Blood Clots and Cancer

Blood clots are a complicated disease that can be caused by many different things, from sitting too long to an inherited genetic risk. One risk factor that many people are unfamiliar with is cancer.

Patients with cancer, diagnosed or undiagnosed, are at risk for developing blood clots, which can occur in up to 20% of these patients. It is the second leading causes of death for these patients. It’s important for patients, those with cancer and those only affected by blood clots, to understand the connection between the two.

**WHY DOES CANCER CAUSE BLOOD CLOTS?**

The answer to “why?” is not a simple one and can vary from patient to patient.

“There are several different factors that increase the risk of blood clots in patients with cancer,” said Dr. Jean Connors, a hematologist that works with both Brigham and Women’s Hospital and the Dana-Farber Cancer Institute.

For some patients, the type of cancer they have can trigger blood clots.

“Some cancers actually produce substances that are pro-coagulant,” explained Dr. Connors. According to Dr. Connors, mucin producing adenocarcinomas, types of cancers that arise from epithelial cells, are especially pro-thrombotic (meaning they can promote the creation of blood clots). They release substances that activate the clotting cascade and produce clots in the areas where they are found.

Blood clots can also be triggered by tumors that cause the ‘Mass Effect.’ “Tumors compress the blood vessels and slow the blood flow, setting up the ideal state for a clot to form,” said Dr. Connors.

Continued on page 3

Patient Perspective – Bart Coyne

Bart Coyne, a heart transplant patient, experienced deep vein thrombosis (DVT) and pulmonary embolism (PE) in April 2017. Here is his story about how a positive attitude and the support of others has helped him manage his life after DVT/PE:

Q: What has your experience with heart disease and blood clots been like?

In 2000, I had a heart transplant.

Immediately before it, I was active. I was playing ice hockey a month before. I didn’t really have any signs or symptoms of needing any serious heart surgery or even knowing that I had a heart issue.

When it started, I developed some breathing complications. I went into the hospital and had an aortic valve replacement, which was calcified, and four days after that pretty much everything went south.

I ended up getting a heart transplant. I got the heart transplant on my birthday, which I guess was a nice birthday present.

After that, things went along very well. Other than the annual evaluation looking for any kind of rejection on the heart, I never really had to visit the hospital. I didn’t have any complications. And then, in April of 2017, I was diagnosed with deep vein thrombosis and bilateral pulmonary embolism, which seemed to come out of nowhere.

Continued on page 2
I really didn’t have any symptoms, other than a small amount of chest pain on a very deep breath intake. With the DVT and PE diagnosis, I didn’t experience a lot of pain. It came totally out of nowhere and was a complete surprise. I didn’t really know what to expect.

Q: How is your recovery from the blood clots going? What kind of treatment are you on?

Right now, I’m on Coumadin. I know there are several other options besides Coumadin, but with my heart transplant that seems to be the basic care my doctors wanted.

I don’t experience any breathing issues right now. I’m very active. I exercise. I swim. I bike ride. But, I really don’t know if the blood clot is growing while I’m on anticoagulants. Is it going to go away? The doctors seem to indicate that that’s a question that really doesn’t have a definite answer for any one individual. I think that all cases are a little bit different. And that’s probably the biggest thing relevant to this diagnosis that I’m not sure about.

Q: What do you feel the most anxious about?

Well, there’s uncertainty with the diagnosis. There’s an anxiousness, because you don’t know a lot. If you get a pain in your leg, is this the pain that’s related to the blood clot or is it just a stretched a muscle?

There’s a lot of just not knowing what some of the symptoms might be or what some of the symptoms may develop to be going forward.

Q: What do you feel the most anxious about?

Well, Diane, my wife, is a nurse and a great support person. She helps me understand what’s going on as far as the diagnosis. She helps me research and look into a lot of it. She understands it a lot better than I do, when it comes to some of the effects and the medications.

In general, I’ve been fortunate that I’m a very positive person. Both the heart transplant and the DVT/PE diagnosis for me did not come with a lot of pain or advanced warning. I really didn’t even know I needed a heart transplant until probably a week and a half before I ended up getting it. I didn’t know there was even a possibility of having a DVT or a PE until the evening I was diagnosed.

I experienced no pain and that’s allowed me to go into all of these experiences with a very positive attitude, because I didn’t labor with a lot of issues in advance. Having been diagnosed, listening to the doctors, and having received great treatment in both cases, I can keep a very positive attitude about going forward.

My make-up is to be extremely positive in pretty much all aspects. It’s not anything that I can change. I certainly can’t go back and prevent either of the two from happening.

With the DVT and PE, which are my newest diagnoses, it’s just a matter of listening to what I’ve been told, doing a small amount of research on my own, talking to the various doctors attending the support groups, and meeting people similar to myself, who have had the same exact experience in their own individual ways.

PATIENT PERSPECTIVE

Continued from page 1

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BLOOD CLOTS AND CANCER
Continued from page 1

For other patients, different cancer treatments can make them prone to blood clots.

“Many chemotherapy drugs are pro-thrombotic, some more so than others,” Dr. Connors explained. “They can cause inflammation and vascular endothelial damage. They create a situation that is prime for clotting.”

Radiation therapy can also leave patients at risk for developing a clot. The radiation can damage the body’s vascular endothelium, making it inflamed and pro-thrombotic.

Additional risks for blood clots can compound the risk from cancer.

If a patient already has established risk factors for a blood clot, cancer only adds to that risk. Additional risk factors can include:

- A family history of blood clots
- Hormone therapies, such as birth control or menopausal treatments
- Surgery, especially on the hip or knee
- Pregnancy
- A sedentary lifestyle
- Smoking
- Obesity

Several of these risk factors can be controlled through living a heart healthy lifestyle. Patients with cancer should try to adopt heart healthy habits to help them lower their risk of developing a blood clot.

BLOOD CLOTS AS A SYMPTOM OF CANCER

For some patients, the blood clot comes before the cancer diagnosis. That was the case for Mark, a business-owner and family man, who was diagnosed with a submassive PE at 49 years old.

After receiving treatment at Massachusetts General Hospital, Mark’s doctors followed up with him to find out why he had experienced an unprovoked blood clot (unprovoked meaning there was no known cause). His doctors discovered that his blood clot had been caused by multiple myeloma, a dangerous form of cancer. Because of this discovery, Mark was able to get the treatments he needed.

“I was a ticking time bomb without anyone knowing,” said Mark. “I feel extremely fortunate.”

“I feel better every day. I get stronger every day,” he remarked, praising the nurses and doctors he’s been working with.

Up to 10% of patients with an unprovoked clot are diagnosed with cancer within a year of their blood clot. Despite the fact that blood clots can be a sign of undiagnosed cancer, screening for cancer is not immediately done for patients diagnosed with an unprovoked blood clot. Studies have shown that screening every patient may be ineffective and not beneficial.

A study, “Screening for Occult Cancer in Unprovoked Venous Thromboembolism,” published by the New England Journal of Medicine in 2015, investigated whether patients with unprovoked blood clots should get extra radiology scans to check for cancer. They found that the screening with abdominal and pelvic CT scans did not detect any more cancers than standard screening tests, such as routine blood work or a chest x-ray. They also found that the screening didn’t detect significantly more occult cancers, shorten a patient’s time to cancer diagnosis, or reduce the number of cancer-related deaths among trial participants.

“Not everyone with a clot has cancer,” Dr. Connors stressed. The best way to prevent cancer is by ensuring patients receive their age appropriate cancer screenings, such as mammograms, regular pap smears, and colonoscopies.

However, Dr. Connors did highlight the importance of doctors reacting to their blood clot patients’ additional symptoms.

“You should check up on symptoms,” she said. For example, if a patient has persistent abdominal pain or unexplained bleeding and an unprovoked blood clot, a CT scan or other tests may be in order.

TREATMENTS FOR BLOOD CLOTS IN CANCER PATIENTS

The American College of Cardiology provides specific outlines for how doctors should treat blood clots. For patients with cancer, they recommend low molecular weight heparin over warfarin or any of the direct oral anticoagulants (DOACs).

The American Society of Clinical Oncology recommends that all hospitalized cancer patients be considered for an anticoagulant to prevent blood clots. As with the ACC, the American Society of Clinical Oncology also recommends low molecular weight heparin as the preferred treatment for the initial blood clot and continuing treatment of cancer patients with blood clots.

When treating patients, doctors must balance these guidelines with patient preference and patient history. Patients on low molecular weight heparin must deal with injecting themselves with the medication every day, which many patients have trouble with.

A very recent report on the use of one DOAC, edoxaban, compared to treatment with dalteparin, a low molecular weight heparin, for patients with cancer and blood clots was published in the New England Journal of Hematology in December 2017. This study found that patients treated with edoxaban had the same composite risk of developing both recurrent blood clots and major bleeding. It appears that edoxaban might have been better at preventing recurrent blood clots than dalteparin, but there was an increase in bleeding. This was primarily seen in patients with GI cancers.

“Even before publication of the results of this study, I would use the DOACs in very carefully selected cancer patients, such as people who have good renal function, who have minimal risk of bleeding, and for whom they’re likely going to be effective,” explained Dr. Connors, referring to the study that compared edoxaban and dalteparin. “While the results of this study are encouraging, I am still cautious about using DOACs in every cancer patient with VTE until more data are available.”

If you’re a patient dealing with blood clots or cancer, talk to your doctor about any concerns that you may have. Only your doctor is familiar with your individual case and can provide personalized care.

Care to share your experience with blood clots and cancer? Email info@natfonline.org for more information.
COMPASS: A new direction for patients with heart disease?

By Aaron P Kithcart, MD PhD

This past fall, at the annual meeting of the American Heart Association, the results of an exciting clinical trial called COMPASS were announced. The study looked at the benefit of adding a low dose of rivaroxaban, an oral blood thinner frequently used for patients with blood clots, to a low dose of aspirin in patients with atherosclerosis. Also known as hardening of the arteries, atherosclerosis can lead to many serious complications, including heart attacks and strokes. More than 90 million Americans are thought to have some form of cardiovascular disease. Let’s take a closer look at the study.

HOW WAS THE STUDY DESIGNED?

COMPASS is a double blinded, randomized clinical trial, meaning that neither the doctors nor the patients knew which drugs enrollees were receiving. Researchers tested three different combinations: rivaroxaban plus aspirin, rivaroxaban alone, or aspirin alone. The dose of rivaroxaban for

A DOAC Deep Dive: Rivaroxaban

For the past several decades, warfarin has been the go-to anticoagulant for doctors, but new treatments have recently emerged in the form of direct oral anticoagulants (DOACs). DOACs are considered more effective and safer than warfarin, especially in relation to serious bleeding episodes. These anticoagulants include apixaban, betrixaban, dabigatran, edoxaban, and rivaroxaban.

Natf is dedicated to offering readers a closer look at each DOAC in order to empower patients to make informed healthcare decisions. In this issue, natf takes a closer look at rivaroxaban:

WHAT IS IT?

Rivaroxaban, also known as Xarelto, is a blood-thinning medication that is used to treat thrombosis and nonvalvular atrial fibrillation patients. It’s used for patients that are at risk for developing deep vein thrombosis (DVT) or pulmonary embolism (PE). It is also used to prevent strokes in patients who have atrial fibrillation.

HOW DOES IT WORK?

Rivaroxaban is a factor Xa inhibitor, meaning the drug binds to a factor Xa molecule, which stops blood from clotting at a certain point in the clotting cascade. The clotting cascade is the process by which the body creates blood clots.

“When it works the way it’s supposed to, the clotting cascade stops patients from bleeding and can save lives. However, it can also cause a problem if a clot is formed in an inappropriate place in the body. It can cause stroke, heart attack, PE, and DVT,” explained John Fanikos, RPh, MBA, Director of Pharmacy Services for Brigham and Women’s Hospital. “The factor Xa inhibitors interrupt the clotting cascade, preventing the blood from clotting when it shouldn’t.”

Other factor Xa inhibitors include apixaban and edoxaban. By interrupting the clotting cascade and stopping clots from forming, these drugs help to prevent DVT, PE, and more.

Patients should take rivaroxaban with food in order to help the body absorb the medication.

WHAT IS UNIQUE ABOUT RIVAROXABAN?

While apixaban and edoxaban are also factor Xa inhibitors, rivaroxaban has several benefits that set it apart from other DOACs.

One benefit is its dosage. Many patients on rivaroxaban for atrial fibrillation or blood clots only have to take it once a day. This can be helpful for patients who have trouble remembering to take their medications.

“Many patients have trouble remembering to take their medications consistently. This can be dangerous for patients on anticoagulants. The once-daily dose of rivaroxaban can be helpful for some patients by simply reducing the number of times a day they need to take their medication,” explained Dr. Fanikos.

WHAT ARE THE RISKS?

Rivaroxaban has its own set of unique risks that all patients should discuss with their doctor prior to taking it. As with warfarin and the other DOAC drugs, patients on rivaroxaban are at a higher risk of bleeding. This risk is increased if a patient is taking aspirin, non-steroidal anti-inflammatory drugs, clopidogrel, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, or other medications to treat blood clots.

Patients on rivaroxaban should call their doctor if they experience any symptoms of bleeding. These can include unexpected bleeding; such as nosebleeds, bleeding from the gums, or menstrual bleeding that is heavier than normal. Patients should also contact their doctors if they feel dizzy or weak and are experiencing headaches.

Unlike warfarin and dabigatran, rivaroxaban does not currently have a reversal drug. Doctors who prescribe anticoagulants without reversal drugs work to balance the bleeding risk against the risk of VTE and stroke.

INTERESTED?

If you would like to explore rivaroxaban as a potential treatment, you must first talk to your healthcare provider. Only your doctor knows your individual health history. They can provide you with the best input on what medications are right for you. Never change or stop taking your medication without talking to your doctor.

Natf’s Anticoagulation Comparison Chart is a great tool that you can use with your healthcare provider to discuss what anticoagulant is right for you.

You can find this on our website at www.NATFOnline.org
COMPASS
Continued from page 4

this trial, 2.5 mg twice a day, was lower than what is commonly used today. The primary question was whether or not a low dose of a blood thinner added additional benefit to aspirin. Currently, patients who have had a heart attack or stroke, or have risk factors for atherosclerosis including high blood pressure, high cholesterol, diabetes, or a family history, are started on a low dose of aspirin to prevent complications from blockages in arteries. In this study, enrollees were followed for nearly two years and regularly evaluated for events including heart attacks, strokes, or death.

WHAT WERE THE RESULTS OF COMPASS?

The study created a lot of excitement because the addition of rivaroxaban resulted in a significant reduction in heart attacks, strokes, and death. Importantly, this was not associated with an increased risk for bleeding, which is unfortunately a complication of patients taking blood thinners. The low risk of bleeding may have been due to the lower dose of rivaroxaban used in this study. There was also a benefit for patients with peripheral artery disease, another form of atherosclerosis in the arms and legs. Those patients taking both rivaroxaban and aspirin had fewer limb complications, including amputations and surgeries. Across the board, patients seemed to benefit from the combination of blood thinner and aspirin without any significant additional risk.

WHAT DOES THIS MEAN FOR ME?

Patients with heart disease are often at risk for future complications, and after the first sign of problems are almost always started on a baby dose of aspirin. The results of COMPASS tell us that someday we may add a low dose of blood thinner as well. Right now, we don’t know if these benefits extend to other blood thinners in the same class, including apixaban, dabigatran, betrixaban, or edoxaban. We also don’t know if patients already on one of these drugs would benefit from the addition of a baby aspirin. Patients with a history of blood clots, including deep vein thromboses or pulmonary emboli, are usually on higher doses of these oral blood thinners. More studies will need to be done to know if there is a benefit for this group of patients.

WHAT HAPPENS NOW?

The dose of rivaroxaban used in this trial was much lower than what is commercially available now. The Food and Drug Administration will look at the results of this trial and determine if this is safe to be used in the appropriate patient population. At the same time, experts from around the world who write international guidelines will take a hard look at whether or not our recommendations for patients should change. The results of big trials like this one often take several years before becoming fully incorporated into patient care. Perhaps most importantly, the people who run clinical studies will now ask if there are other combinations of blood thinners and aspirin that should be tested for the same benefits. Stay tuned!

Dr. Aaron Kithcart is a vascular medicine fellow at Brigham and Women’s Hospital in Boston.

PATIENT PERSPECTIVE
Continued from page 2

I find it very easy to say, “Okay, this is just another development that I have to overcome. I’m not going to dwell on it. I’m not going to be more concerned than I need to be because that can have negative effects.”

So, I pretty much tackle all situations, whether it be professional or personal, with, “Alright, let’s solve this problem.”

You know, life’s really good. I have three children, four grandchildren, and a very supportive wife. That makes it a lot easier to really tackle some of these issues.

Bart and Diane connected with Dr. Samuel Goldhaber, president of NATF, and decided to attend NATF’s in-person support group.

Q: What has your experience with NATF’s support group been like?

It was a brand new experience that neither Diane or I had experienced. We just decided that the support group would be something that we could both learn something from. It really enhances Diane’s ability to support me and help me make some of the decisions I need to make.

The support group has supplied education and the opportunity to meet people who have experienced the same type of thing. It turned out to be a group of really sensational individuals that are dealing with this disease. Support group was very encouraging. It reinforced that it wasn’t just me who had this issue. It became very clear that life after DVT/PE is certainly a possibility and a real positive possibility.

The fact that Diane and I have been able to attend the support group and learn from the experiences of other people has really worked well for my situation. I deal with all these incidents with a very positive attitude. I’m not going to let it slow me down. I know coming out on the other side is going to be a very positive result and the support group has really allowed me to listen to people and listen to the doctors. I get a close, first-hand response from the doctors and that feeds into my very optimistic view of how I’m going to live my life.

I think it’s allowed myself and Diane to go forward in a very positive way to overcome this particular diagnosis and this particular disease.

Thank you, Bart, for sharing your experience!

Would you like to share your patient story?
Email info@natfonline.org.

Are you inspired by stories like Bart’s? You can help patients similar to Bart by starting a support group in your community. Join us in the fight against blood clots and email: info@natfonline.org.
Upcoming Events

In-Person Blood Clot Support Group at BWH
Feb. 13 and March 27
All support groups start at 7:00 p.m. and are held at Brigham and Women's Hospital. To register, email Kathryn Mikkelsen at KMikkelsen@NATFonline.org or call 617-730-4120.

Online Blood Clot Support Group
Feb. 27 with Dr. Rachel Rosovsky – The Importance of Follow-Up Care after a Blood Clot
March 19 with Dr. Aaron Kithcart – Lifestyle Changes After a Blood Clot
April 17 with Dr. Alec Schmaier – Treatment Options for PE/DVT: Demystifying the Drugs

NATF's Online Blood Clot Support Group offers patients the opportunity to share common concerns, offer support to one-another, and learn up-to-date and accurate information, including new research on blood clot prevention and treatments. Dates and speakers for our upcoming meetings can be found at www.natfonline.org/patients/supportgroups. To register for this online support group, please email info@natfonline.org.

Stopping the VTE Epidemic: An Innovative, Cutting Edge, and State-of-the-Art Action Plan
April 19 – Philadelphia, PA; April 27 – Detroit, MI
NATF will be hosting a series of free programs, designed for medical professionals, that will center on protecting medically ill patients across the United States from VTE. Doctors, nurses, pharmacists, and other healthcare providers are invited to join us for the opportunity to earn CME credits and learn about the latest in VTE treatment and prevention. These events are part of NATF’s ongoing “Avoiding the Avoidable: Pathways for VTE Prevention in the Vulnerable Medically Ill” program series.

Vascular Protection: What Every Patient, Physician, Pharmacist, and Nurse Needs to Know
March 29, 2018
Brigham and Women’s Hospital
45 Francis St. Boston, MA 02115

Join NATF for an exciting new program focused on preventing heart attack, stroke, and leg amputations in patients with coronary artery disease (CAD) and peripheral artery disease (PAD). NATF is inviting patients, physicians, pharmacists, and nurses alike to learn about important updates in vascular protection. Attendees will learn about the intricacies of peripheral artery disease, how to prevent heart attack, stroke, and adverse limb events in patients with atherosclerosis, the important results of the recent COMPASS Trial, and more.

Attendees will have the chance to earn up to 2.25 CME credits.

At the end of this program, attendees will be able to:

• Understand the solid rationale for combined anticoagulation and antiplatelet therapy for clinical application based upon advances in translational science.
• Use combination therapy with low-dose anticoagulation and low-dose aspirin to prevent recurrent cardiovascular events in patients with established coronary artery disease or peripheral artery disease.
• Emphasize that carotid atherosclerosis plays a major role in the burden of peripheral artery disease. Secondary prevention with dual antiplatelet therapy and anticoagulation can markedly decrease the risk of stroke.

For information on how to register, please visit: www.regonline.com/vascpro

For more information on any of these events, please email events@natfonline.org. We look forward to hearing from you!