Original Article

Prostate cancer: Relationship between vascular diameter, shape and density and Gleason score in needle biopsy specimens

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Abstract

Background: Tumor growth requires expansion and development of vascular network. An increase in Gleason score is representative of an increase in tumor invasion and extent. In this study, the relationship between Gleason score and vascular characteristics of needle biopsy samples in prostate cancer patients has been evaluated.

Materials and Methods: We evaluated vascular characteristics including density and size of vessels; and percentage of vessels with irregular shape in 62 cancer-positive samples obtained by prostate needle biopsy under ultrasound guide, and compared them to Gleason score.

Result: Gleason scores of 23 patients were ≤6; Gleason scores of 18 patients were 7 and 21 patients had their Gleason score from 8 to 10. An increase in Gleason score was associated with increased vascular density ($P < 0.0001$), increased percentage of vessels with irregular shape ($P < 0.02$) and decreased average vascular diameter ($P < 0.015$), from which the relationship with vascular density was clearer and more evident.

Conclusion: Vascular morphological characteristics can be representative of angiogenic potential of prostate cancer which is required for tumor progression. As Gleason score can prognosticate the behavioral characteristics of prostate cancer in future, vascular characteristics may also be able to express tumor behavior. With attention to vascular characteristics in biopsy samples and apart from Gleason score, we may also be able to divide patients into other subtypes in a way being helpful for the establishment of treatment plan.

Key Words: Gleason score, prostate cancer, vessel density

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INTRODUCTION

Biologically, prostate cancer is heterogeneous. Many of localized cancers, even without treatment, represent a slow growth,[1,2] while, in spite of local treatment, some patients who seem to have organ-limited cancer may become affected by metastases.[3,4] Understanding the molecular characteristics leading to progression of prostate cancer is of particular importance.

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One of the elements that can be applied in prognosticating the outcome of prostate tumor is Gleason score (GS) in needle biopsy samples. Many studies have shown that with an increase in GS, the chance of progression, recurrence and metastasis formation increases, even after local treatment.[5] This has to be considered for treatment planning.

Angiogenesis is one of the ways for tumor progression. Forming vascular network by delivering growth factors, nutrients and oxygen plays a pivot role in growth of solid tumors.[6] Also, angiogenesis increases the possibility of metastasis formation, since it causes tumoral cells to reach the vascular system. Continuance of tumor growth requires a vascular network which is primitive in terms of morphology, function and its formation;[7] however; angiogenesis is dependent on the host vascular system.

In several tumors, expansion of angiogenesis has been associated with increased risk of tumor growth and invasion[8,9] and decreased survival.[10] In prostate cancer, it is shown that an increase in micro vascular density is predictive of poorly differentiated cancers[11] and biochemical recurrence after treatment.[12,13] However, there are a few studies considering the morphologic features of angiogenesis and in none of them it's correlation with GS has been evaluated.[14] Quantitative and qualitative evaluations of angiogenesis and its relationship with GS in prostate cancer biopsy samples can provide an opportunity for dividing prostate cancer into biological subtypes and also express and reinforce new aspects of treatment.

MATERIALS AND METHODS

During a 9-month period, 62 patients with positive needle biopsy for prostate cancer were entered into this study. None of the patients had undergone pelvic radiation. Twelve core samples from right apex, right mid zone, right base, left apex, left mid zone and left base (2 samples from each one) were taken trans rectally, under local anesthesia and ultrasound guide with a semi-automatic 18 gauge needle, and samples were delivered to a pathologist. After hematoxylin and eosin staining, GS of the cancer was determined. To study the vascular characteristics and for displaying vascular endothelial cells, Slides were stained using monoclonal antibodies against CD34 and immunohistochemistry method. Then, from the two grades of cancers occupying the most volume of cancer cells among slides, 10 fields were chosen; shape, number and diameter of observed vessels under high magnification of optical microscope (× 400) were recorded. Vessels, in terms of shape, were divided into two groups of regular or rounded and irregular or jagged and the percentage of vessels with irregular shape over total vessels was calculated. The number of vessels was determined and vascular density was calculated by dividing the total number of vessels by 10. Lastly, diameters of vessels were determined in these 10 fields, in micrometer, and the average of them was calculated. This method is similar to Mucky and Peony, with little variation.[15] The relationship between diameter, shape and density of vessels and GS was evaluated.

All data were analyzed by statistical software "SPSS 18", and Pearson correlation test, One-Way analysis of variance and Duncan were applied for determination of the relationship between diameter and density of vessels.

RESULT

Sixty two patients, with the mean age of 72.6 and the mean PSA of 34.06 mg/ml, entered the study. GS of 23 patients was ≤ 6; GS of 18 patients was = 7 and 21 patients had their GS from 8 to 10. Patients had the average vascular density of 59.9, the average percentage of vessels with irregular shape of 49.7 and the average vessels diameter of 24.4 micrometers. An increase in GS was associated with increase vascular density; the vascular density was 41.7 for GS ≤ 6 and 66 for GS = 7 and 74.5 for GS = 8-10. This increase was statistically significant (P value < 0.0001). By increasing in GS, the average vascular diameter decreased in a way that the average vessels changed to 25.4 micrometer for GS ≤ 6 and 23.9 micrometer for GS = 7-23.7 micrometer for GS = 8-10. This decrease in diameter was statistically significant (P value < 0.02). The percentage of irregular vessels increases in association with GS; they were 45.5, 51.3 and 52.9% for scores under 6, 7 and 8-10, respectively. This increase in percentage of irregular vessels was also statistically significant (P value < 0.015). Among the above mentioned parameters, the most significant correlation was between the GS and vascular density.

DISCUSSION

Considering the fact that an increase in GS is related to worse prognosis and increased biochemical recurrence in treated and untreated patients,[5] we can conclude that increased vascular density and percentage of vessels with irregular shape and decreased diameter of vessels in biopsy samples such as GS is probably associated with poor prognosis. In a study conducted by Lofdei Mucci *et al.*, in 2009, the relationship between shape, diameter and vascular density and metastasis rate

and extra capsular extension in samples obtained by radical prostatectomy has been evaluated and it has been determined that increased vascular density and irregularity and decreased diameter of vessels, regardless of stage and tumor grade, was related to increased metastasis and biochemical recurrence.[15] Also, several studies have shown the same subject,[11,12] so we can be hopeful that vascular characteristics in prostate biopsy sample can estimate the outcome, recurrence rate and tumor expansion after local treatment and surgery. Our findings in this study on vascular morphology and its structure support angiogenesis importance in progression and prognosis of prostate cancer. They may also sustain the theory that progression of disease is due to immediate formation of smaller and more malformed neovasculars in tumor.[16,17] However, all vessels available in the sample are not considered as new ones but as an indicator for neoangiogenesis, since a number of these vessels have been already existed.

One of the prominent features is that vascular characteristics and their relationship with GS have been studied before any treatment. Therefore, according to the fact that an increase in vascular density seems to be associated with increased GS and probably increased disease recurrence and progression rates, we can conclude that if a patient didn't fall into the intended group (regardless of other parameters such as GS, Stage, etc.), he would better to be chosen to a lesser extent for conservative treatments such as watchful waiting and to be under more aggressive treatments from the first stages. However, the relationship between vascular characteristics in biopsy samples and metastasis and recurrence rates after definite treatment of prostate cancer is probably required to be considered in other studies in order for more information to be obtained on this relationship.

One of the limitations of this study was our inability to use computer techniques and software to evaluate the slides and immunohistochemistry characteristics of the vessel so we had to use manual methods and experience of the pathologists.

Moreover, empirical studies have suggested that angiogenic treatments may either normalize or decrease the vascularity of tumor which can consequently prevent disease from progress.[17] Findings of the present study can also fall effective in approval of manufacturing anti-vascular drugs.

Finally, the evaluation of vascular structural characteristics may be useful for the study of neoangiogenesis rate and shape, size and density of vessels may be considered as markers for differentiation between aggressive and indolent tumors.

CONCLUSION

The study of vascular morphological characteristics in prostate biopsy samples is, related to GS, and may be useful for the establishment of treatment plans in future.

REFERENCES

1. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. JAMA 2005;293:2095-101
2. Johansson JE, Andrén O, Andersson SO, Dickman PW, Holmberg L, Magnuson A, *et al*. Natural history of early, localized prostate cancer. JAMA 2004; 291:2713-9.
3. Bill-Axelson A, Holmberg L, Ruutu M, Häggman M, Andersson SO, Bratell S, *et al*. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med 2005; 352: 1977-84.
4. Porter CR, Kodama K, Gibbons RP, Correa R Jr, Chun FK, Perrotte P, *et al*. 25-year prostate cancer control and survival outcomes: A 40-year radical prostatectomy single institution series. J Urol 2006; 176:569-74.
5. William J Catalona, Misop Han. Defnitive Therapy for localized prostate cancer: An overview. In: Alan J Wein, editor. Campbell-Walsh Urology. New York: McGraw-Hill; 2012. p. 2772-85.
6. Folkman J. Angiogenesis in cancer, vascular, rheumatoid and other disease. Philadelphia, PA: Lippincott; 1997: *3075-3085.*
7. Fukumura D, Jain RK. Tumor microvasculature and microenvironment: Targets for anti-angiogenesis and normalization. Microvasc Res 2007; 74:72-84.
8. Folkman J: Tumor angiogenesis: Therapeutic implications. N Engl J Med 1971; 285:1182-6.
9. Hanahan D, Folkman J. Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. Cell 1996; 86:353-64.
10. Weidner N, Semple JP, Welch WR, Folkman J. Tumor angiogenesis and metastasis: Correlation in invasive breast carcinoma. N Engl J Med 1991; 324:1-8.
11. Weidner N, Carroll PR, Flax J, Blumenfeld W, Folkman J. Tumor angiogenesis correlates with metastasis in invasive prostate carcinoma. Am J Pathol 1993; 143:401-9.
12. Borre M, Offersen BV, Nerstrøm B, Overgaard J. Microvessel density predicts survival in prostate cancer patients subjected to watchful waiting. Br J Cancer 1998; 78:940-4.
13. Silberman MA, Partin AW, Veltri RW, Epstein JI. Tumor angiogenesis correlates with progression after radical prostatectomy but not with pathologic stage in Gleason sum 5 to 7 adenocarcinoma of the prostate. Cancer 1997; 79:772-9.
14. Albertsen PC, Hanley JA, Barrows GH, Penson DF, Kowalczyk PD, Sanders MM, *et al*. Prostate cancer and the Will Rogers phenomenon. J Natl Cancer Inst 2005; 97:1248-53.
15. Mucci LA, Powolny A, Giovannucci E, Liao Z, Kenfield SA, Shen R, *et al*. Prospective study of prostate tumor angiogenesis and cancer-specific mortality in the health professionals follow-up study. J Clin Oncol 2009; 27:5627-33.
16. Vaupel P, Kallinowski F, Okunieff P. Blood flow, oxygen and nutrient supply, and metabolic microenvironment of human tumors: A review. Cancer Res. 1989; 49: 6449-65.
17. Jain RK. Normalization of tumor vasculature: An emerging concept in antiangiogenic therapy. Science 2005; 307:58-62.

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