Ordering Practices and Utilization of a Next-Generation Sequencing Panel for Myeloproliferative Neoplasms

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Guest: Dr. Tyler Cooke is a Clinical Pathology resident at Columbia University and New York-Presbyterian Hospital.

Randye Kaye: Hello, and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye. Myeloproliferative neoplasms, or MPNs, are diseases associated with abnormal production of cells from the myeloid lineage that includes white blood cells, red blood cells, and platelets. The three main MPNs are polycythemia vera, essential thrombocythemia, and myelofibrosis. The standard of care for the diagnosis and prognosis of these diseases is molecular testing for driver mutations, like *JAK2*, *CALR*, and *MPL*. However, even though this testing is standard of care, the reimbursement denial rate can be high.

The May 2026 issue of *JALM* features a research article investigating the reimbursement denial rate for these molecular tests for MPNs. The researchers took a deep dive into MPN panel orders at their institution over the entirety of 2023 to identify any areas for better laboratory stewardship. Today, we are joined by the article's lead author, Dr. Tyler Cooke. Dr. Cooke is a clinical pathology resident at Columbia University and New York Presbyterian Hospital. He will be pursuing a molecular genetic pathology fellowship next year and is interested in molecular pathology, quality, and lab operations. Welcome, Dr. Cooke. First, can you give a brief overview of why molecular testing for *JAK2*, *CALR*, and *MPL* mutations is standard of care in the workup of myeloproliferative neoplasms? And what prompted your team to investigate how this testing was being ordered?

Tyler Cooke: Sure. So for the three myeloproliferative neoplasms, or MPNs, that we looked at in this paper, polycythemia vera, essential thrombocythemia, and primary myelofibrosis *JAK2*, *CALR*, and *MPL* mutations are the driver mutations that cause the disease and then cause the progression of them. And so one of the reasons that we test for these mutations in these genes is that it's in the diagnostic criteria for the WHO, the ICC, and then also in the NCCN guidelines. Some institutions will do this testing sequentially since *JAK2* is the most commonly mutated gene. They'll start with that gene and then move on to *CALR* and *MPL* if it's negative. What we do at our institution is a 15-gene NGS panel that looks at those

three as well as some other genes that are implicated in prognosis. That's kind of how we do it at our institution. The reason that we were looking at how this test was being ordered is that our previous work showed a fairly high reimbursement rate for these MPN panels.

So we were curious what was causing that. One of our hypotheses was that it might be related to how physicians were ordering the test and so that was the purpose of this study is to really understand how physicians were ordering and what are the ordering patterns for this test.

Randye Kaye: So what factors did you look at to evaluate clinician ordering patterns?

Tyler Cooke: The first thing we looked at was just the overall test volume as well as the results of the test and along with that, we looked at the ICD-10 codes that physicians put on the requisition forms. We also looked at how many tests were canceled by the lab and why the lab canceled them and then for each test, we looked at a clinician level -- we looked at provider level, i.e., were they a resident, a PA, an attending -- so provider level, and then specialty and then for each patient, we also looked at their pretest CBC, or complete blood count.

Randye Kaye: All right. Thank you. So those are the factors you looked at and were you surprised by any of your findings?

Tyler Cooke: So one of our main findings, I guess, was that -- kind of comparing to what some other people have found -- they'd shown that there were different ordering patterns by different physicians and so that was kind of one of our hypotheses going in was that okay, are there certain providers who maybe don't understand how to order this test or quite understand the clinical context that it was intended and is that causing some of our reimbursement challenges? We were rather pleased to find that was not the case at our institution. The vast majority of tests were ordered in what appeared to be a very appropriate, straightforward clinical context. We looked at all the provider levels and provider specialties, and really that had no association with test results. One surprise that we did find, though, was that 10% of our test volume was actually not for diagnosis of a myeloproliferative neoplasm, but it was for a thrombophilia workup.

So patients who have blood clots, especially in more unusual locations, it's standard of care to order *JAK2* mutation testing and so at our institution, the MPN panel is what they order to get that testing.

Randye Kaye: All right. Thank you. Now, I'm curious, were there any other factors that you would have liked to include in the study?

Tyler Cooke: I think the one factor that we would have liked to include is the final diagnosis, understanding how the results of the assay inform the patient's diagnosis. That would have just been nice to fully close the loop and understand the clinical and diagnostic impact of this testing but unfortunately, we weren't able to get it for the study.

Randye Kaye: Since MPN panel testing is expensive and it has a low reimbursement rate, are there algorithms based on more standard laboratory testing that exist that try to predict molecular test positivity before sending for molecular testing?

Tyler Cooke: Right. So that's a good question and I think the short answer is that -- the short answer is no. People have tried to make algorithms to establish pre-test probability to try and get a sense of who might test positive on an MPN panel and who might not. I think what has been shown is that it's very difficult to create those algorithms without missing some patients. So, for example, most of those algorithms use the CBC as the cutoff, where you do some calculation based on the CBC to determine whether a patient is likely to test positive or negative on MPN gene testing. The reality is that all of those algorithms will miss some patients because there are some patients even in our study who had a normal CBC and still had mutated genes on the test.

Randye Kaye: Okay. So in this space, is there any kind of a role for clinical decision support, or is the picture just too nuanced?

Tyler Cooke: You know, I'm not sure if clinical decision support is the right word since, you know, we looked at our clinical ordering practices and they were -- by and large, appropriate. However, given the challenging reimbursement environment and low test positivity rate, there is potentially an opportunity to reduce testing to conserve resources without impacting patient care -- if we could get a better picture of the pre-test probability and not test some of these patients who -- if we could know in advance that they were already going to have negative test results. Using a CBC-based approach for that is challenging because some patients, even with a normal CBC, will have positive MPN panel results. So there may be an opportunity for something that is, as you said, more nuanced -- something like a machine learning model that incorporates longitudinal CBC data, the patient's clinical notes, history, and physical exam. I think, yeah, something like that could be valuable.

Randye Kaye: All right. Thank you. So, with all this and all that you've learned, is there advice that you would give to other molecular labs that are facing these similar reimbursement

challenges like is the answer better education, better coding, advocacy with payers, or something else entirely?

Tyler Cooke: Yeah, I think really all of the above. One of the things that our lab has found is that certain ICD-10 codes, specifically vague or not entirely accurate ICD-10 codes, are less likely to be reimbursed. So for example, an ICD-10 code for a blood disorder, unspecified, or secondary polycythemia is less likely to be reimbursed than if the clinician just writes polycythemia vera. So I think educating our clinicians on the importance I guess of putting an accurate ICD-10 code on the test requisition form. In terms of billing, many of our test reimbursements are denied due to lack of prior authorization.

So coordinating with the billing team as well as the clinicians to better understand which patients and which payers need prior authorization and making sure we can have that set up in advance before we actually run or order the test. And finally, I think advocacy is really important here because one of the big challenges with reimbursement is this gap between clinical practice and clinical guidelines, which suggest using MPN genetic testing as a screening test, which is how -- that's what the guidelines say, that's how our clinicians are using it, but that is not how insurance companies want to reimburse.

They -- I don't know exactly what they're thinking but it seems like they want this to be used more as a diagnostic test rather than a screening test. I think we do need continued advocacy with insurance companies so that they can update their reimbursement policies with guideline-based, evidence-based, clinical practice.

Randye Kaye: All right. Thank you and thank you so much for joining us today.

Tyler Cooke: My pleasure. Thank you for having me.

Randye Kaye: That was Dr. Tyler Cooke, describing the *JALM* research article, "Ordering Practices and Utilization of a Next-Generation Sequencing Panel for Myeloproliferative Neoplasms." Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.