-analysis (https://pubmed.ncbi.nlm.nih.gov/18408253/) that specifically looked at NSAID use in RA patients found that these drugs do *not* increase the risk of heart disease.

"I'm not too worried about NSAIDs, but some cardiologists are," says Dr. Navarro-Millan. "But I still try to avoid them because they may cause GI distress, ulcers, and gastritis, and they're not disease-modifying for rheumatoid arthritis. We have better options."

If you must use NSAIDs regularly, naproxen is probably your best bet, says Dr. Bartels. It has a slightly different mechanism of action so it's less likely than other NSAIDs to lead to cardiovascular problems.

Disease-modifying antirheumatic drugs (DMARDs)

Most traditional DMARDs like methotrexate as well as newer biologics, such as TNF inhibitors, do not raise the risk of cardiovascular problems. In fact, there's some evidence that they might lower the risk (https://www.clevelandheartlab.com/blog/the-cardiac-risks-of-rheumatoid-arthritis/) of heart disease. TNF inhibitors include adalimumab (Humira), certolizumab pegol (Cimzia), etanercept (Enbrel), golimumab (Simponi and Simponi Aria), and infliximab (Remicade),

Other medications like JAK inhibitors [such as tofacitinib (Xeljanz), baricitinib (Olumiant), and upadacitinib (Rinvoq) and IL-6 inhibitors [such as tocilizumab (Actemra) and sarilumb (Kevzara)] are a bit different, because they may raise levels of cholesterol and triglycerides, says Dr. Bartels.

JAK and IL-6 inhibitors "are still good options for certain patients," says Dr. Bartels. However, they might not be a great fit if you already have high cholesterol.

Dr. Bartels says she checks patients' lipids before they start these drugs, then again six weeks later. If the numbers seem high at the six-week mark, she'll test again at six months to see if they normalize along with better RA disease control.

5. Your doctor might not be keeping tabs on your cardiovascular health

"A large number of RA patients don't even get a cholesterol test," says Dr. Navarro-Millan. The problem, she says, is that many patients treat their rheumatologist as their main health care provider, but rheumatologists expect that primary care physicians, such as internists, are monitoring their patients' heart health.

In the CreakyJoints survey, 20 percent of respondents said they were not monitoring their heart health with a doctor, such as getting regular cholesterol or blood pressure tests.

Rheumatologist Jeffrey Curtis, MD, MPH (https://scholars.uab.edu/display/jcurtis), Professor of Medicine at the University of Alabama at Birmingham, says that "physician ownership" — or lack thereof — is a huge problem when it comes to RA and co-occurring conditions (comorbidities) like heart disease. "There are some blurry domains in medicine for people with chronic medical conditions," he says. "Many rheumatologists might say, 'My job is to take care of your RA.'" They may not have time to manage issues like high blood pressure, high cholesterol, diabetes, and other heart disease risk factors.

This disconnect means that the responsibility can fall on RA patients in a few ways. Not only is it essential to see a primary care doctor (or also a cardiologist), but it's important to bring up heart health with your rheumatologist.

For starters, "ask [one of your providers] for a cholesterol test and an A1C test," which is used to diagnose insulin resistance and type 2 diabetes, says Dr. Navarro-Millan. And when any doctor runs a test, no matter how simple, ask for the results and what they mean.

It's too easy for, say, a nurse to take a blood pressure measurement, enter it into a patient's health record, and then nothing else happens. "Don't assume your doctor would tell you if there was a problem," Dr. Bartels says.

Read more here about tests to assess and prevent heart disease for rheumatoid arthritis patients (http://creakyjoints.org/comorbid-conditions/rheumatoid-arthritis-heart-disease-tests).

Empower Yourself to Take Action

While the link between RA and cardiovascular disease is quite serious, it can absolutely be mitigated by making healthy lifestyle changes, such as incorporating more physical activity into your routine, quitting smoking, losing weight, or eating more nutritious foods. Dr. Bartels often refers patients who smoke to the Quit Line (https://connecthealth.wisc.edu/quit-connect/), a free resource that offers coaching and nicotine replacement.

Read more here about tips to reduce your heart disease when you have rheumatoid arthritis (http://creakyjoints.org/comorbid-conditions/rheumatoid-arthritis-heart-disease-lower-risk).

If any of your doctors have prescribed a statin (cholesterol-lowering medication) because they deemed you high risk, be sure to stay on it, Dr. Bartels adds. Ditto for medication to lower high blood pressure and high blood sugar (as diabetes is very closely tied to heart disease).

Lastly, keeping tight control of your RA inflammation and disease activity is crucial to protect your joints and your cardiovascular health.

“Several studies have found associations between higher disease activity in RA and cardiovascular disease outcomes,” says Dr. Singh, who notes that the longer you are in remission, the lower your odds of having a cardiovascular event.

One such study, which was published in the journal *Arthritis & Rheumatology* (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4446181/), followed nearly 25,000 RA patients in a U.S. registry for an average of 2.7 years. It found that people whose RA was in remission were 53 percent less likely to experience a serious cardiovascular event during that time.

Dr. Bartels adds that some patients are reluctant to change up their RA drug regimen despite not being in remission because they’ve gotten comfortable with it — but that’s a mistake: “Following a ‘treat-to-target’ strategy not only helps preserve joints but also reduces your long-term cardiovascular disease risk by reducing uncontrolled inflammation.”

Treat to target means picking a goal, such as low disease activity or remission (as measured by blood tests, counts of painful and swollen joints, and patient reports of symptoms) and adjusting your RA treatment until you reach the target goal.

This article is part of A Patient’s Guide to Understanding Rheumatoid Arthritis and Heart Disease (https://awareness.creakyjoints.org/ra-heart-health/) *and was made possible with a grant from Myriad Genetics, Inc.*

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