# A Healthy Discussion on Renaming Low-Grade Prostate Cancer as Non-Cancer​

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**Becca Battisfore:**

Welcome to the latest edition of the College of American Pathologists' CAPcast. I'm Becca Battisfore, content strategist with the CAP. In this episode, our guest host, Dr. Gladell Paner, will be talking with two fellow genitourinary pathologists on the ongoing discussion of renaming low-grade prostate cancer as non-cancer. Before we get into the conversation, let's learn more about our guests. Dr. Panner, would you like to introduce yourself?

**Dr. Gladell Paner:**

Thank you, Becca. Good afternoon. My name is Gladell Paner. I am a GU pathologist working at the University of Chicago and I had the pleasure of working previously in CAP committees, including the Cancer Committee and the PERT Committee. And I'm currently working on several educational projects for CAP on prostate cancer.

**Dr. Ming Zhou:**

Good afternoon. My name's Ming Zhou. I'm currently a professor and vice chair for oncological pathology, director of urological pathology service and fellowship program in the Department of Pathology, Molecular and Cell-Based Medicine at Mount Sinai Hospital and Icahn School of Medicine in New York City. I previously served as a chair at the Tufts Medical Center in Boston, Massachusetts.

**Dr. Rajal Shah:**

Hello everybody. My name is Dr. Rajal Shah. I am Dr. Charles Ashworth's Professor of Pathology at the Department of Pathology at University of Texas Southwestern Medical Center in Dallas, Texas. And before that I have taken many academic roles at University of Michigan. I have also been at Cleveland Clinic and also have been also in industry in past. And currently I also serve as a president of United Neuropathology Organization.

**Becca Battisfore:**

Thank you all for joining the podcast, Dr. Paner. I'll let you take it from here.

**Dr. Gladell Paner:**

Thank you, Becca. So today we will talk about a highly controversial subject in renaming of Gleason score 6 or Grade Group 1 prostate cancer. This subject is not new but has gained greater attention. Recently the renaming issue is rooted in the concern of overtreatment of low grade or indolent prostate cancer and that treatment is not free of complications. Renaming of Grade Group 1 prostate cancer will have an impact to our practice as pathologists and it's best to get into the core of the issue, have a healthy conversation and understand the circumstances around this issue. So for my first question, I would like to address this to Dr. Zhou. Dr. Zhou, can you please give our listeners a brief historical background how the idea of renaming Grade Group 1 prostate cancer came about and what are the major benefits for the patients?

**Dr. Ming Zhou:**

Thank you, Gladell. I would be happy to do that. As you mentioned that the proposal for removing the cancer label from the Grade Group 1 cancer is not a new idea. It was first brought up more than a decade ago in 2012 by several groups. The rationale behind the proposal is multifold. The first one is that the biology of prostate cancer has evolved significantly over the last several decades. With contemporary screening detection and management, the low risk of Grade Group 1 cancer has become a disease of excellent prognosis. This is true for Grade Group 1 cancer diagnosed in both radical prostatectomy and biopsies. For example, in radical prostatectomies, Grade Group 1 cancer rarely invades out of the prostate gland and seminal vesicle invasion is even more rare. It is incapable of metastasizing to lymph nodes and other distant sites.

The 15-year cancer specific survival is very high approaching 100 percent. If the low-risk Grade Group 1 cancer is diagnosed in prostate biopsies, the prognosis is also very excellent. The 15-year cancer specific death is around one to 2% regardless of the treatment modalities including active surveillance, surgery or radiation. Therefore, the low-risk Grade Group 1 cancer should be managed conservatively using active surveillance protocol. However, this is not the case at the present time. Despite all the initial enthusiasm, the current intake rate for active surveillance plateaus at 50% and more importantly, around 40% of the patients with a low-risk cancer choose immediate surgery or radiation. But aggressive treatment for low-risk cancer amounts to overtreatment, which in itself has serious and negative implications not only on the patients but also on society as a whole. It is for these reasons that the proposal was brought up to remove the cancer label from the Grade Group 1 cancer.

And the hope is by doing so, it will stop patients from rushing to make a treatment decision and give them time to research and to find out about their disease and ultimately to make an informed treatment decision. There are several major benefits to remove the cancer label from the Grade Group one cancer. The first one is to decrease the over-diagnosis and overtreatment of a low-risk cancer and therefore to reduce the psychological and financial burden on the patients and their families and to minimize the side effect associated with treatment; it can also decrease the burden on the healthcare system as a whole.

**Dr. Gladell Paner:**

Thank you, Dr. Zhou for that very detailed explanation of the historical background on this renaming issue. And I just want to point out there what you said right now that the compliance for active surveillance, it's right there in the 50% range at this point, at least in the US and that's really an important piece of information there. I'd like to turn over to you, Dr. Shah, and I'm going to ask you two related questions. The first question is what are the histologic and molecular features of Grade Group 1 prostate cancer that will make it as cancer? And the second question is, what challenges will pathologists encounter in renaming, especially in biopsy samples?

**Dr. Rajal Shah:**

I think those are really great questions. So first of all, I would like to thank College of American Pathologists for this opportunity to participate in a very timely topic regarding the first question. One of the strongest rationales for considering Grade Group 1 as a cancer is the fact that Grade Group 1 prostate cancer shares many morphologic and canonical molecular alterations which are associated with higher grade prostate cancer. Like high grade prostate cancer Grade Group 1 prostate cancer has a uniform loss of basal cells. Cytologically, it is indistinguishable from high grade cancer. Its architecture is similarly infiltrative with frequent perineural invasion. Rarely one can also encounter extra prostatic tumor extension. It often merges with higher grade cancer. As we know, grade group cancer also exists on a molecular continuum with higher Gleason grade cancer. Similar to high grade prostate adenocarcinoma, we see overexpression of alpha-methylacyl-CoA racemase, loss of PTEN, GSTP1 downregulation, and temporal or gene fusions are present in Grade Group 1 prostate adenocarcinoma like we see in high grade cancer.

It is true that the frequency of some of these alterations, specifically PTEN loss, are substantially less common in Grade Group 1 prostate cancer. But overall the similarities support the similar pathways of tumor development and progression. Now regarding the second question, I believe that removing the cancer label from the Grade Group 1 prostate cancer would have significant challenges and impacts to the pathologist practice. We know that Grade Group 1 is comprised of pure Gleason pattern 3 and this is the integral part of the 5 grade group system, which is essentially made up of Gleason patterns and it is the lowest grade that pathologists use while assigning a grade. Previously we used to call Gleason 6 in biopsy, which we now call Grade Group 1. So this is the lowest grade regardless of the specimen type that you utilize, removing the lowest grade from grading system may create an artificial shift towards higher grading.

So we may be dealing with a more bias higher grade system. There will be also inconsistencies and confusion in the prostate cancer reporting. We know that pathologists typically receive multiple core or multi-part prostate biopsies. So in this setting it is very common to see that one core has a Grade Group 1 and the other core maybe Grade Group 2 or higher. And this could be coming from the same tumor, say for example, index tumor. So from a practical viewpoint, how would needle biopsy be signed out where one part of the tumor is Grade Group 1 and another part is Grade Group 2 or higher? Do we all call part of the same tumor cancer and part not? So there was an interesting survey that Renal Pathology Society did a year ago. We surveyed a very large number of pathology community and 82% of pathologists were opposed to removing the cancer label from the Grade Group 1 cancer. And of these respondents who oppose the name change, 72% were concerned that renaming a Grade Group as a non-cancer can result in a significant modification in diagnosis grading and reporting practices which would practically make the entirely a different practice to some extent.

**Dr. Gladell Paner:**

Thank you. Thank you, Dr. Shah. And that's really, that's a detail. There's a lot of excellent points that you made there, but I think really the crux of the challenge here is that fundamentally Grade Group 1 prostate cancer is histologically cancer. And I think it's hard to go against that because the morphology is pretty much like the way traditionally we diagnose cancer, it is cancer and that's hard to overcome. So Dr. Zhou, I'm going to direct you the second question. So are there ways to overcome these challenges while renaming Grade Group 1 prostate cancer in biopsy?

**Dr. Ming Zhou:**

Yes, there are, but let me first clarify that I am not arguing that Grade Group 1 cancer is not cancer. And I agree with Dr. Shah that the Grade Group 1 is cancer, but what I'm arguing for is to change the name for the sake of the patient management. By dropping the cancer label and calling it the word the name that is somewhat short of cancer but still significant, pathologists will acknowledge their uncertainty regarding the biological behavior of the Grade Group 1 cancer diagnosed in the biopsy. It is very likely to be a disease with a good prognosis and doesn't need aggressive treatment, but it may also be an aggressive disease that indeed needs aggressive treatment. We just need more time to do more studies to be certain before patients pick the right treatment for themselves. Dr. Shah has mentioned a few challenges that the pathologists and other teams will encounter if we want to rename Grade Group 1 cancer.

The first issue is pathologists may incline to over grade a Grade Group 1 to Grade Group 2 if Grade Group 1 is no longer called cancer. I think the answer to this question or to this issue is that we really need to clarify the grading criteria. For example, one of the difficult areas in Gleason grading is how to grade poorly formed glands. It is not uncommon to see a Grade Group 1 with a few poorly formed glands being over graded as Grade Group 2. It is actually a mistake that may have important clinical implications as it may preclude patients from getting on active surveillance. About 10 years ago, Dr. Shah and I put forward a grading recommendation for poorly formed cancer glands. The second issue Dr. Shah brought up is this change, namely renaming a Grade Group 1 cancer, will cause some confusions and inconsistencies in cancer reporting. But what I'm proposing is to just drop the cancer label and call it something like prostatic neoplasm. Pathologists will still provide Gleason score, Grade Group, and tumor volume measurements. If the entire case has only Grade Group 1 cancer, we'll add a comment that the tumor has uncertain biological behavior. It may represent a tumor of good prognosis or carcinoma. Additional workup is needed. If other parts of the same biopsy have Grade Group 2 or higher cancer, then this comment may be omitted and may not be needed.

**Dr. Gladell Paner:**

Thank you, Dr. Zhou. I'd just like to encapsulate what you said, and this is a very important point that you made in terms of the renaming and renaming is not really renaming Grade Group 1 prostate cancer. That's a benign entity. It still has histologic features of cancer, but the renaming would be something else, something that is not cancer to avoid the overtreatment of this indolent low grade prostate cancer.

So for the next question I would address to Dr. Shah and you briefly mentioned, alluded to this earlier about the impact we are pathologists and of course something of this nature of this change will have an impact in our practice as pathologists. So with this change of nomenclature of Grade Group 1 prostate cancer and kind of shift really the boundary of the diagnosis between benign or non-cancer to cancer, it'll shift right there between Gleason score 6 and of course 3 plus 4. And that will be a critical boundary now for pathologists making this diagnosis. So having said that, my question to you Dr. Shah, what is the potential negative impact of renaming Grade Group 1 first from the patient's perspective and then for the diagnosing pathologist as well?

**Dr. Rajal Shah:**

Yeah, I believe there will be several negative consequences both from patients as well as pathologist's perspective regarding renaming Grade Group 1 as a non-cancer. So let me first address a patient's perspective. So in a previous question we address that frequently we receive multiple core prostate biopsies, multiple part coming from different sites of the prostate. So it is very common to see prostate cancer with different grade groups in different cores. One core may be Grade Group 1 other course could be Grade Group 2 or higher. So in setting like this is we call the Grade Group 1 as a non-cancer and the other Grade Group 2 or higher as a cancer. So patients might assume that do they have two separate tumors? That is one fundamental confusion that in my opinion would be a significant one that I might dealing with the two separate tumors. In addition, in certain situations I think we may end up, I think because we don't have a about this particular terminology as well as I think we know that there are some borderline situations. So we may end up calling atypical proliferation or uncertain malignant potential. So patient may have anxiety whether they have cancer or not. And that may create a lot of, I think potential second opinions. And I think subsequent challenges we also very important thing to know, Dr. Zhou already discussed that, that active surveillance is currently the well accepted treatment for Grade Group 1 prostate cancer. Dr. Paner mentioned that I think the acceptance of this treatment in United States is somewhat less than optimal, but in certain European countries it's very good. It's almost in the range of 95% to 100%. So the success of this treatment depends on a committed and motivated patient who comes for a regular follow-up. It is logical and expected that renaming Grade Group 1 as not cancer will lead to less compliance with the follow-up. We know that we can let the patient off the hook that because I call this the neoplasm you are completely free of subsequent follow-up.

So I think that is one very significant concern that I have from patient's perspective, patient may not feel it necessary that they need to have a periodic follow-up visit as they no longer have cancer. Finally, we may end up pre classifying some of the non-cancer as cancer in follow-up biopsies. We know that several Grade Group 1 prostate cancer in current practice may end up being Grade Group 2 or 3 which could be due to either tumor progression or grade progression or sometime due to unsample higher grade cancer which was not sample in the initial biopsy. So in this situation it may become very difficult to explain to patient that why suddenly what happened from a tumor which was not cancer to suddenly I ended up having a more significant cancer. From a pathologist's perspective, the threshold between Grade Group 1 and Grade Group 2 is often blurry and is not without interobserver variability.

If the cancer label is removed from Grade Group 1 in borderline situations between Grade Group 1 and Grade Group 2 pathologists may choose a bit of a defense you practice and may are on the side of calling Grade Group 2 to avoid the potential consequences of missing a significant cancer. And Dr. Zhou mentioned about the study. I think in that study we saw that I think in borderline situations the interobserver variability could be significant. So this could be one of the major challenge in the gap survey that I mentioned. 74% of the pathologists raise concern about pathologists over grading of Grade Group 1 to Grade Group 2 to avoid potential litigation type of situation. So we may basically err on the side of towards being a defensive.

**Dr. Gladell Paner:**

Thank you, Dr. Shah. So to your point, there is potential migration in grading to kind of gear towards the higher grade, the Grade Group 2 instead of Grade Group 1 especially of course for those borderline cases.

**Dr. Ming Zhou:**

So now one of the issues is when prostate biopsies have several parts which have different Grade Groups. One part has Grade Group 1, the other part has Grade group two. If you rename the Grade Group 1 as non-cancer, the patient may be confused. So, I just want to first make sure that, Gladell also mentioned that, if we rename a Grade Group 1 cancer as something else, I really don't like to call it benign. I want to use a terminology that is not cancer, but yet significant enough such as prostatic neoplasm so that both patients and doctors understand this is not just something benign, not benign prosthetic tissue, and not that patients can be told they can go away and don't have to come back.

It is still something significant. They still need to come back for further and additional workup. So that's one of the comments I want to make. Second comment is if we don't call Grade Group 1 cancer, then a patient may not come back for follow-up during which Grade Group 2 or higher cancer is detected. And how do you explain that discrepancy? This is very easy. Pathologists constantly deal with the situations like that. For example, if a patient has a prior diagnosis of cancer, he comes back for a repeat biopsy which is negative. We don't tell the patient, oh, you no longer have cancer. We just explain to the patient that this is a part of the sampling problems because prostate biopsy is known to have sampling issues.

**Dr. Gladell Paner:**

Thank you, Dr. Zhou. Yeah, so to your point in terms of the terminology and really that's the follow-up question, right? We talked about renaming and the issue of to rename or not to rename is really the first step. And then the second step if it was true, is that how to rename? Yeah. And as you pointed out something like indefinite for carcinoma or something of that nature. For the next question, I like to pull out the GPs survey that Dr. Shah alluded to earlier, and there's an interesting piece of information here. In the survey, among the respondents, 51.5% supported the change or name change for radical prostatectomy only and for biopsy it's 12%. And then for renaming in both biopsy and radical prostatectomy is 36%. I mean all of these are low numbers. We can argue that renaming in radical prostatectomy is above midline above half or there's a small majority there. But clearly to my point is that the type of specimen or the situation has an effect to the idea of renaming as shown by this data. So my question, and this is addressed to both of you, the question is that, is renaming possible if a Grade Group 1 prostate cancer, the entire lesion is fully examined in a radical prostatectomy specimen? I would like to start with your Dr. Zhou.

**Dr. Ming Zhou:**

Okay, yeah. Let me clarify. Yes, both GUPS and ISUP did a survey of their members on whether the Grade Group 1 cancer should be renamed as something non-cancer. So I'm familiar with the GUPS results. I want to clarify the results a little bit further. Yes, there are only 12% of the members who supported the renaming, the Grade Group 1 cancer as non-cancer. Of those supporters, only 50% support the renaming in radical prostatectomy specimens. So if you do the math, only about 6% of its members support the renaming of the Grade Group 1 cancer in the radical prostatectomies. Having said that, I am fully behind that. I support dropping the cancer label and renaming Grade Group 1 cancer for the reasons that I mentioned earlier, the Grade Group 1 cancer in radical prostatectomies have excellent prognosis. The extra prostatic extension is very rarely reported in about 4% of the cases.

Seminal vesicle invasion is even rarer, reported in less than 0.05% of the cases. Grade Group 1 cancer is incapable of the lymph node and distant metastases. Long-term survival is also excellent, approaching 100 percent. For these reasons I support removing the cancer label from the Grade Group 1 cancer in the radical prostatectomies.

But there are two key issues here. If we choose to do that, dropping the cancer label from the Grade Group 1 cancer in the radical prostatectomy specimens, we need to make sure, number one, the radical prostatectomy specimens need to be entirely submitted and examined by pathologists. Number two, pathologists need to use strict contemporary grading criteria for the Grade Group 1 cancer, especially for the poorly formed glands. We need to follow the recommended criteria for grading poorly formed glands as Grade Group 1? If you just see a few poorly formed glands that are right next to well-formed glands, it's not Gleason pattern 4, it's still Gleason Pattern 3, therefore Grade Group 1 cancer.

**Dr. Gladell Paner:**

Thank you, Dr. Zhou. And for you Dr. Shah, the same question.

**Dr. Rajal Shah:**

Yes. Yeah, I completely agree with what Dr. Zhou said. In fully examined radical prostatectomy, I would fully support that Grade Group 1 prostate cancer can be classified as a non-cancer, non-cancerous proliferation. But it is very, very important that we have a fully examined prostatic evaluation and use contemporary criteria. And that's based on the data that Dr. Zhou mentioned that we don't see any extra prostatic metastasis in lymph nodes or distance metastasis. There is no disease specific death that has been reported with Grade Group 1 prostate cancer. So data fully supports it, but this is completely different in the biopsy setting. In the biopsy setting, the problem is that we cannot know with certainty whether a patient harbors only pure Grade Group 1 cancer.

**Dr. Gladell Paner:**

Thank you, Dr. Shah. So far we've been talking about the renaming issue, but we really have not talked about the root cause of this issue. And really the root cause of this issue, why this controversy arose is that there's this issue of overtreatment of low grade or indolent prostate cancer. And having said that, the next question is for both of you. I will start with you, Dr. Shah. So the question is, what will be the necessary steps from the pathologist's perspective that would help alleviate the over-diagnosis and over-treatment of Grade Group 1 prostate cancer?

**Dr. Rajal Shah:**

I think this is a very important question. So first of all, let me emphasize that there is a universal agreement amongst pathologists and clinicians alike that Grade Group 1 prostate cancer should not be overtreated and active surveillance should be the default option for its management. It is also very important that pathologists remain a critical part of this important debate because ultimately diagnosis is made by pathologists. However, what I believe is that the burden of alleviating over diagnosis and overtreatment of Grade Group 1 prostate cancer does not rest on pathologists alone. The optimal detection of indolent prostate cancer would require a multidisciplinary team approach from clinical colleagues, radiologists, and pathologists, instead of relying on pathologists alone. We need to ensure that patient does not have unsampled high grade or clinically significant cancer through very careful clinical evaluation.

Multiparametric imaging studies, adequate biopsy sampling, specifically targeted and systemic sampling, careful morphological examination by an expert GU pathologist and in some situation molecular studies as well. So it is important to keep in mind that Grade Group is only one of the many prognostic factors that influence prostate cancer outcomes. So finally, instead of focusing on its name change from Grade Group 1 to non-cancer, I believe the focus of debate can be shifted to better educate patients to understand their cancer diagnosis and how we can refine the risk stratification to identify patients with Grade Group 1 who can be conservatively followed or who may eventually need a treatment.

**Dr. Gladell Paner:**

Thank you, Dr. Shah. I couldn't agree more with what you emphasize that this is really a multidisciplinary issue and it has to be addressed in...

**Dr. Rajal Shah:**

I think one point if I can make currently both societies, Genitourinary Pathology Society and International Society of Urologic Pathologists have come together to develop a consensus statement which will address this particular issue in detail. So please be on lookout for that. That will be hopefully coming out by end of the 2024 or early 2025.

**Dr. Gladell Paner:**

That's a great endeavor there. So there will be an ISUP and GUPS combined white paper on low grade indolent prostate cancer. So for the audience, watch out for that likely at the end of the year or probably early next year. And the same question for you, Dr. Zhou.

**Dr. Ming Zhou:**

I agree with both of you that we need to reduce the over diagnosis and over treatment of the low-grade Grade Group 1 cancer. And it takes an entire village, it takes entire patient care teams to do that. That includes oncologists, urologists or radiologists and pathologists and even patient advocacy groups. However, I do want to emphasize that pathologists can play an oversized role in this process. And we do have precedence in pathology that we change the name of the disease entities in order to provide better patient management. For example, in kidney cancer there is a form of clear cell renal cell carcinoma with extensive cystic changes and it actually has an excellent prognosis. No reports of the recurrence or metastases have been reported after the surgical resection, therefore the name has been changed to multilocular cystic neoplasm of low malignant potential. And the cancer label was dropped and it conveys the message that this is a tumor of excellent prognosis. The patient does not need excessive postoperative follow-up or treatment.

**Dr. Gladell Paner:**

Thank you, Dr. Zhou. Now I'm going to shift a little bit here. And to our pathologist audience, I like to emphasize that about a year ago we released the latest edition of the CAP prostate Cancer Protocols and we have four protocols. There were two biopsy protocols, one for specimen level reporting, and at the other is for case level reporting. We also have a radical prostatectomy protocol and then the TERP protocol. And the next couple of questions are related to that. And my first question will be addressed, Dr. Zhou. And actually Dr. Zhou was my predecessor in the cancer committee. He was previously in charge of creating the GU protocols and he did a wonderful job there. And my job was really just to continue what he had started. So my question to you, Dr. Zhou, is that in addition to reporting grade, what other grading related futures should be included in the cancer protocol for prostate biopsy?

**Dr. Ming Zhou:**

Thank you, Gladell, for those compliments. I really enjoy my time on the Cancer Committee. To answer your questions. Now obviously Gleason score and the Grade Group are one of the most important pathology parameters for reporting prostate biopsies. But there are several other grading related features that are also important for the prognosis and patient management, therefore should be included in the biopsy report, including the cribriform cancer glands and intraductal carcinoma. I think pathologists should also be aware of the recent updated recommendations for the grading reporting. I would just mention a few of these recommendations. The first one is the reporting of the percentage of the Gleason pattern 4 in Grade Group 2 and 3 cancers. Unfortunately, the reporting of the Gleason pattern 4 is quite variable amongst the pathologists. So we really need to focus on the cut points that are important for the clinical management.

For example, 10%, 40%, 60%, and 90%. Because a Grade Group 2 cancer with 10% Gleason pattern 4 may still be eligible for active surveillance. So it is very important to accurately quantify the Gleason pattern 4 in that scenario. And 40%, 60% really distinguishes between Grade Group 2 and Grade Group 3 cancer. And 90% distinguish grade three from Grade Group 4 cancer. So by focusing on these critical cut points, the Gleason pattern 4 quantification can be more reproducible. Second point I'll try to make is the small focus of cancer, usually less than one millimeter in length with a Gleason pattern 4. The accurate grading and quantification of Gleason pattern 4 is often difficult and sometimes can be misleading in this scenario. In these cases, I would diagnose these cases as a small focus of cancer with the Gleason pattern 4 present but mention in a comment that the focus is too small to accurately grade and quantify the Gleason pattern 4. The last point I want to make is the grading of the targeted biopsies. Usually several biopsy cores, 3 to 4 cores, will be taken from an MRI suspicious lesion. When more than 1 course is positive for cancer, a combined Gleason score of all the positive cores is usually better than individual core Gleason score to predict the Gleason score of the radical prostatectomy specimen.

**Dr. Gladell Paner:**

Thank you, Dr. Shah, to emphasize your last point. So one MRI target lesion 1 Grade regardless of the number, of course.

**Dr. Ming Zhou:**

Correct.

**Dr. Gladell Paner:**

Alright, so I would reiterate the question for the benefit of our audience. This is address to Dr. Shah. So what other grading related features should be included in CAP Cancer Protocols and this time for radical prostatectomy?

**Dr. Rajal Shah:**

So CAP prostatectomy protocol also has several important grading-related reporting elements that pathologists need to report. These elements are specifically important in the setting of Grade Group 2 or higher prostate cancer. So one important thing is that if you have a Gleason score 7, which could be 3 plus 4, Grade Group 2, or 4 plus 3, which is Grade Group 3. So you need to differentiate. That's an important prognostic parameter, even though both represents Gleason score 7. And that is the advantage of grade grouping that we can better differentiate between two. But we also need to provide percent pattern 4 in radical prostatectomy, which is an important prognostic feature. Studies have shown that very small amount of pattern 4may not be harmful specifically in the setting of a non cribriform pattern 4. In comparison, a very high percentage of pattern 4 patients in certain situations may benefit from additional adjuvant treatment such as androgen deprivation treatment modality.

Dr. Zhou already mentioned about cribriform pattern 4 and intraductal carcinoma. These are proven prognostic adverse pathological parameters. So they must be reported whenever, particularly in the situation when you have 3 plus 3 with intraductal carcinoma or even in Grade Group 2 or Grade Group 3, these elements are critical to report and both societies recommend reporting these two important adverse pathological features in the setting of Gleason pattern 5. It is important to determine in specifically radical prostatectomy situation whether it is primary, secondary or tertiary pattern. If it is less than 5%, we can utilize that as a tertiary pattern. But if it is greater than 5%, then it can be technically utilized as a secondary pattern and primary pattern the recommendation that is pretty much same as what it used to be. So these kind of are my overall recommendations for and CAP Protocols have adequately addressed this elements.

**Dr. Gladell Paner:**

Thank you Dr. Shah. We have a very interesting conversation. Unfortunately that's the only time we have. So I would like to thank Dr. Shah and Dr. Zhou for giving us their insights in this healthy discussion in the pro and cons of renaming Grade Group 1 prostate cancer. And as we hear each other's point, I can say that there are really no two sides here, only one side. And that is the one side that wants to achieve the best healthcare for patients with prostate cancer. And we can all agree that those who are renaming and those who are against renaming wants the best care for patients with prostate cancer. And thank you and I'll pass now to Becca.

**Becca Battisfore:**

Thank you, Dr. Paner for leading the conversation and to our guests for sharing their perspectives on this topic. And I want to thank you all for listening to this CAPcast. The CAP has four prostate Cancer Protocols available to support pathologists in reporting out cases. If you have questions or comments about any of the protocols, please email CancerProtocols@cap.org. And for more information about the CAP, visit cap.org.