

**Anticoagulation in Obese Patients:  
Applied Clinical Practices in the Non-specialist Setting**



**Rachel Rosovsky:** Hello. My name is Rachel Rosovsky. I'm a hematologist at Massachusetts General Hospital, and I am thrilled to moderate this second webinar with two of my colleagues, Stephan Moll and Bishoy. I will have them introduce themselves in a minute. This is *Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting*.

## Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting

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**Rachel:** This is the second of two webinars, and I encourage you to listen to the first one if you haven't already. We're going to be using first names. Stephan, if you want to introduce yourself, tell us where you're from.

**Stephan Moll:** Yes, thank you, Rachel. I'm Stephan Moll. I'm an adult hematologist. I do mostly coagulation thrombosis, but other benign hematology, and I'm at the University of North Carolina in Chapel Hill.

**Rachel:** Wonderful. Great to have you. Bishoy?

**Bishoy Ragheb:** Yes, thank you, Rachel. I'm Bishoy Ragheb. I'm a Clinical Pharmacist practitioner at the Eastern Colorado VA Healthcare System.

**Rachel:** Wonderful.

## Learning Objectives

- Summarize the role of DVT prophylaxis in obese patients with and without a history of VTE
- Outline issues of obesity, VTE, and DOAC use in special populations, including considerations for heavy menstrual bleeding, renal issues and bariatric surgery
- Apply strategies for patient education and engagement that support improved medication adherence and outcomes

**Rachel:** Our objectives today are going to be discussing the role of DVT prophylaxis in obese patients with and without a history of VTE. Then the second part is going to explore issues of obesity, venous thromboembolism, and direct oral anticoagulant use in special populations. Those will include patients with heavy menses, diabetes, and renal issues, and bariatric surgery.

Just to remind you, the first one focused on obesity as a major healthcare crisis. VTE is a major cause of morbidity and mortality worldwide, but we really identified the impact of obesity on VTE pathophysiology. We've reviewed DOAC absorption and distribution and metabolism. We explored anticoagulation management strategies for obese patients.

## Case Presentation: DVT Prophylaxis

- Patient, 48 years old
- BMI 48
- Developed DVT after major orthopedic surgery
- Treated on DOAC for 3 months

**Rachel:** We're thrilled to have this one, and I'm going to start with a case. This is a 48-year-old woman who unfortunately developed a DVT after undergoing major orthopedic surgery. She was treated with a direct oral anticoagulant for three months, and as we know, based on our first webinar, that having a BMI of 48 does not preclude her from being on a direct oral anticoagulant for the treatment of her DVT. She has completed therapy, and remember, this is a major transient risk factor.

The question is now she's going to be stopping her direct oral anticoagulant. Stephan, I'm wondering, could you talk us through and talk to us about what the role of perhaps having her on 81 milligrams of aspirin for a kind of secondary prevention. Is there any data about this?

**Stephan:** Well, first of all, I would not do that. She's been treated with three months of full dose anticoagulation, and that's appropriate for major surgery-associated clot. Yes, she is at somewhat higher risk for clots in the future, particularly with transient risk factors. In general, we know that aspirin is ONLY a little bit effective in the secondary DVT prevention, and there have been two New England Journal of Medicine articles on how aspirin does not have very much effect in preventing VTE.

If there's any indication, or if there's high enough risk for a future clot, one would decide to have a patient on anticoagulation rather than aspirin. In this patient, he essentially had a major risk factor, I would stop after three months and not put on aspirin. The question then comes up, in what situations in the future should she be on DVT prophylaxis?

**Rachel:** Exactly.

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**Stephan:** Often there's no good data for the daily things like long-term travel by car, anything more than six hours or airline travel more than six hours. Yes, she will be at a higher risk for clots, however, is it high enough that you would use some anticoagulation prophylaxis? Maybe I would since she is obese and may be cramped in airline seat. What I typically think is anything more than six hours uninterrupted flight, maybe it's worthwhile to take one pill of a DOAC, one to two hours before flights, and maybe one to two hours before long distance travel more than six hours. That's a very individualized decision. They just take one pill before, and then on return travel, do the same thing.

**Rachel:** Well, thank you for sharing that. I think long travel is a question that comes up a lot. Again, because she's had a major transient risk factor, it makes sense that anytime she's perhaps in another situation, which places her at increased risk of clotting, such as long travel, it makes sense to put her on a low dose prophylactic anticoagulant.

Bishoy, can you talk us through what other situations you think she would need to be placed on DVT prophylaxis? What other situations have you come across, or what other situations would you recommend, for example, primary care doctors think about putting her back on DVT prophylaxis? If you can just let us know what your thoughts are about the dose. Should she be on a therapeutic dose, prophylactic dose is enough, especially given her BMI of 48?

**Bishoy:** Yes, sure. With regards to travel, I would agree that the issue with travel, we're talking about a single-dose anticoagulant for that. While there isn't much evidence one way or the other, typically travel isn't considered a very high risk. And I would tell my patients, if it was, I would have just stopped working where I'm working and would have set up shop at a major international airport and would have retired by now. But on the flip side, we're really just talking about a single dose. The risks of that single dose are very, very low. If it provides ease and comfort for the patient, that's fine.

**Bishoy:** The other thing for primary care providers and clinicians to think about is if the patient undergoes any other type of surgery that would place them again at a high risk for a clot.

Ensuring that she is communicating this to her surgeons and proceduralists that she's had a previous provoked clot by surgery before, this ensures that the necessary steps are taken care.

If she's a young patient and she ever gets put on birth control or something, it could be considered at that point but anything, again, that would increase the risk, we take all those factors in together thinking is prophylaxis necessary at that point?

**Rachel:** I think it's very important for her to let her providers know. I think that's a key message. I also think it's important for providers to ask patients, "Have you ever had a blood clot in the past?"

When you're thinking about if she needs surgery again. God forbids, she breaks a leg and needs to be in a cast, she's hospitalized. I think it's interesting. You do mention if she's going to be placed on oral contraceptives or becomes pregnant, is this someone you would feel okay being placed on oral contraceptives, given that she's had a blood clot already after major orthopedic surgery?

**Bishoy:** Probably not, but again, if it comes up in the sense that that was the only option that the patient had, that's again where it would come up, but it would be discouraged initially from that offset.

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**Rachel:** Okay. Stephan, what about you?

**Stephan:** Well, two points. Number one, whenever the patient, obese or not, stops anticoagulation after being treated with three or six months or what have you.

I always tell the patients, "Whenever you have surgery in the future, whatever surgery, tell your surgeon I've had a DVT or PE, should I get DVT prophylaxis?" How long they should get DVT prophylaxis depends on the degree of surgery. If it's major surgery, you may go up for six weeks. If it's a minor surgery, you may go for two weeks, maybe one week, or maybe not even at all.

The fact that they are severely obese, BMI of about 40 or weight more than 120 kilos, is probably another reason to think you had a DVT, plus you're obese, maybe we should be a little more aggressive with DVT prophylaxis in the future.

Yes, the ISTH guidance document, International Society on Thrombosis Hemostasis Publication from 2021 that summarized what's been known about DOAC dosing, states that the appropriate DVT prophylaxis dose is the prophylactic dose as approved for other people as well. You do not have to increase the dose.

The second thing, Rachel, I would like to add, even though that's obesity independent but you brought it up, is the birth control issues.

I would clearly state somebody with a DVT & PE in the past should not be on estrogen-containing combination pills, but I do make a strong point that the progestin-only CONTRACEPTIVES, particularly the IUDs, are safe from a thrombosis point of view. It also includes the Nexplanon rod, the implantable rods. Those are really good choices.

**Rachel:** Thank you. I completely agree. If someone's had a DVT in the past, I would be very reluctant to put them on estrogen-containing contraception. Again, the progestin-only ones. I would caution against the Depo-Provera because it has an increased risk of clotting.

Although that is progestin-only, I would not advise that one. I have had patients that have PCOS, polycystic ovarian syndrome, and have to be on estrogen. In those situations, I will often put them on a low-dose anticoagulant just because I feel like that risk is so high.

Again, Bishoy, going back to your statement, really having that discussion with the patient, shared decision-making, exploring their values, really laying out what those risk factors are.

That was a great discussion. Thank you both so much.

We're going to pivot, and now we're going to explore issues of obesity, venous thromboembolism, and DOAC use in special populations.

I'm not so sure I would call this a special population, but a potential complication that comes from placing patients on anticoagulants.

## Case Presentation: Heavy Menses

- 42-year-old woman
- BMI 52
- PE with no underlying cause
- Long-term, full-dose anticoagulation
- Presents with heavy menstrual bleeding (HMB), causing her to miss 1 – 2 days/cycle
  - Began shortly after initiation of DOAC therapy

**Rachel:** This is a 42-year-old woman. She has a BMI of 52. She developed sudden shortness of breath and workup revealed a severe pulmonary embolism. There is no underlying cause identified, and she was started on a direct oral anticoagulant, which, as we know, is safe in patients with any BMI.

Because we couldn't identify a cause, she will need to remain on long-term anticoagulation. She's on full dose. Again, as discussed in our last webinar and based on the ISTH guidelines, patients with a BMI greater than 40 or weight greater than 120 should remain on full dose.

She presents to you complaining of heavy menses, and they're so heavy that she actually has to miss one or two days of work for each cycle because of that.

She does tell you that she started having this and experiencing these very heavy menses right after starting her direct oral anticoagulant.

**Rachel:** My first question to both of you is, how common is this? Do you see this a lot in your own practice? Bishop, is it 50% of people, 100% of people? How common do you see this?

**Bishop:** Working at the VA, we have predominantly male population. We don't encounter this too much. However, in terms of the general population, unfortunately, it is a very common issue that occurs. The numbers are up to 70% of patients or women who are on anticoagulation will experience heavy menstrual bleeding while on anticoagulation.

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**Bishoy:** It's even so prevalent or so prominent that between the bleed rates between men and women with VTE, women have much higher. But when you take away and account for the uterine bleeding, those bleed rates then fall in line with each other and there's almost no difference between men and women. It's a major driver in bleeding with women. With DOACs, I think in the pivotal trials, we saw anywhere between 5% to 10% of women experienced the heavy menses. It's common, unfortunately.

**Rachel:** I always advise my patients and say, "Look, you're going to expect an increase in your menses." I'm wondering Stephan, when you talk to patients and you know that they're menstruating and they're about to start DOAC, what do you tell them? Do you say, "Hey, you may experience a 5% to 10% increase, and don't worry about that." At what point do you tell them "you need to alert me to what's going on?" What's the threshold?

**Stephan:** Well, I don't give percentages. I just tell them, "Your menstrual bleeds may well increase in intensity and length, or they may not change." Typically, they don't turn to me as a hematologist, initially. It may go through the primary care physician first, but then I hear about it at some point. We can talk about treatment options because there's certainly a number of treatment options that should be applied relatively early and not have the woman suffer through this too long.

**Rachel:** Yes. I would mention one other thing before we go into how to treat. Just in terms of workup, and you mentioned this, that oftentimes people will present to their Ob/Gyn. I think it is important to explore whether or not they have something underlying that they've unmasked. For example, a fibroid. I always encourage my patients to think about that.

If they've had a mild increase in the number of days or the degree of bleeding, I usually don't. But if it has been a significant amount, I want to make sure there's not something underlying that's been unmasked by the anticoagulation. How we should treat it seems that there's a lot of different options.

Stephan, if you could talk us through how you approach your patient that presents with increase in heavy menses after starting a DOAC?



## Heavy Menstrual Bleeding on Anticoagulants

### Management options

- Gyn evaluation
- Switch to apixaban
- Dose reduce DOAC
- Interrupt anticoagulation at time of menstrual bleed

Godin R, Marcoux V, Tagalakis V. *Vascul Pharmacol*. 2017 Aug;93-95:1-5. doi: 10.1016/j.vph.2017.05.001. Epub 2017 May 4. PMID: 28479313.

**Stephan:** I fully agree with you, Rachel. The first thought is, is there something morphologically going on and atomically that gynecology should address? One doesn't assume it's just the anticoagulant. It could be a polyp, it could be early malignancy fibroid.

So, gynecology evaluation first, but then from a hematology point of view, it depends on what anticoagulant the patient is on. One could certainly think about switching anticoagulants.

And there's some data, even though not absolutely solid, but to suggest that maybe menstrual bleed is more with rivaroxaban than with apixaban.

If the patient is on rivaroxaban, my next step would be to switch to apixaban.

The other thought is to dose reduce the DOAC. Now, that wouldn't be in the first three months after the acute DVT or PE, but once we are beyond the acute setting, dose reduction is certainly something one could consider.

I feel comfortable in the non-severely obese patient, but even in the severely obese patient, if menstrual bleeding is such heavy, that would be a consideration.

Then sometimes, again, not in the acute setting, but after three, six months of treatment, interrupting the anticoagulation for two or three days at the times of the severe bleeding is something to consider even though it's not typically my first main go-to thing.

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### Management options

- Gyn evaluation
  - Switch to apixaban
  - Dose reduce DOAC
  - Interrupt anticoagulation at time of menstrual bleed
- Progestin IUD (progestin implant)
- Endometrial ablation
- Oral contraceptive pills (OCPs)
- Tranexamic acid po

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**Stephan:** Really important is to offer or to discuss with the patient the progestin IUD which may be a really good way to deal with the menstrual bleeds, so they need to discuss it with gynecologist.

If they're done with having children, endometrial ablation. While not 100% successful, and I don't know what the gynecologist would scientifically quote, even though the data I've seen is it's effective in about two-thirds of patients will decrease the bleeding.

Now, every so often, but that's not common, if the bleeding is significant and these interventions didn't help one could consider estrogen-progestin combination pill, but at that time, I would want to make sure that the patient is on full dose anticoagulation because we're treating for DVT and PE.

Then, as a non-hormonal or non-gynecological intervention, tranexamic acid, which as hematologist we know from people with bleeding disorders is quite effective in decreasing menstrual bleeds. That's really a nice thing to offer to the woman as well, to take that orally at the times of the menstrual bleeds, either just in the first few heavy days or for the whole menstrual bleeds and that may be very successful.

**Rachel:** Thank you for really walking us through that. I just want to comment one thing about the dose reduction that you would dose reduce during the heaviest days and then go back up because, again, the ISTH guidelines do not recommend dose-reducing obese patients with VTE on long-term anticoagulation.

But in this, once a month for that two to three days that they have very heavy periods, dose reducing. Again, the interruption is just for those two to three days, they then would go back to the full dose.

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**Stephan:** Well, Rachel, the ISTH guidance document does not take a reference and does not say you should not dose reduce in the severe obese patients. The data are such that we don't know whether you can safely dose reduce. The EINSTEIN CHOICE Trial for rivaroxaban, and then the AMPLIFY EXTENSION for apixaban showed you can safely and effectively dose reduce in the patient population studied, which was mostly non-obese, that can be done after the initial six months of full dose.

Maybe that could be done in severely obese patients, but we don't know. My tendency and the tendency for many hematology colleagues is not to dose reduce in the severely obese patients, but if the patient has significant issues with bleeding, then you will highlight-- well, we don't know scientifically. Maybe it is okay to dose reduce and it could certainly be considered.

**Rachel:** Thank you for clarifying that. Yes, something to talk to your patient about. We just don't have the safety and efficacy data like we do for non-obese patients.

**Stephan:** Right.

**Rachel:** Bishoy, can you talk a little bit more about the tranexamic acid? I've had some colleagues say to me, "Won't that increase the risk of clotting?" What's the data behind that? Is that something we need to worry about?

**Bishoy:** Yes, actually, if you look at the prescribing information, it's a contraindication because the patients had a previous clot. Really, that's more so theoretical. The studies that looked at patients who are at high risk VTE actually failed to demonstrate an increased risk of VTE in those patients.

**Bishoy:** Now, they didn't have a clot in the past, granted that. Currently, there's been no trials looking at patients who have had a clot on anticoagulation and use tranexamic acid. There were a few patients in the Einstein trials that reported use, but again, it was very, very minimal. There is one trial that's currently being conducted, I believe, in the Netherlands that's going to look at a subgroup of patients that are looking at that as well.

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Hopefully, we'll have some answers, but actually now, it's a recommendation to use tranexamic acid during that period, just the period during the heavy menses. One thing to consider as well is not to use it during the first month or during the very high acute treatment phase, and to avoid it during that time because the fibrinolysis process is going to be very important.

**Rachel:** I have another question for both of you, not necessarily this case, but let's say there was a patient that developed a blood clot on oral contraceptives, and you were starting her on direct oral anticoagulant. Would you stop her oral contraceptives, or would you have her stay on it? Let's say she was on it because of a history of heavy menses?

**Stephan:** Good question. In general, the tendency is to stop it because it is prothrombotic. However, the patient will be on anticoagulation, so it is mostly protected from clots, so maybe it's okay to stay on estrogens, and if the patient was on the estrogen pill because of heavy bleeds, even without anticoagulation, you probably expect that she will bleed even more so if you take the pill off and if she's on anticoagulation. It is an option and that's discussed in the literature. It's a reasonable option to continue the estrogen pill and see how things go. I would feel comfortable with that because she is on full-dose anticoagulation.

**Rachel:** Yes, and I would too, and I will say that our European colleagues do that all the time. I think in the US we are a little hesitant, although I think practice is changing especially for what you just said. It's that the patient, if she stopped it even without her having been on anticoagulant and she was on it for heavy menses, that's going to come back. Now you've had an anticoagulant and she's going to be on full-dose anticoagulation, so that will hopefully protect her. Bishoy, any comments about that?

**Bishoy:** No, I absolutely 100% agree. Now they have the protection. Now, again, risks and benefits here would typically favor continuing now that they have the anticoagulant.

**Rachel:** Yes, that was a great discussion.

## Case Presentation: Diabetes with Poor Renal Function

- Patient with diabetes mellitus (DM)
- BMI 48
- Creatinine 2.5
- Recently diagnosed with pulmonary embolism (PE)

**Rachel:** I'm going to change to a second situation. This is a patient with diabetes, has a BMI of 48. They've just been diagnosed with a pulmonary embolism, but they have a creatinine of 2.5, so Bishoy, my first question is what is the best way to assess renal function? Do we use creatinine clearance? Do we use GFR? Do we just use creatinine? How do you think about that?

**Bishoy:** Yes, so just for the sake of time, everything that has been discussed about the use of assessing renal function revolves around using creatinine clearance and using actual body weight, Cockcroft-Gault equation. The GFR, while it's typically used, isn't what was done in the trial, so evidence-based would be using creatinine clearance, actual body weight.

Unfortunately, in obese patients, what that can tend to do is it could possibly overestimate the creatinine clearance. That would just need to be taken into consideration. What do you do if that becomes the case? There's really no evidence. Probably the cleanest way or the easiest approach is just to use apixaban and avoid all of the renal issues at that point if possible.

## Apixaban and Renal Function

- Apixaban recommended in cases of poor renal function
  - Lowest rate of renal clearance of all DOACs
  - Data in end-stage renal disease
  - Most experience in patients with renal disease

Jones A, Swan D, Lisman T, et al. *J Thromb Haemost*. 2023 Sep 29;S1538-7836(23)00722-5. doi: 10.1016/j.jtha.2023.09.020. Epub ahead of print. PMID: 37778512.

**Rachel:** Can you just talk us through why you would choose apixaban versus a different DOAC?

**Bishoy:** Sure, apixaban is the least renally cleared, so therefore, it's going to be less impacted by all of the renal issues. It has data in end-stage renal disease hemodialysis patients, so it's the one at least with the most current field experience in those patients.

**Rachel:** Okay, and if she has a creatinine clearance of 2.5, 3.5, whatever, would you ever consider dose reducing? Now remember this is an obese patient, creatinine clearance of 2.5 or 3.5, what's the data behind dose reducing in patients with VTE?

**Bishoy:** Yes, so overall, if the patient meets the criteria for the dose reduction per AMPLIFY-EXT, it's within the consideration.

Just as Stephan pointed out in the ISTH guidance, I mean there's no evidence to suggest against it nor support it. But now if the creatinine clearance does go up, it may be worth a consideration at this point and then again, they're part of the shared decision-making process.

**Rachel:** Okay. Stephan, I'm going to ask you the same question. Do you dose reduce if patients are in renal failure, and is there a creatinine level at which point you would not recommend a DOAC?

**Stephan:** The first answer is the same that we just heard from Bishoy. The apixaban is a go-to drug in significant renal impairment, and I don't have a problem using it independent of the GFR. As discussed, it's been used in end stage renal disease and hemodialysis patients. In the severely obese patient, BMI above 40, weight above 120 kilos, I would tend to use full dose, and even long-term, I would not dose-reduce unless there's some bleeding issue.

It's the very light patient, the elderly patient, high-risk for bleeding who has significant renal impairment. There, I would dose-reduce for the DVT treatment, but in the obese patient, I would tend to use the full dose.

## DOAC Dose Reductions with AFib

- For patients with renal failure or renal issues who are prescribed DOACs for Afib, DOAC dose reduction should occur when 2 of the following 3 criteria are met
  - Creatinine clearance  $\geq 1.5$
  - Age  $\geq 80$
  - Weight  $\leq 60$

**Recommendations DO NOT APPLY to DOACs for VTE**

Agnelli G, Buller HR, Cohen A, et al. *N Engl J Med*. 2013 Feb 21;368(8):699-708. doi: 10.1056/NEJMoa1207541. Epub 2012 Dec 8. PMID: 23216615.

**Rachel:** I think there's some confusion. Bishoy, if you can shed some light on this. If you look at the package insert, it's different in terms of dose reduction for renal failure or renal issues if you're using a DOAC for AFib. Can you just briefly mention that?

**Bishoy:** Sure.

**Rachel:** Because I think there's a lot of confusion with that.

**Bishoy:** Yes. For AFib specifically, it's three dose reduction criteria, which is creatinine clearance greater than or equal to 1.5. Age, equal to greater than 80, or a kilogram of equal to or less than 60. If you meet two of those three criteria, you dose reduce for AFib. VTE however does not apply. Those three don't apply. The dose reduction is mainly based off of the Amplify Extend, which is you've been treated for six months, you're now at clinical equipoise, and then taking it a step further with ISTH guidance, specifically with obese patients, whether or not we dose reduce and creatinine clearance. That doesn't really apply or factor into that.

**Rachel:** Yes. Thank you for clarifying that because that does come up a lot.

## Case Presentation: Bariatric Surgery

- 38-year-old man
- BMI 50
- Long-term anticoagulation for unprovoked PE
- Considering bariatric surgery or weight loss drugs

**Rachel:** We're going to go to the next case. This is a gentleman who is 38 years old. He has a BMI of 50, and he's on long-term anticoagulation for unprovoked PE, and he comes to you to discuss bariatric surgery versus weight loss medications.

Bishoy, my first question is are there any drug interactions with these new weight loss medications?



## New Generation Weight Loss Medications

	Semaglutide	Tirzepatide
CYP	No effect	No effect
Pgp	No effect	No effect

- Delayed Gastric Emptying (minor)
  - Reduced drug absorption?
- Nausea/Vomiting
  - Especially during initiation → Missed doses
- Reduced Appetite
  - Rivaroxaban precaution
  - Dehydration → AKI

Semaglutide injection package insert. Accessed online January 16, 2024 at <https://www.ozempic.com/prescribing-information.html>. Tirzepatide injection package insert. Accessed January 16, 2024 at <https://uspl.lilly.com/mounjaro/mounjaro.html#pi>. Frías JP, Davies MJ, Rosenstock J, et al. *N Engl J Med*. 2021 Aug 5;385(6):503-515. doi: 10.1056/NEJMoa2107519. Epub 2021 Jun 25. PMID: 34170647.

**Bishoy:** Yes. The two that are on the market now, that have been released and FDA approved are semaglutide and tirzepatide. To date, there's nothing to suggest that there's an actual significant drug interaction between the two, since there's really no SIP or PGP interactions from that front, but just a couple things to keep in mind as again we're thinking about the big picture.

These medications do cause a little bit of delayed gastric emptying, which could possibly reduce absorption, but again, there's no data to suggest it's anywhere near clinical significance, but just something to keep in mind.

These drugs are associated with nausea, vomiting, especially during initiation. Just be sure that if the patient does experience that, that they're reporting it because then if the patient starts vomiting because they're unable to hold anything down, then they could be missing doses. If it's significant, then we need to be aware.

Then the last thing is reduced appetite. These medications do suppress the appetite fairly significantly. This would be a precaution for rivaroxaban, for the food requirements for the 15 milligrams and the 20 milligram rivaroxaban.

The last thing is dehydration. We have seen some reports of dehydration resulting in acute kidney injury because again, people just stop drinking water. It's not on their minds anymore. Just something to keep in mind. Again, if folks are using apixaban, shouldn't be an issue from using the drug, but again, just from a precautionary standpoint of acute kidney injury and renal function to keep that in mind.

**Rachel:** Yes. So really important if these patients are coming to their primary care doctors and want to start one of these weight loss medications, that they really highlight those issues that you mentioned, especially the hydration, and the appetite.

## Post-operative Considerations and DOACs

- ISTH Guidelines advise heparin followed by transition to DOAC
- Consider site of DOAC absorption and impact of bariatric surgery
- Consider impact of small meals on rivaroxaban administration
- Apixaban preferred

Martin KA, Beyer-Westendorf J, Davidson BL, et al. *J Thromb Haemost*. 2021 Aug;19(8):1874-1882. doi: 10.1111/jth.15358. Epub 2021 Jul 14. PMID: 34259389.

**Rachel:** I think you highlight the ISTH guidance, which does say post-op patients should not immediately go back on a DOAC but heparin, and then you very eloquently described, where the DOACs are absorbed and which ones. It sounds like it really doesn't matter which kind of surgery he has. Whether it's a Roux-en-Y or a sleeve gastrectomy because it sounds like rivaroxaban is absorbed both in the stomach and farther down in the GI tract. But if you're going to have any kind of surgery, because the apixaban site of absorption is farther down, it makes more sense to start on that one regardless of the surgery. Bishoy, I'm wondering what your thoughts are.

**Bishoy:** Yes, and actually I speak as a bariatric surgery patient myself. [chuckles] The apixaban would be the go-to here. The meal size is a huge, huge issue, especially initially as patients get used to it. Sticking with the apixaban and seeing how that works. The trough level is something to consider as we mentioned previously. However, if that trough level does come back outside of the range, it doesn't mean that we are supposed to adjust the dose of the DOAC and increase it because the trough levels are off. It should just be used as something to say, "Okay, you're out of the expected levels. Do we want to continue this or switch it to something else more conventional like warfarin going forward?"

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**Rachel:** Both of you are on the expert panel that we recently published, and this was one of the questions we asked people. When do you check peak, when do you check trough, and what do you do about it? It sounds like, first of all, do both of you check a trough level in all of your bariatric patients. Yes or no? Stephan, do you?

**Stephan:** My volume is not that huge, but I do see two or three patients per year where this comes up and I tend to do a trough level. Yes.

A peak level would not be meaningful because typically with bariatric surgery, the peak is reached after DOAC intake; 2, 3, 4 hours after intake. There's quite a bit inter-individual variation, but the trough level is always before the next dose. The trough level, you really know what you're dealing with. Peak level, not meaningful. Trough level, yes.

**Bishoy:** We haven't had the capability to draw it at our facility. We are actually in the next month going to have that. Again, keeping in mind that these drugs have a very wide therapeutic margin, so it's not necessary, but it would be ideal. I think the wording would be it makes us sleep better at night knowing it's within the range, but if you can't, it shouldn't completely deter us, but it's nice knowing it for data purposes and having it with us.

**Rachel:** This patient decides to actually have the bariatric surgery. My first question, Stephan, if you can walk us through, there's a lot of different options and, in particular, I think it's important to look at those because we talked in the first webinar about absorption, metabolism, excretion and all of that with these DOACs. If you can just first talk us through, what are those different options?

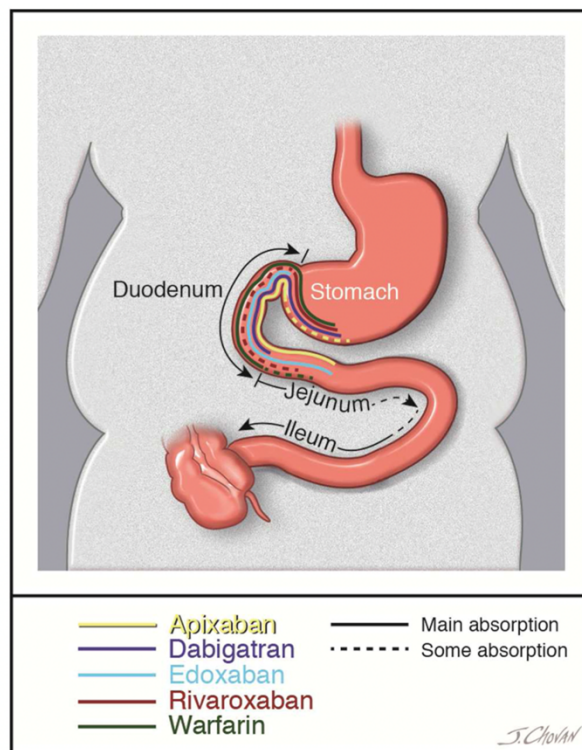
## Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting

### Location of Absorption of Anticoagulants

DOACs primarily absorbed in the  
PROXIMAL SMALL INTESTINE

- Rivaroxaban also absorbed in the distal stomach (can be influenced by surgery)
- Apixaban also absorbed in distal small intestine (not influenced by surgery)

Martin KA, Lee CR, Farrell TM, Moll S. *Am J Med.* 2017 May;130(5):517-524.  
doi: 10.1016/j.amjmed.2016.12.033. Epub 2017 Feb 1. PMID: 28159600; PMCID: PMC5401640.

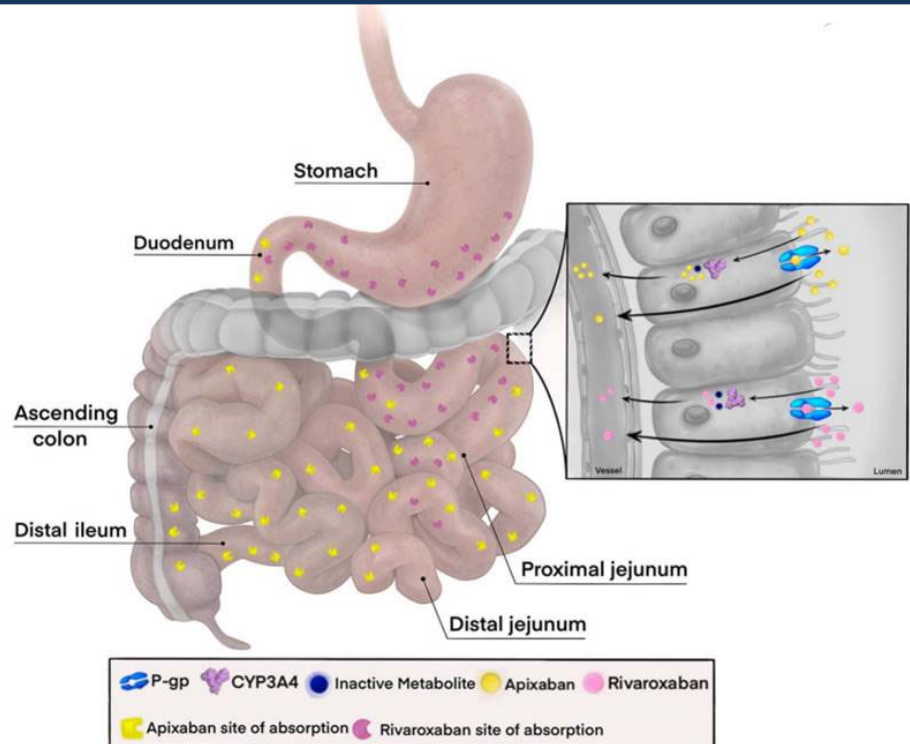


**Stephan:** Obviously, as a hematologist, we don't make that decision. We send them to the bariatric surgery clinic, and they decide what would be the appropriate one. We've all heard about the Roux-en-Y, the sleeve gastrectomy, the gastric banding, and there's a duodenal switch surgery.

From a DOAC point of view and hematology point of view, or primary care physician for that matter, it doesn't really matter. What's important to know is where the anticoagulants are absorbed. They're all absorbed in the more proximal small intestine, particularly rivaroxaban that's also absorbed in the distal stomach.

## Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting

### Location of Absorption of Anticoagulants



Hakeam HA, Alkhani M, Alyahya Z, et al. *J Cardiovasc Pharmacol.* 2021 Dec 1;78(6):867-874. doi: 10.1097/FJC.0000000000001142. PMID: 34882113.

**Stephan:** Rivaroxaban is not a great choice with any of these procedures because it's influenced, because part of the stomach is cut away or bypassed. The transit time is different.

The important part to know is apixaban is also absorbed in the more distal small intestine, which is not influenced by these procedures. Apixaban is really, if one uses a DOAC, the go-to drug in patients after bariatric surgery. However, in the acute setting after the surgery, the DOACs are not absorbed very well. There's a lot of change there. Not just the absorption surface. I mentioned the transit time, the meal size, the weight changes.

## Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting

### Peri-operative Management

Direct Oral Anticoagulant	Procedure Bleeding Risk	Pre-Procedure DOAC Interruption						Surgery/Procedure (Day 0)	Post-Procedure Resumption*			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4
Apixaban	High											
	Low/Mod											
Dabigatran (CrCl ≥ 50 ml/min)	High											
	Low/Mod											
Dabigatran (CrCl < 50 ml/min)	High											
	Low/Mod											
Edoxaban	High											
	Low/Mod											
Rivaroxaban	High											
	Low/Mod											

 No DOAC administered that day

\*DOAC can be resumed ~24 hours after low/moderate-bleed-risk procedures, and 48-72 hours after high-bleed-risk procedures. In selected patients at high risk for VTE, low-dose anticoagulants (i.e., enoxaparin, 40 mg daily or dalteparin, 5,000 IU daily) can be given for the first 48-72 hours post-procedure.

Martin KA, Beyer-Westendorf J, Davidson BL, et al. *J Thromb Haemost*. 2021 Aug;19(8):1874-1882. doi: 10.1111/jth.15358. Epub 2021 Jul 14. PMID: 34259389.

**Stephan:** The ISTH guidance documents suggests appropriately, for the first few weeks, to use a parenteral anticoagulant because there you have at least somewhat reliable anticoagulation uptake into the bloodstream and not use the DOACs. After a few weeks, once the patient has more adjusted to the surgery, then one can consider DOAC and then in that case, apixaban would be the best choice given where it's absorbed. But, since you still don't know how well is it absorbed, is there less absorption, the ISTH guidance document suggests that it may be worthwhile to consider the trough DOAC level, i.e. just before the next dose is to due, so that one is clear. Is one roughly in the expected range? Is this patient absorbing the apixaban well?

**Rachel:** Yes, and I think that's a good point that you both made in both in the last webinar and this one is that even if you get it and it's not within range, it's hard to know what to do with that information and you can't really make up a new dose for your patients then when you have a conversation of whether you're going to switch them to something else or you're going to keep them on that. Stephan, you want to comment about that?

**Stephan:** Rachel, I also want to include rivaroxaban is not the wrong drug to use after bariatric surgery. A number of patients are on rivaroxaban for various reasons. The once daily is advantageous, cost issues maybe. So it's not wrong, but again, in those patients, I also would do a trough level to know where we are.

**Rachel:** The person undergoes surgery, they're put on a direct oral anticoagulant and Bishop, they come to you two months after the surgery, and you ask how things are going and they say they're taking it only a few times a week. How do you address that?

Really discussing the importance of why they need to be on it and then thinking about maybe what's behind them not taking it, barriers to taking medications, and then strategies for talking to patients about how to be on it.

## Thoughtful Strategies for Patient Engagement & Education

### Addressing poor adherence:

- Reframe conversation about risks of drug discontinuation or intermittent dosing
- Emphasize that "feeling fine" does not reflect risk
- Educate patients about recurrent VTE

**Bishoy:** Yes, it's a very good question and I think sometimes, as clinicians, we might take for granted the information and the risks that are associated with not taking a medication. A lot of patients may not be aware, so we try to reframe the discussion and reframe it in a way of, "If you don't take it, here are your risks for not taking it." A lot of times what we'll hear is the patient says, "Well, I've been off of it for a month and I feel fine." I believe just because of the environment that we're in, we usually are treating things and we feel better.

This is more preventative and explaining to the patient we are preventing a blood clot from occurring, so it's good that you're not feeling anything, and we want to keep it that way. Explaining the risks of recurrent VTE with patients and having them see the big picture so they can appropriately make that decision whether or not to take, it should encourage them. If there are issues with obviously just forgetting to take it, pill reminders, pill boxes, alarms, and those types of things can be implemented.

If it's a cost issue, whether it be copays, there are patient assistance programs that can be used. Side effects and those types of things. Again, drilling down exactly as to why we're not taking it. Is it just a lack of information or what it might be? Then we drill down to the bottom of that and make sure we address it for them.

**Rachel:** Yes, and I think what you mentioned is really explaining the importance of being on this. Especially, we know obesity is a huge risk factor for VTE and it can contribute to recurrent blood clots if they've already had one. Especially in people who have an unprovoked blood clot and really talking about that importance and exploring the barriers as to behind their not taking it. Stephan, any comments?

## **Anticoagulation in Obese Patients:**

### **Applied Clinical Practices in the Non-specialist Setting**

**Stephan:** I think Rachel, one of the most important things that I see in clinic is that often patients don't know about the copay cards that exist for these various drugs. If a patient has some insurance, very often the copay cards grip and they can get the drug for \$10 a month. Now, unfortunately, that does not grip if they're uninsured or if they're Medicare, Medicaid, or Tricare. I always ask them what is your copay, and make them aware of the copay cards.

**Rachel:** That's a great point. I just want also to mention it's important to make sure that they're taking the right dose of medication. There was a study that showed if patients were not on the right dose, that there was a several fold higher risk of adverse events, so really making sure people are on the right dose.

I think we talked a little bit about patient engagement and education just a second ago. In the previous video, we do talk about this and to really remind PCPs how important it is to talk to patients about the risk of VTE and obesity. Stephan, in the last video really, walked us through how the more risks you have, the higher risk of you getting a VTE, and then really important that patients know the signs and symptoms of having a blood clot. Bishoy really talked to us about obesity and VTE pathophysiology and why reducing the BMI is so important to decrease that risk.



## Key Resources for PCP

- ISTH 2021 Guidance Document<sup>1</sup>

Access at: [https://www.ithjournal.org/article/S1538-7836\(22\)01848-7/fulltext](https://www.ithjournal.org/article/S1538-7836(22)01848-7/fulltext)

- Resource Center at the Anticoagulation Forum Centers of Excellence<sup>2</sup>

Access at: <https://acforum-excellence.org/Resource-Center/>

- Recent consensus manuscript, DOACs in Obese Patients with VTE: Results of an Expert Consensus Panel<sup>3</sup>

Access at: <https://pubmed.ncbi.nlm.nih.gov/36803697/>

1. Martin KA, Beyer-Westendorf J, Davidson BL, et al. *J Thromb Haemost*. 2021 Aug;19(8):1874-1882. doi: 10.1111/jth.15358. Epub 2021 Jul 14. PMID: 34259389.

2. Centers of Excellence Resource Center. December 2023. Accessed January 18, 2024 at: <https://acforum-excellence.org/Resource-Center/>

3. Rosovsky RP, Kline-Rogers E, Lake L, et al. *Am J Med*. 2023 Jun;136(6):523-533. doi: 10.1016/j.amjmed.2023.01.010. Epub 2023 Feb 16. PMID: 36803697.

**Rachel:** I guess this next part I just want to talk about is where would you recommend primary care doctors find information and guidance when thinking about obesity and VTE both? What we just talked about in the previous webinar and all the things that we talked about today, really what guidance or other sources of recommendations are available? Where can clinicians find them? Stephan, what would you tell providers.

**Stephan:** Well, for me, a key one is the ISTH guidance document from 2021 that lays out with seven or eight points how to consider using the DOACs in the obese patients. That might be a good resource for healthcare providers.

**Rachel:** Bishoy, what about you? Where do you tell providers to go?

**Bishoy:** As a part of the AC forum, you can go to the Centers of Excellence, there's some resources there. We also had our recent consensus manuscript, which also added a little bit to the ISTH guidance from the sense of what were the updated evidence from the ISTH guidance, the release until that manuscript.

**Rachel:** You can find that both Stephan and Bishoy were part of that. It really walks through some of the issues that we've talked about that might not have a straightforward answer in terms of checking peaks and troughs, and decreasing to lower doses, and what you do where the guidance isn't there, when the guidelines don't have the information.

## Dr. Moll's Take-Home Points

### A. In any patient with VTE

1. Patient has a DVT/PE: VTE is **multifactorial** – obesity is one of the risk factors. Identify ALL risk factors: A....., B....., C....
2. How long to treat? Try **Recurrence triangle** (this is independent of obesity)
3. Try **DOAC “Hate Factor”**, talk about cost and copay cards (independent of obesity)

**Rachel:** This has been a great discussion and I just want to review that we spoke about the role of DVT prophylaxis in obese patients and thoughts around that. Then we really explored the majority of this webinar on the issues surrounding obesity, venous thromboembolism, and DOAC use in patients who present with heavy menses, renal failure, and bariatric surgery. I'd like to ask both Bishoy and Stephan for their take-home points. What is the most important point you want people to walk away from this talk?

**Stephan:** Thank you, Rachel. It's been nice to be part of this discussion. My take-home points is pretty simple and it really summarizes what we had in our first program.

Just to highlight that VTE is typically multifactorial. Obesity is only one of the risk factors. In the clinician who sees a patient with DVT & PE, the role is to identify each of the individual risk factors in some a, b, c manner. That one really addresses the various issues and knows was it a provoked or unprovoked VTE.

Secondly, one of the most important questions is how long does a patient need to be treated with anticoagulation. We discussed in our first session the recurrence triangle, and I find that a helpful tool.

Thirdly, some patients hate to be on an anticoagulant, and others love to be on it because it gives them safety. It says that with a DOAC hate factor that we also discussed in our first session.

## Dr. Moll's Take-Home Points

### A. In any patient with VTE

1. Patient has a DVT/PE: VTE is **multifactorial** – obesity is one of the risk factors. Identify ALL risk factors: A....., B....., C.....
2. How long to treat? Try **Recurrence triangle** (this is independent of obesity)
3. Try **DOAC “Hate Factor”**, talk about cost and copay cards (independent of obesity)

### B. In the very obese patient with VTE

4. Use DOAC at full dose up to BMI 55 kg/m<sup>2</sup>; above that make individual decisions
5. I do not lower DOAC dose at 6 months in very heavy patients on long-term anticoagulation
6. Caveat: **bariatric surgery**. Decreased absorption? Consider parenteral anticoagulant after surgery for a few weeks; if DOAC used: I get a trough level.

**Stephan:** Then what we discussed mostly today is if the DOAC is considered, it's fine to use apixaban or rivaroxaban in the very obese patient, i.e. the BMI above 40 or 120 kilos at standard doses.

Now, when it comes to the extremely heavy people, a BMI of 55 or 60, people are a little uncomfortable. What do we do? There are different approaches. It seems reasonable to use a DOAC. Maybe in that patient's worthwhile to get a trough level.

Then I do not lower the dose of the DOACs at six months, as one may do in none of these patients, based on the Amplify Extension EINSTEIN CHOICE trial. I tend to use full dose if they tolerate it well.

Then really there's a lot of caveats about the bariatric surgery and we discussed that today.

## **Dr. Ragheb's Take-Home Points**

- HMB remains challenging in anticoagulated women
- Various options exist for managing HMB
- Apixaban preferred for bariatric surgery patients
- Patients on rivaroxaban should be monitored with trough level assessment
- Utilize SDM when considering dose adjustments

**Rachel:** Thank you, Stephan, for those very wise words. I'm wondering, Bishoy, what is your take-home message for our audience?

**Bishoy:** Specifically for our talk today, and I appreciate, again, allowing me to be a part of this, and then joining you in this conversation.

For our patients who are women who have heavy menses, to understand that this is an issue for our patients who are in anticoagulation. It's good to get a baseline assessment of what their current bleeding looks like, and then when they're on anticoagulation, to alert us to any type of increase.

If the bleeding does increase, at that point, to start exploring and evaluating all the options to ensure that we reduce the bleeding. Whether it be switching DOACs or things like that.

For bariatric surgery patients, those who are put on it, apixaban is most likely the best choice.

While rivaroxaban also may be a choice, but if a trough level is assessed to keep that in mind and not to use that as the driving force behind a dose adjustment, but more so, again, within shared decision making.

## Anticoagulation in Obese Patients: Applied Clinical Practices in the Non-specialist Setting

Thank you.

**Rachel:** This concludes our discussion of special clinical circumstances in the treatment of obese patients with risk of VTE, as well as a discussion of DVT prophylaxis in this population.

I'd like to thank both Stephan and Bishoy, really, for your incredible expertise on this topic, and talking with me today. I'd like to provide our audience for further information on the use of direct oral anticoagulants in obese patients, with and without the many issues that we talked about. Please, look back at our previous video, where we really talked about obesity as a major health crisis, VTE as a major cause of morbidity and mortality, and really the impact of obesity on VTE pathophysiology. Talking about DOACs in this setting, and really exploring lots of different anticoagulation management strategies. As well as how to educate our patients about the key aspects of anticoagulation management.

Again, thank you, everybody, Stephan and Bishoy. Please don't forget to complete your CE evaluation to claim your CE credit. Thank you very much for your attention.