

Prostate, an Age Based Conundrum- Development at Early and Old Age- A Review

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Abstract:

Background: With rapidly changing lifestyle, increasing life expectancy and screening using Prostate-Specific Antigen (PSA), the males are becoming more prone to prostate cancer. The condition is generally associated with older ages, 50 and beyond but in recent records, it has been found that the condition has also been targeting the men of younger ages, 20 and beyond. Early onset prostate cancer a newly identified, more aggressive subtype often linked to genetic mutations. Data from the Indian national cancer registries show that incidence of prostate cancer has been on an unprecedented high, among all other forms of cancers in males.

The article aims to review the condition in general information that needs reckoning is the epidemiology and the statistics of prostate cancer. Reviewing the incidence rates, mortality, and trends over time for prostate cancer as the data collected from national population-based cancer registries. The Prostate is the second leading site of cancer among males in large Indian cities like Delhi, Kolkata, Pune and Thiruvananthapuram, third leading site of cancer in cities like Bangalore and Mumbai and it is among the top ten leading sites of cancers in the rest of the population-based cancer registries (PBCRs) of India. The PBCRs at Bangalore (Annual Percentage Change: 3.4%), Chennai (4.2%), Delhi (3.3%), Mumbai (0.9%) and Kamrup Urban District (11.6%) recorded a statistically significant increasing trend in incidence rates over time^[1].

According to the Department of Defense Center for Prostate Disease Research, Prostate cancer is traditionally more actively found in men aged 50 years and above. The younger men traditionally have accounted for approximately 1% of those diagnosed with prostate cancer^[2]. Prostate-related prior studies have led many clinicians to believe that they have a less favorable outcome than older men with respect to prostate cancer. However, most of these studies were conducted before the advent of PSA screening programs^[2]. There were several evaluations around a surgically treated cohort of men age 50 years or younger to determine whether disease recurred more frequently among them than in those 51 to 69 years old in the PSA era. Which brought the researchers closer to the prognosis of prostate cancer and its thriving conditions in younger men^[2].

The paper also aims to provide insights into the importance of dietary inclusions and improvement that can and are reported to support and accelerate the treatment and benefit the patient of prostate cancer. The dietary influence is an important and elementary provision for patients suffering from prostate cancer and other prostate conditions in particular and for a healthy life with longevity in general. Various foods for prostate cancer during the treatment, post the treatment and to be considered in general for a better health are discussed.

Keywords: Prostate Specific Antigen (PSA); Carcinoma of the Prostate; Epidemiology; Statistics of prostate cancer; Foods for prostate cancer

Methodology

The primary methodology incorporates the secondary data coalition from various journals from sources like the internet data collaboratively has been studied and arranged for a prognosis to diagnosis basis for age-based conundrums of prostate cancer, its symptoms, its treatment options and treatment methods. The methodology also involves the study of varying stage, age, and therapy that based on references from the innumerable studies that were conducted throughout the last two-three decades. The data is also incorporated to represent the Indian condition of males suffering from Prostate cancer. The condition has been discussed as a clinical entity and the chances and trends of mortality are

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also discussed. The generalities of the condition differing in the two competing age groups have been the focal point of discussion here.

Research Findings

Research-based results for prostate cancer conditions in males from varying age

During the late 1980s to late 1990s, a research was conducted that included comprehensive sample medical records of 477 men who underwent radical prostatectomy^[2]. Age, ethnicity, preoperative PSA, clinical and pathological stage, margin and seminal vesicle involvement, and recurrence were compared between 79 men age 50 years or younger (study group) and 398, 51 to 69 years old (comparison group). Disease-free survival rates were compared using Kaplan-Meier and Cox regression techniques^[2]. As a result, there were 6 (7.6%) recurrences in the study group (79) and 107 (26.9%) in the comparison group (398). The disease-free survival curves were significantly different (log-rank $p = 0.010$). Age remained a significant prognostic factor (Wald $p = 0.033$) in multivariate Cox regression analyses that controlled for race, clinical and pathological stage, and pre-treatment PSA. Similar results were found when the comparison group was limited to 116 patients 51 to 59 years old (log-rank $p = 0.034$, Wald $p = 0.069$). Conclusively, these data suggest that patients in the PSA era who underwent radical prostatectomy and were age 50 years or younger have a more favorable disease-free outcome compared to older men^[2].

Influence of stage, grade and therapy in men less than 45 years old with Prostate cancer

An analysis was conducted with the patients with histologically proved adenocarcinoma of the prostate to determine the natural history of prostatic cancer in men less than 45 years old. The mean age of the patients was 41 years (range 36 to 44 years). The analysis had varying results. At presentation 5 patients were found asymptomatic, 5 had voiding symptoms, 3 had bone pain, 3 had hematuria and 1 had testicular pain. They were followed up from 19 to 270 months, with a mean of 111 months^[3]. Six patients with clinical stage B disease at diagnosis underwent radical retropubic prostatectomy. These patients had survived for a projected 10 and 15-year survival rates of 100 and 82 percent, respectively. However, four patients with stage C disease had also died of prostatic cancer, with only 1 surviving for 204 months. Four patients with stage D that were analyzed, 3 had died within 13 months, while 1 was still alive at 48 months^[3]. Conclusively, no patient with a Gleason tumor score of 8 to 10 had survived for more than 13 months. Here, the severity is given a close look at, with patient age at presentation appearing to be less important than the clinical stage, histological grade or treatment modality in the prediction of the course of prostatic cancer. The projections and the analysis reports suggest that young men with localized disease at presentation should be treated aggressively and they should have survival rates comparable to actuarial expectancy^[3].

Increasing Indian trend in the incidence of prostate cancer

Among the several incidences collected as analytical assessment and several Indian registries suggest that incidence of prostate cancer and the mean annual percentage change has dramatically ranged between 0.14 - 8.6. Age-adjusted incidence

rates (AAR) of prostate cancer for the period 2005 - 2008 ranged from 0.8 (Manipur state excluding Imphal west) to 10.9 (Delhi) per 105 person-years. Age-specific incidence rates (ASIR) increased in all PBCRs especially after 55 years showing a peak incidence at +65 years clearly indicating that prostate cancer is a cancer of the elderly. MAPC in crude incidence rate (CR) ranged from 0.14 (Ahmedabad) to 8.6 (Chennai). Chennai also recorded the highest MAPC of 5.66 in ASIR in the age group of 65+. Estimated annual percentage change (EAPC) in the AAR ranged from 0.8 to 5.8 among the three registries. Increase in trend was seen in the 5 - 64 year age group cohort in many registries and in the 35- 44 age group metropolitan cities such as Delhi and Mumbai^[4].

Prostate cancer as a clinical entity in young men

The disease, prostate cancer is invariably related to older men. The condition is rampantly digressing in its trends and younger males are also entailed under this condition and critically severe too. The factors may be varying. According to Kathleen A. Cooney, MD, Professor of Internal Medicine and Urology at the University of Michigan, "*Early onset prostate cancer tends to be aggressive, striking down men in the prime of their life. These fast-growing tumors in young men might be entirely missed by screening because the time frame is short before they start to show clinical symptoms*"^[5]. The study that was recently conducted to determine the age-related propensities of the disease discusses that prostate cancer is generally related to a man is 55 years of age and if younger, then it is a distinct phenotype of the disease, and it should be treated and researched accordingly.

The research paper also included that, based on a review of studies of prostate cancer especially in younger men, the University of Michigan Comprehensive Cancer Center, found that more than 10% of prostate cancer cases occur in men in this younger age group, with the rest occurring in older men. The occurrence of the disease in men in the younger group increased by 5.7-fold, from 5.6 to 32 cases per 100,000 person-years, between 1986 and 2008, according to the authors, who added that the rise in cases in younger men cannot be entirely attributed to increased use of screening for the disease^[5]. The study clearly deduces that the disease differs in the younger population, compared to in older men, in three ways-

➤ The abstract of the authors mentions that "*Among men with high-grade and advanced-stage prostate cancer, those diagnosed at a young age have a higher cause-specific mortality than men diagnosed at an older age, except those over age 80 years. This finding suggests that important biological differences exist between early-onset prostate cancer and late-onset disease*"^[5].

➤ As mentioned above, the early onset of the disease can be aggressive and can also be entirely missed in the screening due to lesser symptomatic developments in the early age.

➤ In the cases when prostate cancer begins at an earlier age, it "*has a strong genetic component, which indicates that young men with prostate cancer could benefit from evaluation of genetic risk.*" In fact, in certain cases, such tests for diagnosing the condition have proven to perform better in younger men. In addition, the study also mentions that science could benefit from studying this younger cohort of men because their cancers are more likely to hold secrets about the genes associated with prostate cancer susceptibility and development^[5].

➤ These are the reasons that pose severe challenges to the patients with early age prostate conditions. The challenges are, however, accompanied with opportunities for scientific research and treatment development, for clinical and research communities. According to Kathleen A. Cooney, the “*Current data suggest that early-onset prostate cancer is a distinct phenotype—from both an aetiological and clinical perspective—that deserves further attention*”^[5].

The prognosis

The majority of men diagnosed with prostate cancer today have a favorable prognosis, with the most recent estimates for five and ten-year relative survival being 100.0% and 98.7%, respectively, based on data from men diagnosed between 1994 – 2009 in 17 Surveillance, Epidemiology, and End Results (SEER) registries^[6]. These estimates reflect the fact that the majority of prostate cancers are identified early in the natural history of the tumor when they can be treated with curative intent and advanced stage disease makes up only a small proportion of total diagnosis^[6].

Several clinical studies report no significant difference in survival across age groups or an improved prognosis in the youngest men after radical prostatectomy, brachytherapy or radiation therapy^[5]. However, other studies, based on cancer registry or other data point to consistently lower survival for the youngest patients worse than for all other age groups except men diagnosed at over 80 years. The data from the SEER cancer registries suggests, 28% of the population, reveal that recently diagnosed (1994 – 2008) men between 20 – 54 years have a 5-year relative survival of 98.0% whereas the survival of men diagnosed during the same period but aged 55 – 79 years was 100.0%. This is not a novel observation. The notion that early age at onset is associated with worse prognosis was common among physicians in the pre-PSA era^[7].

Prostate cancer as a clinical entity in old men

Most studies before the advent of PSA screening have suggested that Prostate cancer is a disease limited to older men. However, it is not the case. But with the advent of the screening process, a large number of old men also have been able to diagnose properly the exact nature of the condition and the malignancy. Besides PSA serum levels and Gleason score, age is considered to be a key prognostic factor in terms of treatment decisions. In men older than 70 years, treatment without curative intent may deprive the frail patient of years of life. Modern radical prostatectomy techniques are associated with low peri-operative morbidity, excellent clinical outcome, and documented long-term disease control^[8]. Thus, radical prostatectomy should be considered because local treatment of organ-confined prostate cancer potentially cures disease. The huge extent of PSA screening programs may lead to over-diagnosis of prostate cancer. Not every man who is diagnosed with prostate cancer will develop the clinically significant disease. This has led to the concept of expectant management for screen-detected, small-volume, low-grade disease, with the intention of providing therapy for those men with disease progression^[8].

Older age as a risk factor

The death ratio has fallen over the last decade, primarily as a result of improved screening and diagnosis, improved

treatments, and better risk assessment to guide therapy. Moderate incidence increases in the last decade are most likely attributable to wide spread PSA screening among men younger than 65 years. Prostate cancer incidence rates have leveled off in men aged 65 years and older^[8].

A study by the Defense Center for Prostate Disease Research indicated that the percentage of men older than 65 years diagnosed with prostate cancer decreased from 53% in 1990 to 27.8% in 1996 and remained stable thereafter. The number of patients diagnosed with prostate cancer who are younger than 60 years old increased from 18.6% in 1991 to 40.7% in 2000^[8].

The probability of developing prostate cancer increases from 0.005% in men younger than 39 years to 2.2% in men between 40 and 59 years and 13.7% in men between 60 and 79 years. The current life time risk of developing prostate cancer is 16.7%, for about 1 in 6 men^[8]. The probability of developing histological evidence of prostate cancer is even higher. Some more research data by Carter and others showed that 50% of men between 70 and 80 years of age showed histological evidence of malignancy. A lifetime risk of 42% for developing histological evidence of prostate cancer in 50-year-old men has been calculated. In men at this age, however, the risk of developing the clinically significant disease is only 9.5%, and the risk of dying from prostate cancer is only 2.9%^[8].

Treatment impacted by age

The high rise in the diagnosed cases of prostate cancer in the last two decades have majorly been attributed to increasing life expectancy as well as the current practice of screening by PSA blood tests. Gleason score is also considered one of the attributes for rising diagnosed cases; however, age is also considered an important prognostic factor in treatment decision-making. Observational studies of older men with early-stage disease have suggested conservative management as a viable option. A study conducted by Albertson and colleagues during 1971 and 1984, involved long-term outcomes of 767 men diagnosed with localized prostate cancer. The study aimed at analyzing the estimate survival rate based on a competing risk analysis. The sample of men between 55 and 74 years of age treated with either immediate or delayed hormonal therapy and followed for 10 to 20 years after diagnosis^[8]. During the observation time, most of these men died from prostate cancer; approximately one-third of the older men died from competing for medical hazards. The 20-year follow-up analysis of this cohort published by Albertson and coworkers clearly demonstrated that men with low-grade prostate cancer are at low risk for disease progression even after 20 years of watchful waiting or androgen deprivation therapy. Men with Gleason tumors were found to be at high risk of dying from prostate cancer. After 20 years, only 3 of 217 patients survived. Men with the moderate-grade disease have an intermediate cumulative risk of prostate cancer progression after 20 years of follow-up^[9].

These results are in compliance with earlier findings on the outcomes of prostate cancer patients depending on Gleason scores. Johansson and colleagues in 1997 published a 15-year follow-up analysis of a cohort of 642 prostate cancer patients who received no immediate therapy when diagnosed. Only 300 patients had organ-confined prostate cancer. Eighty-five of patients were younger than 70 years. Fifty percent showed well-differentiated tumors.

Chodak and associates evaluated 828 men who were managed expectantly in a series of non randomized trials. Median follow-up was approximately 6.5 years. Patients with poorly differentiated cancers had a 10-fold increased risk of death from prostate cancer as compared with men showing highly differentiated prostate cancer. These findings revealed that it is reasonable to withhold active therapy in elderly patients with well or intermediately differentiated prostate cancers, thus avoiding the associated risks and impact on quality of life^[10].

Making right decisions for treatment

Current expert guidelines for treatment of localized prostate carcinoma recommend potentially curative therapy for patients whose life expectancy is at least 10 years. Patients with limited life expectancy are more likely to die from health conditions other than prostate cancer. Men with a life expectancy of more than 10 years are more likely to die from progressive prostate cancer. Conservative management proved to be an acceptable treatment option for men with low-grade Gleason scores, clinically localized disease, and life expectancies of less than 10 years. Increasing age was described as a risk factor for receiving inadequate treatment for prostate cancer. Thus, older men have been shown to receive potentially curative therapy (radical prostatectomy or radiotherapy) less often than younger men. Radical prostatectomy is preferred treatment in men younger than 70 years, whereas radiation therapy is applied predominantly in patients older than 70 years. Conservative therapy such as watchful waiting or androgen deprivation by luteinizing hormone-releasing hormone analogs is preferentially applied in men older than 80 years. Watchful waiting or hormonal therapy is used to treat 82% of men older than 80 years^[11].

Age, clinical stage, PSA level, histological grade, and co-morbidities should be carefully balanced before making a treatment decision, especially in elderly men suffering from prostate cancer. In order to choose the appropriate option, patients should be selected for potentially curative treatment on the basis of age, remaining life expectancy, tumor grade, and co-morbidity. Various studies have demonstrated that potentially curative therapy of men with prostate cancer is applied less often in older men and men with significant co-morbidity. In contrast, 2 other studies failed to demonstrate any impact of co-morbidity on treatment decisions. Potentially curative therapy should be offered to those patients with the greatest potential to benefit^[11].

Undertreatment of elderly, choice-based treatment decisions

Schwartz and colleagues reviewed the treatment decisions and factors influencing them in a cohort of men with localized prostate cancer. Age, co-morbidity, and Gleason score were found to be independent predictors of suboptimal treatment. It was conclusively found that most men older than 70 years with moderately or poorly differentiated tumors and no to mild co-morbidity were given suboptimal treatment. Most of these men were undertreated, receiving watchful waiting therapy when potentially curative therapy could have been applied. With optimal treatment, clinical outcomes could have been improved^[12].

Prostate cancer is subjected to a detrimental impact on health and life quality of elderly men as well as the young patients. Healthy elderly men should be checked routinely by PSA measurements and undergo biopsy when PSA is elevated. There

is general medical agreement, men with life expectancies of less than 10 years are unlikely to benefit because of the long natural history of untreated localized prostate cancer and other age-based causes of death^[13]. Patients with poorly differentiated prostate cancers with localized tumors need an aggressive modality even at an older age. However, there are clinicians, who may be reluctant to offer aggressive treatment to older men because of an increased risk of short-term and long-term treatment-related adverse effects^[14]. But the treatment should be tailored according to the condition and life requirements of the patient. Urologists may also apply age thresholds for radical prostatectomy^[15].

The predilection for prostate cancer screening among health-care providers in general declines with increasing patient age but then persists for a small proportion of patients. A more selective screening practice is recommended for men older than 75 years. Medically, age does play a crucial factor in treatment preferences. Older patients have been found to be either less willing to sacrifice quality of life for prolongation of life or prefer surgery over conservative treatment even if no survival benefit can be expected because of the psychological impact of cancer and its life-threatening potency, all depending upon their personal view on their health vis. Future with a prostate condition.

As part of the correlation between hormones and prostate, many of the men treated by androgen deprivation therapy also reported side-effects like reduced sexual functioning before treatment and the additional decline during hormonal treatment^[16].

Food and Diet as a regulative measure to prevent and reduce the risk of Prostate Cancer

Food plays a vital role in regulating almost every process in the body. Diet and the kind of food intake one has, plays a leading role in germination, cultivation and even prevention of diseases that might be simmering to breakout eventually. Good nutrition may help reduce the risk of developing prostate cancer, slow progression of the disease and prevent aggressive disease. Better food and a healthy diet make preventive layers against prostate related issues, as severe as Prostate cancer and can also help expedite the treatment results towards positive sides. The further discussion contains a section on diet and healthy food that helps to prevent disease risk and reduce the severity in the affected body.

Experts believe our dietary choices account for the vast majority of prostate cancer cases. So it becomes important to evaluate the dietary choices to keep prostate risks at bay. Scientists have slowly uncovered a list of cancer super foods and supplements to optimize in your diet while also discovering foods and supplements that could actually contribute to cancer risk and aggression.

As part of a healthy diet plan, your food choices should primarily be plant-based, inclusive of fruits and vegetables, high fiber, low fat, and lesser simple sugars. But in the case of protecting prostate concerning diseases like prostate cancer and improve metastasis, a special variety of foods need inclusion in the diet. Fruits and vegetables contain large amounts of cancer-fighting and inflammation-reducing substances like vitamins, polyphenols, antioxidants, minerals and natural fiber. The inclusion of cruciferous vegetables like broccoli, cauliflower, Brussels sprouts, kale, and cabbage is important as they have phytochemicals that reduce Oxidative stress or oxygen free radi-

cals in the body which means a lower risk of prostate cancer and its aggression. Carrots are a rich source of nutrients and contain antioxidants beta-carotene and falcarninol that reduce the risk of cancer. Tomatoes have abundant lycopene which attacks free radicals helping the body lower the risk of prostate cancer and its aggression. Mushrooms, pomegranates, grapes, lemon and citrus fruits, avocados, pepper, jalapenos, apples, and berries are a great source of cancer-preventing foods^[16].

Apart from increased intake of fruits and vegetables, reduced intake of animal protein is suggested by the doctors to lower the aggression of prostate cancer. Plant protein, green tea, whole grains, limited sugars, organic foods are generally recommended by most of the cancer specialists in this case^[16].

During cancer dietary recommendations include- watching the calorie intake, to begin with. Essential nutrients the body needs, such as protein, carbohydrates, fiber, vitamins, minerals, phytonutrients, such as carotenoids, and water will improve the ability to recover faster during the treatment. Coupled with a regular walk is considered an accelerating mechanism for the patient to recover^[16].

Food safety as an important factor to deal with side effects

Patients under treatment of prostate cancer need to be excessively careful of contracting any kind of infection as their low immune system is prone to infections. Wash your hands before and during the handling and preparing of food. Wash vegetables and fruit thoroughly before eating them. Handle and store food appropriately. Keep raw meat away from other foods when cooking. Eat thoroughly cooked foods. Avoid drinking unpasteurized beverages, such as unpasteurized cider, raw milk, and fruit juices. Milk should be especially not past expiry date^[16].

Post-cancer nutrition includes a diet of fresh fruits and vegetables and unprocessed, low-fat foods that help regaining strength after prostate cancer treatment. Recent research suggests that making healthy food choices in your survivorship may lower your risk of recurrence and help you live longer. According to many experts, foods recommended during prostate cancer are also recommended post the treatment unless the doctor treating you has special recommendations to make^[17].

The diet patterns are however country and region-specific, many experts believe that countries with more red meat consumption have more men prone to prostate concerning issues than the countries with more plant-based diets. However, not much research has been able to provide the basis for this hypothesis. Scientists are doing deep research on it though. The diet recommendation made by experts that are mentioned above are, therefore, very generic and suitable for most of the cases^[18].

These diet patterns are also applicable for almost all the age brackets prone to or suffering from Prostate conundrums. However, according to William Faloon, Cancer cells are present in the prostate glands of many aging men, yet only one in six men are ever diagnosed with prostate cancer. If one looks at what is required for a single cancer cell to develop into a detectable tumor, it becomes obvious that natural barriers exist to protect men against full-blown cancer. Unfortunately, dietary choices in the Western world circumvent the body's protective barriers. The end result is that most men unwittingly provide, through their food choices, biological fuel for existing prostate cancer cells to propagate and metastasize^[19].

Conclusion

Reviewing the analysis of incidences, treatment methods, age discrepancies side-effects of prostate cancer in both young and old men, various conclusions based on various researches from the secondary data source, the internet, and journals, some conclusions have been drawn. It needs to be stated at the beginning of the conclusive arguments only, that due to lack of primary evidence the scope of robust conclusions has been compromised and the research findings are open to further discussion. Comparisons, however, have not been made directly between the old and the young age groups. Although they have been put against each other at various times to bring direct correlation between the patient and the condition depending on their age and malignity. This paper focuses on the general observations found during the last two decades in the field of Prostate cancer and its age-based treatment methodologies, the first age group discussed is the younger patient demography. The findings have been as follows-

The incidence of prostate among the youngest group of at-risk men has increased sharply over the last two decades, making early-onset prostate cancer an important emerging issue for public health. Increased screening activity in young men 55 years of age and under may account for some, but not all of the increase in early-onset cases. Young men diagnosed with advanced higher grade prostate cancer may have a distinct clinicopathologic form of prostate cancer with more aggressive progression to disease-specific death than similar stage and grade prostate cancer in their older peers.

Men diagnosed with early-onset prostate cancer are likely to have a greater genetic risk of prostate cancer than older cases, making this group an especially rich resource for investigating genetic susceptibility to prostate cancer. Various features of early-onset prostate cancer present unique opportunities for prostate cancer treatment and clinical research. Susceptibility of inheritance of prostate cancer plays a greater role in prostate cancer diagnosed in younger men than in older men and may indicate a richer group of cases for cancer susceptibility gene discovery. In addition, prostate cancer in the youngest group of men may also lead to further understanding and identification of the role of otherwise rare alleles, such as HOXB13 mutations and possibly others with pleiotropic phenotypes that may contribute more to the development of disease in younger men. Finally, because the majority of men diagnosed at younger ages tend to have a lower grade, organ-confined tumors, they are likely to represent a unique group of cancer survivors who will experience any morbidities that result from the treatment of their cancer for a longer period of time than their older peers. Since early-onset prostate cancer is enriched for genetic compared to environmental risk factors, future research focusing on these uncommon cases has the opportunity to identify additional risk alleles that may help improve our understanding the etiology of this cancer. Unique challenges have been put across especially in elderly men. There is an urgent need to predict more accurately its natural history and growth characteristics in order to avoid unnecessary treatment. At present, clinical criteria such as PSA serum levels, DRE, and transrectal ultrasound provide the best way of determining the presence of a small-volume disease. Careful selection and monitoring of older men with small volume cancers may provide a reasonable alternative to treatment

of all screen-detected cancers. New approaches to managing prostate cancer in older men are necessary to decrease health-care costs and morbidity and reduce unnecessary therapy.

Declaration of interest Policy: Here by the authors also declaring that there is no conflict of interest.

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