SPEAKER 1: Hello, my name is Matthew Tollefson. I'm a urologic oncologist at the Mayo Clinic in Rochester, Minnesota. And I'm here today to discuss one of our really interesting findings that are going to be published in the *Mayo Clinic Proceedings.* The paper is entitled "Prostate Cancer Ki-67 Expression, Perineural Invasion, and Gleason Score as Biopsy-Based Predictors of Prostate Cancer Mortality." We put these together-- these factors together-- to create The Mayo Model of Prostate Cancer Mortality After Surgery.

Prostate cancer is the most common solid tumor that's diagnosed in American men. Studies show that one in six American men are diagnosed with prostate cancer at some point in their life, yet it's clear that many men diagnosed with prostate cancer ultimately die of other causes because of the cancer can be so slow growing and indolent. However, there are some men and some cancers that are much faster growing than that, and many men die of prostate cancer.

In the United States, prostate cancer still is the second or third most common cause of death from cancer in men in America. With this, it's clear that not every man that's diagnosed with prostate cancer needs aggressive treatment. It's also clear that not every man diagnosed with prostate cancer doesn't need any treatment. So one of the real difficulties we have in managing prostate cancer is trying to identify the cancers that are really life threatening, and distinguishing those from the cancers that are more benign and more indolent and that men might die with rather than die from. This is a really critical question that we have in the management of prostate cancer.

There are many treatment options for prostate cancer. It can be really just dizzying for some men who get diagnosed with this and are confronted with the possibilities of radiation, which can be done with external beam radiation therapy, proton therapy, or seeds-- which can be put in the prostate to emit the radiation in that manner. Also surgery-- surgery can be done traditionally through an open incision-- it can be done robotically.

There are other treatments, such as cryotherapy, HIFU, and hormonal therapy that are all used in prostate cancer. And it becomes really difficult for men to decide which treatment to go with. These questions become really important because they play a big role in the side effects that one can expect after treatment. And especially with the emergence of active surveillance for patients with lower-risk types of prostate cancer, the identification of which prostate cancers really are lower risk becomes a real critical question in trying to decide which type of treatment one should have.

We, in this study, reviewed our experience with radical prostatectomy in more than 450 men. And we basically went back and looked at all of the features that have been shown to be associated with outcomes from prostate cancer and re-looked at everything. So we took a series of men who underwent radical prostatectomy from 1992 to 1995 and we looked at their biopsies. We looked at their PSA values. We looked at all of the other factors that are known to contribute to aggressive types of prostate cancer and came together with a model that we termed The Mayo Model for prediction of prostate cancer aggressiveness.

This model is really notable that it takes features that are seen on the biopsy and incorporates them into that risk prediction. Many of the features that are used in existing models come from tools that are used to diagnose prostate cancer rather than tools that are used to stratify risk from it. For example, PSA is one of the most common reasons that men get diagnosed with prostate cancer, and it's clear that very high PSA levels are bad or indicate more aggressive cancers. It's not clear, however, that somebody with a PSA of four or a PSA of eight have really much of a different prognosis.

Also, a feature that's commonly used in most predictive algorithms is clinical stage. So when a doctor feels the prostate, if they can feel the prostate tumor, it's considered to be a stage two tumor. If they can feel it outside the prostate, then it becomes a stage three tumor. But that can be very difficult, and at times just feeling the prostate doesn't give one a clear answer as to how aggressive it is.

And so we looked back and came up with the criteria that we found were most predictive of outcomes. And in this analysis, we found that the Gleason score of the cancer was predictive. So the Gleason score is when the pathologist diagnosis a cancer, they can look under the microscope and try to gauge how aggressive it appears.

Another factor that was important was perineural invasion. So perineural invasion represents the cancer invading into some of the nerves that travel through the prostate. And we found that if the cancer does invade into those nerves that men, in general, have a more aggressive type of prostate cancer.

Probably the most intriguing and interesting finding that we found in this study was that the proliferation index was an important factor, in fact one of the most important factors that predicted the aggressiveness of the prostate cancer. Proliferation index is an assessment of how quickly the cells are growing. When cells grow, they express a protein, and that protein can be detected using common histopathologic techniques.

The fascinating part with this is that Ki-67, which is the marker that's used to assess for proliferation, is not a new marker. It's been around since the 80s. However, it's never been used in prostate cancer before. And we found that it was the most predictive of all of the tools that we commonly use in prostate cancer risk stratification.

So the central findings of our study that are coming out in the *Mayo Clinic Proceedings* are that the biopsy Gleason score, the presence of perineural invasion, and the amount of proliferation as assessed by this Ki-67 index were the strongest predictors of prostate cancer mortality after surgery. And we think that these findings can really be used to try to identify the patients who need aggressive treatments and maybe identify the patients who can just be watched with their cancer and maybe don't need to have the aggressive treatment that surgery or radiation have. Hopefully, we can avoid some of the complications and the side effects of treatment in some men who did not need aggressive treatment for their slower growing, more indolent types of cancer. Thank you.

SPEAKER 2: We hope you found this presentation from the content of *Mayo Clinic Proceedings* valuable. Our journal's mission is to promote the best interests of patients by advancing the knowledge and professionalism of the physician community. If you are interested in more information about us, our homepage is www.mayoclinicproceedings.org. There, you will find access information for our social media content, such as additional videos on our YouTube channel or journal updates on Facebook.

You can also follow us on Twitter. More information about health care at Mayo Clinic is available at www.mayoclinic.com. This video content is copyrighted by Mayo Foundation for Medical Education and Research.