Venyo AKG. (April 2017). A Review of Carcinoma of The Prostate Gland in the younger age group: An Update. Jour Of Med Sc & Tech; 6(2); Page No: 136 – 151.

RA Publications
Journal of Medical Science & Technology

Review article Open Access

A Review of Carcinoma of the prostate gland in the younger age group: An Update

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Abstract

Carcinoma of the prostate gland is very common globally and majority of such tumours had been diagnosed in older men and hence many clinicians may be unfamiliar with the biological behaviour of the disease in the younger age group. Literature obtained from 39 references had revealed that more and more cases of carcinoma of the prostate gland are now being diagnosed in the younger age group. Cancer Research UK had documented that between 2011 and 2013, 474 cases of carcinoma of the prostate gland (1.06%) had been reported in males in the United Kingdom whose ages had ranged between 0 years and 49 years out of a total of 44,833 cases of carcinoma of the prostate gland reported in all age groups within the United Kingdom. In some cases of carcinoma of the prostate gland involving the younger men there had been a family history of the disease. A large number of cases of carcinoma of the prostate gland diagnosed in the younger age had been tumours of low-grade and low-stage which had tended to be associated with good prognosis in the long term. On the other hand carcinomas of the prostate gland that are diagnosed in younger men as higher staged/advanced tumours had tended to be associated with poorer long-term prognosis in comparison with similar higher-staged tumours in older men. Perhaps early detection of carcinoma of prostate in younger men by means of serum PSA testing of men with a family history of carcinoma of prostate and or other malignancies might help detect more prostate carcinomas at a lower stage which would enable clinicians guide the men regarding all the treatment options to enable the patients opt for the best opinion of treatment of their choice including active surveillance and curative treatment option of their choice. Younger men who are diagnosed with high-staged / advanced carcinomas of the prostate should be encouraged to enter a multi-centre trial that would identify treatment options that would hopefully improve the long-term survival of their type of disease.

Key Word: Carcinoma of prostate; adenocarcinoma of prostate; active surveillance, radical radiotherapy, brachytherapy, radical prostatectomy; hormonal therapy; Serum prostate-specific antigen; chemotherapy.

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Received: December 20, 2016 Accepted: March 1, 2017. Published: April 20, 2017.

Introduction

Primary adenocarcinoma of the prostate gland is a very common malignancy that is encountered globally year in year out and it tends to be associated with lots of morbidity and mortality. Other types of malignant neoplasms on rare occasions affect the prostate gland and these tumours tend to exhibit biological behaviours which tend to differ from the biological behaviour pattern of the classic and more common adenocarcinoma of the prostate gland. Some of these rare types of malignancies of the prostate gland include: small cell carcinoma of the prostate gland, [1] leiomyosarcoma of the prostate gland, [2] rhabdomyosarcoma of the prostate gland, [3] lymphoepithelioma-like carcinoma of the prostate gland, [4] synovial sarcoma of the prostate gland, [5] angiosarcoma of the prostate gland, [6] sarcomatoid carcinoma (carcinosarcoma) of the prostate gland, [7] fibrosarcoma of the prostate gland, [8] lymphoma of the prostate gland, [9] squamous cell carcinoma of the prostate gland. [10] These rare malignancies of the prostate gland do not

tend to be associated with raised serum levels of prostate-specific antigen (PSA); hence serum PSA level is not relevant to the diagnosis and follow-up of patients who have these malignancies. On the other hand generally adenocarcinomas of the prostate gland tend to be associated with raised serum levels of PSA. Adenocarcinoma of the prostate gland tends to affect older men more commonly; nevertheless, some young men occasionally are also affected by adenocarcinoma of the prostate gland. With the advent of increasing use of serum prostate-specific antigen tests men are being diagnosed as having adenocarcinoma of the prostate gland at an earlier age. Additionally, there has been the trend to investigate men with a family history of adenocarcinoma of the prostate gland to detect adenocarcinoma of the prostate gland at an earlier age when hopefully the carcinoma would be localized and amenable to treatment options of curative intent to enable such patients live longer. It is also known that not all adenocarcinomas of the prostate gland are aggressive and lead to death and based upon this it would be argued that some patients are undergoing overenthusiastic aggressive treatments that could be adjudged to be unnecessary and associated with lots of morbidity that affect the quality of life of these patients. A number of questions may be asked regarding the detection of adenocarcinoma of the prostate at an earlier age and some of these questions include:

- Would the detection of adenocarcinoma of the prostate gland at an earlier age, necessarily be associated with prolonged survival without necessarily interfering with or impairing the quality of lives of such patients over a longer period of the life span of such patients?

- With regard to men whose adenocarcinomas are diagnosed at an earlier age which ones should undergo active surveillance and which patients should immediately undergo treatment of curative intent.

- What should be done with regard to minimizing impairment of the quality of life and sexual lives, as well as psychological trauma sequels of young men who are diagnosed as having adenocarcinoma of the prostate gland at an early age?

This paper which has been focused mainly on adenocarcinoma of the prostate gland because other types of malignancies of the prostate gland are rare is divided into two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some reported cases and studies related to carcinoma of the prostate in the younger age group.

Method

Various internet data bases were searched including: Google, Google Scholar, Educus, and PUB MED to search for literature on Carcinoma of the prostate gland affecting the younger age group. The search words that were used included: Carcinoma of the prostate gland in the younger age group, carcinoma of the prostate in young men, adenocarcinoma of prostate in younger men, prostate cancer in younger men, and prostate cancer in the younger age group. Thirty nine references which contained literature relating to case reports, case series, studies and statistical documentations on carcinoma of the prostate gland that related to the younger age group and at times in correlation with all age groups were used to write the literature related to various aspects of carcinoma of the prostate gland in the younger age group

Literature Review

(A) Overview

General comments on world-wide carcinoma of prostate: estimated incidence, mortality, and prevalence in 2012.

- It has been documented that more than 1.1 million cases of carcinoma of the prostate gland had been recorded globally in 2012 which would account for approximately 8% of all new cases of carcinoma and 15% of cases of carcinoma in men. [11]

- It has been stated that carcinoma of the prostate gland is the 4th most common cancer that occurs in men. [12]

- Out of the estimated 1.1 million men globally that were diagnosed in 2012 as having carcinoma of the prostate gland which accounted for 15% of carcinomas diagnosed in men, almost 70% of the cases (759,000) had been reported in more developed regions. [12]

- Other salient points on global data related to carcinoma of the prostate gland include: [12]

  - The incidence of carcinoma of the prostate gland tends to vary more than 25-fold globally; the rates of carcinoma of the prostate gland are highest in Australia/New Zealand and North America (ASR

111.6 and 97.2 per 100,000 respectively) and Western and Northern Europe, in view of the use of prostate-specific antigen (PSA) testing and subsequent prostate biopsy had become wide spread in those regions. The incidence rates of carcinoma of the prostate gland, adenocarcinoma of the prostate had become wide spread in those regions. The incidence rates have also been relatively high in some less developed regions including the Caribbean region (79.8 per 100,000), Southern Africa (61.8 per 100,000), and South America (60.1 per 100,000). The incidence rates of carcinoma of the prostate gland remain low in Asian populations with estimated incidence rates of 10.5 per 100,000 and 4.5 per 100,000 in Eastern and South Central Asia.

o With an estimated 307,000 deaths globally in 2012 attributable to carcinoma of the prostate gland, carcinoma of the prostate gland is the 5th leading cause of death from cancer in men and this would constitute 6.6% of the total deaths in men. Because serum PSA testing tends to have much greater effect on the incidence of carcinoma of the prostate gland than on mortality due to the disease there tends to be less variation in the mortality rates globally (ten-fold from about 3 per 100,000 to 30 per 100,000) than is observed for incidence of carcinoma of prostate, with the number of deaths from carcinoma of the prostate gland larger in less developed than in more developed regions (165,000 and 142,000 respectively). Mortality rates generally tend to be high in predominantly black populations (Caribbean 29 per 100,000 and sub-Sahara Africa, ASRs 19 to 24 per 100,000). The mortality rates tend to be very low in Asia (2.9 per 100,000) and in South-Central Asia, for example, and the mortality rate tends to be intermediate in Americas and Oceania.

The incidence statistics of carcinoma of the prostate gland in the United Kingdom

J It has been stated that 47, 300 new cases of carcinoma of the prostate gland had been reported in the United Kingdom in 2013 [13] and that within the United Kingdom in 2013 carcinoma of the prostate gland did constitute 13% of all cases of cancer. Cancer Research UK had documented that greater than half (54%) of the cases of carcinoma of the prostate gland that were diagnosed within the United Kingdom 2011and 2013 were older than 70 years. Cancer Research UK furthermore had intimated that the incidence of carcinoma of the prostate gland within the United Kingdom since the late 1970s has been rising. [13]

The incidence of carcinoma of the prostate gland by age

It has been stated that the incidence of carcinoma of the prostate gland is strongly related to age of the patient and that the highest incidence rates of carcinoma of the prostate gland tend to be seen in older men. [13] A number of authors had reported that within the United Kingdom between 2011 and 2013, generally per year, greater than half of all cases of carcinoma of the prostate gland (54%) had been diagnosed in men who were 70 years old or older than 70 years. [14] [15] [16] [17]

J Cancer Research UK had documented that the age-specific incidence of carcinoma of the prostate gland tends to rise from about the ages of 50 to 54 years, and the incidence tends to peak within the 75 years to 79 years age group, but between the 80 years to 84 years age group the incidence of carcinoma of the prostate gland tends to drop and additionally, the incidence of prostate cancer again increases steadily in men older than 84 years until the 90+ age group [13]

J Cancer Research UK had documented that between 2011 and 2013, 474 cases of carcinoma of the prostate gland (1.06%) had been reported in males in the United Kingdom whose ages had ranged between 0 years and 49 years out of a total of 44,833 cases of carcinoma of the prostate gland reported in all age groups within the United Kingdom between 2011 and 2013. Based upon the small proportion of reported cases of carcinoma of the prostate gland in the younger age group in the United Kingdom, it would be understood that very few people would have the opportunity of managing carcinoma of the prostate gland in the younger age group in the United Kingdom and this would appear to be the case globally.

Mortality due to carcinoma of the prostate gland in the United Kingdom

J In the United Kingdom in 2014, 11,287 deaths had been attributed to carcinoma of the prostate gland and this constituted the second most common cause of cancer deaths in males in 2014 [13]

J Carcinoma of the prostate gland has been stated to be the 4th commonest cause of death attributable to cancer in the United Kingdom in 2014 [13]

- Reports related to deaths attributable to carcinoma of the prostate gland in the United Kingdom between 2012 and 2014 had shown that 6 out of 10 (about 57%) of the deaths each year had occurred in men who were 80 years old or older than 80 years but the highest mortality rate had been in men who were older than 90 years [13].

- Reports had also indicated that pursuant to the 1970s death rates attributable to carcinoma of the prostate gland in the United Kingdom had increased by about 21%; however, over the preceding decade mortality rates attributable to carcinoma of the prostate gland had decreased by greater than 13%. [13]. Furthermore it has been stated that in England deaths attributable to carcinoma of the prostate gland had not been associated with deprivation. [13]

- It has been stated that within Europe in 2012, it had been estimated that approximately 92,300 men had died of a cause attributable to carcinoma of the prostate gland and that deaths attributable to carcinoma of the prostate gland in the United Kingdom in 2012 had ranked as 15th in Europe. [13]

- It had been estimated that in 2012 globally more than 307,000 men would have died as a sequel of carcinoma of the prostate gland. [13]

- At the moment there is no way of knowing what the mortality rates due to carcinoma of the prostate would be if all the carcinomas of the prostate are detected at much earlier ages and the patients are offered treatment of curative intent. There is also no definite way of predicting categorically which patients tumours would never progress in the future and hence there is no way of knowing in advance those patients who would not require treatment for their prostate cancers because they would not die of a cause attributable to carcinoma of the prostate gland.

Carcinoma of the prostate survival in the United Kingdom

Cancer Research UK had summarized salient features of recent survival figures related to survival from carcinoma of the prostate gland as follows: [13]

- Cancer Research UK had documented that in England and Wales between 2010 and 2011, 84% of men who had carcinoma of the prostate gland had survived 10 years or longer. [13]

- About 9 in 10 (85%) of men, who were diagnosed as having carcinoma of the prostate gland between 2010 and 2011 in England and Wales had survived their disease for five years or more than five years. [13]

- Between 2010 and 2011 almost 95% (94%) of men who were diagnosed as having carcinoma of the prostate gland had survived for one year or for more than one year [13]

- Between 2009 and 2013 almost 95% of men who had been diagnosed as having carcinoma of the prostate gland and whose ages were between 50 years and 59 years or between 60 years and 69 years old had survived for five years or more than five years in comparison with two thirds of those who were diagnosed as having carcinoma of the prostate gland who were 80 years old or older than 80 years who had survived for five years or more than five years. [13]

- Within the United Kingdom over the preceding 40 years, there have been improvements in survival figures related to carcinoma of the prostate gland, perhaps as a result of serum prostate-specific antigen (PSA) testing. [13]

- In the 1970s one quarter of men who had been diagnosed as having carcinoma of the prostate gland did survive for more than 10 years with their disease; however, recently more than 8 out of 10 men survive for more than 10 years after they have been diagnosed as having carcinoma of the prostate gland. [13]

- All men who are diagnosed with carcinoma of the prostate gland at its earliest stage would survive their disease for a period of 5 years or more than 5 years in comparison with one third of men who are diagnosed as having carcinoma of the prostate gland at the latest stage. [13]

Risk for the development of carcinoma of the prostate gland

- It has been stated that generally the risk for a person to develop malignancy tends to be dependent upon a variety of factors and some of these include: age, genetic factors, exposure to risk factors and some of these risk factors may be associated with potentially avoidable lifestyle factors. [13]

- There are so far no clearly documented proven avoidable or preventable risk factors that have been linked to the development of carcinoma of the prostate gland [13]

- It has been stated that perhaps some factors could relate to a higher risk for the development of carcinoma of the prostate gland including occupational exposures (ionising radiation) and some medical conditions; however, there is no clear cut evidence in support of this suggestion [13]

- It has been suggested that certain types of foods and supplements may lower the risk for the development of carcinoma of the prostate gland but this has not been clarified or conclusively proven [13]

Prevention of carcinoma of the prostate gland

- It has been documented that generally carcinoma of the prostate gland has not been clearly linked with any preventable risk factors [13]; in view of this there are no clear cut ways of preventing the future development of carcinoma of the prostate gland in any man. [13]

Cancer diagnosis

- In the United Kingdom a two week wait is the commonest route by which patients are seen and investigated to establish diagnosis of carcinomas like in other countries [13]

- It has been documented that screening to detect cancer is the route by which the highest proportion of carcinomas of the prostate are diagnosed at an early stage. [13]
- Diagnosis of adenocarcinoma of the prostate tends to be made following pathological examination of specimens of prostate gland obtained via trans-rectal ultrasound scan biopsy, and trans-urethral resection of prostate. Raised serum levels of PSA and abnormal digital rectal examination of prostate generally alert the clinician in most cases to undertake prostate biopsies; however, incidentally histological examination of prostatic chips obtained following trans-urethral resection of prostate performed for a presumed benign prostatic hypertrophy may reveal carcinoma of the prostate in parts of the specimen. Histology reports obtained tend to give the Gleason score, the number of cores that contain the tumour, the percentage of the prostatic specimen that contain the adenocarcinoma, whether or not there is neurovascular permeation/ involvement, as well as if the tumour is another type of tumour within the prostatic specimen which would make the tumour a mixed malignant tumour.

Treatment and management

Chodak and Kim [18] had made the ensuing summations regarding the guidelines to the approach to the management of carcinoma of the prostate gland from the latest guidelines of the American Urological Surgeons Association (AUA) that had recommended that the first evaluation of and treatment discussion with a patient who has carcinoma of the prostate gland should focus on the following two factors: [19]

- The overall life expectancy of the patient, as determined by the patient's age, and co-morbidities, as well as the overall health status. [19]

- The biologic characteristics of the tumour, together with its predicted aggressiveness and behaviour. [19]

- The AUA guidelines had recommended that decisions relating to treatment should take into account the preferences of the patient for the various treatment options, with consideration of complications, adverse effects, relative efficacy, and quality-of-life issues. Health-related quality of life tends to be a particularly important concern for patients who have clinically localized carcinoma of the prostate gland. [19]

- Standard treatment options for clinically localized carcinoma of the prostate gland include the ensuing: [19]
  - Active Surveillance
  - Watchful waiting
  - Radical prostatectomy
  - Radiotherapy
  - Hormonal treatment

- Cryotherapy has also been used in the treatment of carcinoma of the prostate gland; however, there is lack of long-term survival studies. Other new treatment options that have been used include photon beam radiation and High-intensity focussed ultrasound but so far there are no long-term survival reports as well as no reports on the complications associated with these treatments. [19]
- With regard to locally advanced carcinoma of the prostate gland, radiotherapy together with androgen deprivation therapy (hormonal therapy) tends to be recommended generally; nevertheless, in some cases radical prostatectomy could be an appropriate alternative treatment to radiotherapy. On the other hand, a combination of external beam radiotherapy, brachytherapy, and hormonal therapy has been used in treating other cases; however, it is not known for certain whether or not this option of

treatment has more advantages over external beam radiotherapy and hormonal therapy alone but it tends to be associated with increased complications. [19]

- It had been iterated that metastatic carcinoma of the prostate gland tends to be rarely curable [20] In these sorts of cases management tends to be directed at symptomatic including pain control as well as attempts at slowing down further progress of the disease. [19]
- Various types of approaches to radical prostatectomy that are currently available include: nerve-sparing techniques, laparoscopic radical prostatectomy, robotic assisted radical prostatectomy, retro-pubic radical and perineal radical prostatectomy [19]
- Various types of radiotherapy techniques available at present for the treatment of carcinoma of the prostate include: Conventional external beam radiotherapy; Three dimensional (3D) conformal radiotherapy; Intensity modulated radiotherapy; Temporary and permanent brachytherapy; Proton-beam radiotherapy; Sterotactically-guided radiotherapy. [19]
- Hormonal treatment options include androgen deprivation therapy including surgical castration (orchidectomy), medical castration (luteinising hormone releasing hormone (LHRH) analogues or antagonists, anti-androgens and other androgen suppressants

Other treatment options available for advanced and locally advanced disease include Strontium and chemotherapeutic agents (for example Docetacel)

Whilst there has been evidence to suggest that younger men who had been diagnosed as having low grade-low stage (low-risk) disease had tended to have good long-term disease-free survival following treatment, evidence does exist which would indicate that younger men who have high-risk, high-stage disease tend to have inferior prognosis in comparison with older men who have high-stage high-risk disease which would indicate that available treatment options at the moment would tend to be ineffective in the treatment of younger men with high-stage disease. It would therefore appear that there is a great need for research into finding alternative treatment options that would improve the survival of younger men with high-stage, high-risk disease. Perhaps new forms of chemotherapy regimens would need to be developed through research

(B) Miscellaneous narrations and discussions from some reported cases

Salinas et al. [21] stated that carcinoma of the prostate gland has been considered a disease that tends to affect men who are older than 65 years; however, these days greater than 10% of newly diagnosed cases of carcinoma of the prostate gland in the United States of America tend to occur in men who are either 55 years old or younger than 55 years. Salinas et al. [21] also stated that early onset carcinomas of the prostate gland, namely, carcinomas of the prostate gland in men who are aged 55 years or less than 55 years tend to differ from carcinomas of the prostate gland that are diagnosed in the older age group in a variety of ways. Salinas et al. [21] further stated that in the first instance, with regard to men who have high-grade carcinoma of the prostate gland and advanced carcinomas of the prostate gland, patients who were diagnosed at a younger age tend to have a higher cause-specific mortality in comparison with those men who had been diagnosed at an older age with the exception of men who were greater than 80 years old and that the aforementioned findings would indicate that important biological differences exist between early-onset and late-onset carcinomas of the prostate gland. Secondly, Salinas et al. [21] intimated that early-onset carcinomas of the prostate gland tend to have a strong genetic component, which would suggest that young men who are diagnosed with carcinoma of the prostate gland could benefit from assessment of their genetic risk. Salinas et al. [21] also iterated that even though majority of men who are diagnosed with early-onset carcinoma of the prostate gland tend to be diagnosed with low-risk disease but the extended life-expectancy of these patients with low-risk disease tends to expose them to the long-term effects of disease progression which tends to lead to death from carcinoma of the prostate gland. Salinas et al. [21] are of the opinion that because of the aforementioned reasons, patients who are diagnosed with early-onset carcinoma of the prostate gland would tend to pose challenges and opportunities for research. They also indicated that current data on early-onset carcinoma of the prostate gland is a distinct phenotype with regard to clinical and aetiological perspectives which would warrant further attention and studies.

Lin et al. [22] reported their study of 318,774 individuals who were aged between 35 years and 74 years old who had been diagnosed with adenocarcinoma of the prostate gland between 1988 and 2003. Lin et al. [22] reported that the proportion

of patients who were aged between 55 years and younger and diagnosed with adenocarcinoma of the prostate gland had increased during the period of study from 2.3% between the years 1988 to 1991, to 9.0% between the years 2000 to 2003; the median age of the patients at the time of diagnosis had decreased from 72 years in 1988 to 68 in 2003. Lin et al. [22] also reported the following: Younger men were less frequently diagnosed with organ confined disease ($P < 0.001$) but less likely to be diagnosed. with high-grade carcinoma of the prostate gland ($P < 0.001$); Older men were likely not to receive any local therapy or external beam radiotherapy in comparison with young men ($P < 0.001$ for trends); With regard to men who have Gleason 5 to 7 tumours, the overall survival was found to become worse with advancing age; With regard to all age groups with high grade and stage tumours, the youngest men who were aged between 35 years and 44 years were found to be at the highest risk of all cause and cancer specific death. Lin et al. [22] made the following conclusions: Age at the time of diagnosis of carcinoma of the prostate gland was on the decline; Younger men tend to be more likely to undergo prostatectomy for carcinoma of the prostate gland, they tend to have lower grade carcinomas, As a group younger men with carcinoma of the prostate gland tend to have better overall and equivalent cancer specific survival at 10 years in comparison with older men; With regard to men who have high grade and locally advanced carcinoma of the prostate gland the youngest men tend to have a particularly poor prognosis in comparison with older men.

Sakr et al. [23] reported that they had evaluated 152 prostate glands from young men who were aged between 10 years and 49 years. Ninety eight of the prostate glands were from African American men and fifty four of the prostate glands were obtained from white men. Sakr et al. [23] did identify prostatic intraepithelial neoplasia in 0%, 9%, 20% and 44%, and small foci of histological carcinoma in 0%, 0%, 27% and 34% of the male patients in the second, third, fourth, and fifth decades of age respectively. Most of the cases of prostatic intraepithelial neoplasia were of the low-grade type. High-grade intraepithelial neoplasia, which was found in five prostates, was first identified within the fifth decade of life. All of the five cases did occur within prostate glands that did contain histological carcinoma of the prostate gland. Sakr et al., [23] reported that incidental carcinoma of the prostate gland was found with similar frequency in white and in Black men. The foci of carcinoma were of similar size with a tendency of carcinomas in black men to be multi-focal, particularly in those patients in their fifth decade of life. Sakr et al. [23] made the following conclusions: Intraepithelial neoplasia of the prostate gland and histological neoplasia of the prostate gland tend to be surprisingly common in young men of both white and black races; the evolution of intraepithelial neoplasia of the prostate gland and focal histological carcinomas of the prostate gland is not clear but it would appear to present several decades earlier than clinically detected carcinoma of the prostate gland; the natural history of carcinoma of the prostate gland must encompass many more years perhaps decades than had previously been realized; the initiating events that lead to clinically relevant carcinomas of the prostate gland likely do occur at a remarkably young age.

Kotsis et al. [24] reported their study which comprised of 257 men who had carcinoma of the prostate gland which was diagnosed at an age 55 years or less. Kotsis et al.[24] reported that: the median age of the patients at the time of diagnosis was 51 years (and this had ranged between 34 years and 55 years); almost half of the participants had reported a negative family history of carcinoma of the prostate gland; logistics regression analysis of data of the participants did show that having an affected father, an affected first-degree relative, or an affected relative of any relation, was each a significant predictor of well differentiated Gleason 6 or less carcinoma of prostate gland in comparison with moderately and poorly differentiated adenocarcinoma of the prostate gland Gleason 7 to Gleason 10 after adjusting for confounding variables; men who have an affected relative were nearly twice as likely to be diagnosed with well-differentiated carcinoma of the prostate gland in comparison with men who do not have a relative diagnosed with carcinoma of the prostate gland. Kotsis et al. [24] concluded that: family history of carcinoma of the prostate gland would appear to predict the development of well-differentiated tumours independently; the results of their study did show that men who did not have any family history of carcinoma of the prostate gland had higher-grade tumours which tended to be associated with a more serious prognosis. Kotsis et al. [24] recommended that future studies relating to early-onset carcinoma of the prostate gland should be aimed at identifying additional risk factors which could be relevant for men who do not have a family history of carcinoma of the prostate gland.

Khan et al. [25] did analyse data from 2897 men who had undergone retro-pubic radical prostatectomy from between April 1982 and September 2001. Khan et al. [25] compared pre-operative serum PSA level, clinical and pathological stage and biochemical recurrence between 341 men who were younger than 50 years-old and 2,556 men who were either 50 years-old or older. Khan et al. [25] compared disease free (serum PSA < 0.22 ng/ml) survival rates by means of Kaplan-Meier analysis. They compared pathological stage by using logistic regression analysis. Khan et al. [25] reported that men who were aged less than 50-years old did have pathological variables and 5-, 10-, and 15-year biochemical disease-free survival rates that were comparable with men who were aged between 50 years old and 59 years old (88%, 81%, and 69% versus 87%, 78%, and 71%, respectively). Nevertheless, they found that younger men did have lower incidence of extra-prostatic extension (25% versus 31% P < 0.02), seminal vesicle involvement (2% versus 6%; P < 0.03), and positive surgical margins (3% versus 9%; P < 0.03), a greater organ-confined disease rate (65% versus 49%; P < 0.001), and a trend towards greater,5-, 10-, 15-year biochemical disease-free survival rates, which on statistical analysis was not statistically significant, in comparison with men who were aged between 60 years old and 69 years old (84%, 74%, and 67% respectively; P < 0.09). Additionally, younger men apart from having a lower rate of extra-prostatic extension (25% versus 35%; P < 0.001), seminal vesicle involvement (2% versus 10%; P < 0.001), and positive surgical margins (3% versus 9%; P < 0.001), as well as a greater organ-confined disease rate (65% versus 36% P < 0.001), they did demonstrate significantly (P < 0.003) greater 5-,10-, and15-year biochemical disease-free survival rates in comparison with men who were aged 70-years-old or older (72%, 58%, and 58% respectively). Khan et al. [25] made the following conclusions from their study: Men who are diagnosed as having carcinoma of the prostate gland at an age younger than 50 years and who are candidates for radical retro-pubic prostatectomy do tend to have a greater probability of having organ-confined disease in comparison with older men; Additionally, younger men tend to demonstrate long-term cancer control rates in comparison with older men.

Rosser et al. [26] determined the biochemical failure rates in patients who were aged 60 years or younger.as well as in patients older than 60 years who had undergone external beam radiotherapy for localized carcinoma of the prostate gland or locally advanced carcinoma of the prostate gland. Rosser et al. [26] additionally evaluated prognostic factors within the two age groups. Rosser et al. [26] reviewed the medical records of 964 patients who had undergone full dose radiotherapy as the only modality of treatment for carcinoma of the prostate gland. All the patients had had follow-up serum prostate-specific antigen level studies at 3 to 6 monthly intervals pursuant to completion of their radiotherapy sessions. Biochemical failure was based upon the criteria laid down by the American Society for Therapeutic Radiology and Oncology Consensus Panel. Rosser et al. [26] reported that the median follow-up interval of all the patients amounted to 48 months. With regard to the results, Rosser et al. [26] reported that out of the 98 men who were aged 60 years or younger 46 men which constituted 47% of men younger than 60 years, had biochemical failure in comparison with 261 men out of 866 men older than 60 years which constituted 30% of men older than 60 years who had biochemical failure pursuant to having external beam radiotherapy. Rosser et al. [26] also reported that the 5- and 7-years biochemical disease-free survival rates were 55% and 47% in the case of the younger age men, in comparison with 65% and 59% in the case of men older than 60 years. Rosser et al. [26] intimated that the aforementioned biochemical disease-free survival rates were significantly lower in the case of the younger men (P = 0.017, and 0.027 respectively). Furthermore Rosser et al. [26] reported that multivariate regression analysis did show that with regard to the men who were 60 years or younger, the initial serum prostate-specific antigen level, Gleason score, and lower radiotherapy doses were predictive of biochemical failure. Rosser et al. [26] concluded that men who are diagnosed with carcinoma of the prostate gland at the age of 60 years or younger and who are treated by means of radiotherapy may be at a significant risk for the development of long-term biochemical failure. Considering the findings of Rosser et al. [26] a number of arguments could be considered. Firstly it would be argued that if men 60 years-old or younger are diagnosed with localized or locally advanced carcinoma of the prostate gland then they should be treated by means of radical radiotherapy plus neo-adjuvant treatment and or adjuvant treatment with hormonal therapy and or chemotherapy to see if this would lead to significant improvement of the biochemical disease-free survival or long-term overall survival. Since the answer is not known the only way clinicians would know the answer would therefore have to be through a large scale multi-

centre trial. It could also alternatively be argued that if the long-term biochemical disease-free survival rate following radical radiotherapy for localized carcinoma of the prostate gland or locally advanced carcinoma of the prostate gland is low then clinicians should consider an alternative treatment option in the form of radical prostatectomy with adjuvant therapy plus or minus neo-adjuvant therapy with the aim of improving the prognosis. In the absence of a consensus opinion on the best treatment for localized prostate cancer in the younger age group there is also a need for a large-scale multi-centre study which would compare various treatment options including radical prostatectomy alone, radical prostatectomy with neo-adjuvant / adjuvant radiotherapy, radical prostatectomy with adjuvant / neo-adjuvant hormonal treatment, radical radiotherapy alone, radical radiotherapy with neo-adjuvant / adjuvant hormonal therapy, and radical radiotherapy plus adjuvant / neo-adjuvant chemotherapy before guidelines could be formulated with regard to treatment of localized and locally advanced carcinoma of the prostate gland in the younger age group.

Smith et al. [27] reviewed the records of 477 men who had undergone radical prostatectomy between 1988 and 1997. Smith et al. [27] compared a number of factors which included: age, ethnicity, pre-operative serum prostate-specific acid (PSA), clinical and pathological stage, margin and seminal vesicle involvement, and recurrence between 79 men who were 50 years-old or younger called the study group and 398 men who were aged between 51 years and 69 years called the comparison group. Smith et al. [27] compared the disease-free survival rates between the two groups by using Kaplan Meier and Cox regression techniques. With regard to the results, Smith et al. [27] reported that: 6 patients (7.6%) had recurrences in the study group of 79 patients, and 107 patients (26.9%) in the comparison group of 398 patients had developed recurrences; the disease-free survival curves were found to be significantly different, (log-rank P = 0.010); age had remained a significant prognostic factor (Wald P = 0.033) in multivariate Cox regression analyses which controlled for race, clinical and pathological stage, and pre-treatment serum PSA; similar results were obtained in the situation when the comparison group was limited to men who were aged between 51 years old and 59 years old (log-rank P = 0.034, Wald P = 0.069). Smith et al. [27] concluded that the results of their study did indicate that the patients in the serum PSA era who had undergone radical prostatectomy either at 50-years-old or younger than the 50-years-old, would tend to have a more favourable disease-free outcome in comparison with older men.

Loeb et al. [28] undertook a study to assess the biochemical outcome of patients pursuant to radical prostatectomy (RP) which was aimed specifically at men whose ages had ranged between 30 years and 39 years in view of the fact that previous studies had suggested that carcinoma of the prostate gland in young men might be more aggressive. Loeb et al. [28] identified 42 men who were aged 30 years to 39 years, 893 men who were aged 40 years to 49 years, 4085 men who were aged between 50 years and 59 years, 3766 men who were aged between 60 years and 69 years, and 182 men who were 70 years old or older than 70 years, from a large database of 15, 899 radical prostatectomies that were carried out between 1975 and 2007. Loeb et al. [28] compared the clinical characteristics and clinical outcome of the men whose ages had ranged between 30 years and 39 years with the clinical characteristics and outcome of older men. With regard to the results, Loeb et al. [28] reported that 81% of the men who were in their thirties were found to have organ-confined disease in comparison with 62% of men who were 40 years old or older who had organ-confined disease. Loeb et al. [28] also reported that at a mean follow-up of 5 years, biochemical progression was found in 4.8% of men whose ages had ranged between 30 years and 39 years in comparison with 16.1% of men who were either 40 years old or older than 40 years who had biochemical progression (P = 0.055). Additionally, Loeb et al. [28] reported that the corresponding 5-year biochemical progression free survival estimates were 95% for men who were in their thirties and 83% in the case of men who were 40 years old or older than 40 years (P= 0.045). Multivariate analysis undertaken by Loeb et al. [28] did indicate that increasing age was a significant independent predictor of biochemical progression of disease. Loeb et al. [28] made the following conclusions: In contrast to earlier reports, their study had shown that men in their thirties did not have more aggressive disease but instead they did have more favourable pathological features and progression-free survival rates in comparison with their older counterparts. After controlling for other prognostic variables on multivariate analysis, being in the fourth decade of life was independently associated with a lower risk for the development of biochemical progression of disease. Their results did suggest that early aggressive treatment for these patients with a long life-expectancy is associated with favourable long-term biochemical outcomes.

Freedland et al. [29] stated that previous studies had suggested that younger men have lower prostate-specific antigen recurrence rates pursuant to radical prostatectomy; nevertheless, none of the previous reported studies had controlled for the year of study. Freeland et al. [29] examined data obtained from 1753 men who had undergone treatment by means of radical prostatectomy between 1988 and 2002 at 5 equal access medical centres. Freeland et al. [29] compared age, as a categorical variable according to the decade of life which included: 50-years-old or younger, 51 years to 60 years, 61 years to 70 years, and older than 70 years, with the clinical and pathological variables at radical prostatectomy, as well as the time to biochemical recurrence with the use of multivariate Cox proportional hazards model. With regard to the results, Freeland et al. [29] found that age was significantly related to the year of surgery, with more recently treated patients being younger than less recently treated patients ($P < 0.001$). After controlling for the year of surgery, the younger men were found to have smaller prostate glands, fewer high-grade tumours on histological examination of their biopsy specimens, and less lymph node metastases, but they tended to have a greater percentage of cores that had carcinoma. Freedland et al. [29] reported that multivariate analysis of the data revealed that the men who were 50 years old or younger did have significantly lower recurrence rates in comparison with older men. Additionally, the men that were older than 70 years had significantly higher prostate specific antigen failure rates in comparison with men who had been in the 51-years to the 70-years age group, and the men who were aged 50 years or less than 50 years. Freedland et al. [29] made the following conclusions: The average age of men undergoing radical prostatectomy had decreased with time and independent of this, young men tend to have more favourable outcomes following radical prostatectomy in comparison with older men. Continued screening in order to detect carcinoma of the prostate gland among younger men when it is most curable would appear warranted.

Rouprêt et al. [30] gathered data on men who were 50 years old or younger than 50 years old among 5880 patients who had undergone treatment for carcinoma of the prostate gland between 1994 and 2004. Rouprêt et al. [30] recorded the age, ethnic origin, clinical- presentation, family history of carcinoma of the prostate gland, pre-operative serum prostate-specific antigen level, treatment, Gleason score, 2002 TNM stage, surgical margin status, and disease progression. All of the patients had undergone radical prostatectomy as first-line treatment for localized carcinoma of the prostate gland (T1-T2N0M0) and negative lymph nodes. Rouprêt et al. [30] calculated the serum PSA-free survival of the patients. With regard to the results, Rouprêt et al. [30] reported that they had analysed data from 110 patients (1.9%), of whom 37 of the patients had been identified as having had familial cancer (33.6%), and 15 (13.6%) had hereditary cancer. A total of 85 patients (77.3%) had been treated by means of radical prostatectomy and out of these patients 39 (45.9%) had undergone open retro-pubic radical prostatectomy and 46 patients (54.1%) had undergone laparoscopic radical prostatectomy. The surgical margins were found to be positive in 11 patients (12.9%). The mean follow-up pursuant to the prostatectomy was 39.1 + / - 36.8 months and this had ranged between 4 months and 125 months. Nine of the patients (10.6%) did develop biochemical recurrence with serum PSA level, greater than 0.2 ng/ml. Longer serum PSA-free survival pursuant to surgery was found to be significantly associated with high-risk, and intermediate-risk patients with $P = 0.001$, and $P = 0.02$ respectively; nevertheless, this was not found with the surgical procedure ($P = 0.6$), and it was also not found with a family history of cancer ($P = 0.46$). Rouprêt et al. [30] made the following conclusions: Radical prostatectomy is an effective option of treatment for localized carcinoma of the prostate gland in patients who are younger than 50-years-old. Nearly half of their cases of carcinoma of the prostate gland in young men were forms of familial cancer. The detection of familial forms of carcinoma of the prostate gland is the key objective in early screening and in the timely identification of candidates for prostatectomy.

Edwards et al. [31] evaluated the contribution of BRCA2 mutations to early-onset carcinoma of the prostate gland by screening the complete coding sequence of BRCA2 for germ-line mutations, in 263 men who were diagnosed as having carcinoma of the prostate gland who were 55 years old or younger than 55 years. Edwards et al. [31] found protein-truncating mutations in six men (2.3%, 95% confidence interval 0.8% - 5.0%), and all of the mutations were found to be clustered outside the ovarian cancer cluster region. The relative risk for the development of carcinoma of the prostate gland by age 56 years from a deleterious germ-line BRAC2 mutation was 23-fold. Four of the patients who had mutations had no family history of breast or ovarian cancer. Edwards et al. [31] also identified twenty-two variants of uncertain

significance. Edwards et al. [31] concluded that their results did confirm that BRCA2 is a high-risk prostate cancer susceptibility gene which has potential implications for the management of early-onset carcinoma of the prostate gland in both patients and their relatives.

Tomokazu et al. [32] undertook a study to ascertain whether the disease characteristics and prognosis of stage IV carcinoma of the prostate gland treated by means of primary androgen deprivation differ between young and elderly patients. Tomokazu et al. [32] identified 3006 patients from the database of the Japan Study Group of Prostate Cancer whose data were included in the analysis according to the ensuing entry criteria: age of 75 years or less than 75 years and stage IV disease. The patients were divided into three stratified groups which included (a) young aged men who were aged 55 years or less than 55 years old, (b) middle aged men whose ages ranged from 56 years to less than 66 years, and (c) elderly men who were aged between 66 years up to more than 75 years. Their outcomes were analysed both within the age groups and according to whether or not there was metastasis. With regard to the results, Tomokazu et al. [32] reported the following: The proportion of lymph node metastasis was significantly higher in the young group in comparison with the elderly group (P = 0.007), and no significant differences were found in other factors among the age groups. The overall survival at 5 years in the young group was significantly worse in comparison with the middle age group and the elderly age group (26.6%, 59.7%, and 55.3%, respectively) in patients who had stage IV disease with metastasis, even though there was no difference among the age groups in patients who had stage IV disease without metastasis. Multivariate analysis did show that younger age was an independent strong prognostic factor in patients who have stage IV metastatic carcinoma of the prostate gland who are treated by means of androgen deprivation.

Tang et al. [33] stated that studies had shown that initial serum prostate-specific antigen level higher than the median in young men is predictive of a subsequent higher risk for the development of carcinoma of the prostate gland and that to their knowledge the aforementioned relationship had not been studied in patients that had been stratified by race. Tang et al. [33] retrieved from the prostate cancer database of their institution, a cohort of 3,530 black, and 6,118 white men who were aged 50 years or younger, whose serum prostate-specific antigen (PSA) levels were 4ng/ml or less than 4 ng/ml. Tang et al. [33] divided the patients into groups that was based upon prostate specific antigen levels: 0.1 – 0.6; 0.7 – 1.4; 1.5 – 2.4; and 2.5 – 4.0 ng/ml. Univariate and age-adjusted multivariate logistic regression analysis was undertaken to estimate the cancer RR in the aforementioned serum PSA groups. Tang et al. [33] calculated the prostate cancer rate at subsequent follow-ups. With regard to the results, Tang et al. [33] reported the following: The median serum prostate-specific antigen in black and white men was 0.7ng/ml at the age of 50 years or less than 50 years. The prostate cancer rate was found not to be significantly different in the groups with serum prostate-specific antigen less than 0.6ng/ml and 0.7 to 1.4ng /ml in black or white men. Black and white men whose initial serum PSA levels were in the 1.5 to 2.4ng/ml range did have a 9.3- and 6.7- fold increase in the age-adjusted prostate cancer RR, respectively. At up to 9 years of follow-up, Tang et al. [33] reported that initial serum prostate-specific antigen 1.5ng/ml or greater than 1.5ng/ml was associated with a gradually increased detection at follow-up in both black and white men. Tang et al. [33] concluded that an initial serum prostate-specific cut off point of 1.5ng/ml, could be better than median serum prostate-specific antigen level of 0.7ng/ml, to determine the risk for the development of carcinoma of the prostate gland in black and white men who are aged 50 years or less.

Merrick et al. [34] undertook a study to assess the biochemical progression-free survival in hormone naïve men who were aged 62 years or younger and who had organ-confined carcinoma of the prostate gland who had undergone brachytherapy with / or without supplemental-external beam radiotherapy. Merrick et al. [34] reported that between April 1995 and December 2000, 119 hormone-naïve men who were aged 62 years or younger had undergone permanent interstitial brachytherapy for T1b – T2cNxM0 (2002 American Joint Committee on Cancer) carcinoma of the prostate gland. None of the patients had seminal vesicle biopsy or pathological lymph node staging. The median follow-up of the patients was 5.4 years. Biochemical progression-free survival had been defined by either serum prostate-specific acid (PSA) level 0.4ng/ml or less after a nadir or by the American Society for Therapeutic Radiology and Oncology Consensus definition. None of the patients was lost to follow-up. The clinical, treatment, and dosimetric parameters that had been evaluated for biochemical progression-free survival did include:

age, clinical T stage, Gleason score, pre-treatment serum PSA level, risk-group, percentage of positive biopsies, isotope, supplemental external beam radiotherapy, prostate volume, brachytherapy planning volume, percentage of the target volume receiving 100%, 150%, and 200% of the prescribed dose, minimal percentage of the prescribed dose covering 90% of the target volume, and tobacco status. With regard to the results, Merrick et al. [34] reported the following: For the whole group, the actuarial 7-year biochemical progression-free survival rate was 96.1% and 98.3% for a PSA cut-off point of 0.4 ng / ml or less and for the American Society for Therapeutic Radiology and Oncology Consensus definition, respectively. By the use of a PSA biochemical control definition of 0.4 ng / ml or less, 93.1%, 100%, and 95.2%, of the low-risk, intermediate-risk, and high-risk hormone-naïve men had been free of biochemical progression. The median post-treatment serum PSA level for the biochemically disease-free group was noted to be 0.1 ng / ml in multivariate analysis studies. The analysis also showed that only the pre-treatment serum PSA level did predict the biochemical outcome. Merrick et al. [34] concluded that hormone-naïve patients who are 62 years old or younger than 62 years have a high probability of 7-year biochemical progression-free survival pursuant to permanent interstitial brachytherapy with or without supplemental external beam radiotherapy.

Madan et al. [35] reported a 28-year-old man who presented with dysuria and back pain. He had a rectal examination which revealed an enlarged and asymmetric prostate gland with a separate hard nodule. His serum PSA was 5.85 ug / ml, (normal range 0 - 4.0 ug / ml). He had contrast enhanced magnetic resonance imaging scan which showed multi-lobulated enlarged prostate gland and a large tumour with extra-capsular extension to both seminal vesicles and the neck of his urinary bladder as well as enlarged pelvic lymph nodes. Pathological examination of biopsy specimen of his prostatic tumour showed Gleason 4+5 = 9, poorly differentiated adenocarcinoma. Immunohistochemistry studies showed that the tumour cells had exhibited positive staining for Pan-cytokeratin and PSA, and focal positivity for alpha-methylacyl-CoA racemase (AMACR) and synaptophysin but the tumour exhibited negative immunohistochemistry staining for CK7, CK20, TTF-1, MIC-2, myogenin, and chromogranin. Based upon the histology and immunohistochemistry features of the tumour a diagnosis of poorly differentiated adenocarcinoma of prostate with neuroendocrine differentiation was made. He had isotope bone scan which indicated metastases to the skull, the right 6th rib, scapula, the 11th and 12th thoracic vertebrae as well as the 2nd lumbar vertebra. He received palliative treatment for his metastatic disease. He underwent bilateral inguinal orchidectomy and was commenced on anti-androgen therapy. He subsequently received radiotherapy to his painful bone metastatic lesions. At his 1-year follow-up his serum PSA was 4.11 ng / ml, and his pelvic disease had been illustrated on a repeat magnetic resonance scan to have persisted. There was no long-term report of the case; however, Madan et al. [35] stated that the rarity of carcinoma of the prostate gland in the younger population had limited the study of the natural history and prognosis in the younger population.

In 2000, D'Aprile et al. [36] stated that carcinoma of the prostate gland tends to occur infrequently in men who are younger than 50-years-old with an incidence of 0.8 % to 1.1% and that up to 2000 less than 20 cases of carcinoma of the prostate gland had been reported in men who are younger than 40 years. D'Aprile et al. [36] reported a 36-year-old man who presented with a two months history of lower back pain, anorexia and weight loss. On clinical examination he was found to have mild inguinal lymph node enlargement, scrotal oedema and oedema of his right lower leg. He had computed tomography (CT) scan of abdomen and pelvis which showed marked enlargement and fusion of pelvic, inguinal, sacral, and para-aortic lymph nodes and a pelvic mass which had caused obstruction of flow of urine and hydroureteronephrosis. He had an X-ray which showed osteoblastic bony metastases. He had bone scan which showed metastatic areas in lumbar vertebrae, pelvis, femurs, the left humeral head, the acromio-clavicular joint, and multiple ribs. His serum prostate-specific antigen (PSA) level was 500 mgr / ml and **h**is prostatic acid phosphatase (PAP) level was 208 U/l. Histological examination of his prostate biopsy specimen showed undifferentiated carcinoma. He had a right-sided percutaneous nephrostomy and he also received 6 cycles of combination chemotherapy (PEB, cisplatinum, etoposide, and bleomycin) and hormonal therapy (LHRH analogue) which resulted in partial response. At his 6-month follow-up his disease had been noted to have progressed so he was given second-line chemotherapy. At his 18-month follow-up his disease was noted to be still progressing. D'Aprile et al. [36] stated that their patient was a case of an original case

of undifferentiated carcinoma of the prostate gland in a young man associated with high levels of serum PSA and PAP as well as osteoblastic bone metastases. D'Aprile et al. [36] recommended that in order to detect carcinomas early in young patients, further studies would be useful. The lesson learnt from this report would indicate that even though it would be expected that majority of cases of the occasional carcinomas of the prostate gland encountered in the younger age group may be low-grade and low-staged localized disease unexpectedly clinicians may encounter high-grade, high-stage metastatic complicated cases of carcinoma of the prostate gland that would require multi-disciplinary team management approach.

Astiqueta et al. [37] undertook a study to identify the clinical features, diagnostic approach, and treatment of metastatic carcinoma of the prostate gland in young adult patients. Astiqueta et al. [37] undertook a retrospective review of the clinical histories of patients whose ages were less than 50 years who had been diagnosed as having carcinoma of the prostate gland in their institution from 1952 to 2005. Astiqueta et al. [37] collected the demographic characteristics and data on history, symptoms, diagnostic procedures, treatment, and course of the disease. Astiqueta et al. [37] statistically analysed the data and compared the results with information they had obtained from search of the literature. With regard to the results, Astiqueta et al. [37] reported that there were 69 patients who were aged less than 50 years who had been diagnosed as having carcinoma of the prostate gland and 60% of these patients had metastatic carcinoma. The mean age of the patients was 45.5 years with a lower range of 29 years. All of the patients had reported bone pain associated with other signs and symptoms including spinal cord compression in 19.5%, lower limb oedema in 17% of the patients, peripheral adenopathies in 36.5% of the patients, and abdominal tumour in 2.4% of the patients. All of the patients did have bone metastases, of which 14.6% were in the solid organs which included the lungs and liver, 48.7% were in the retro-peritoneum, and 7.3% in the mediastinum. In the first instance, three of the patients had been diagnosed as having lympho-proliferative-syndrome; one patient was diagnosed as having retro-peritoneal tumour of unknown aetiology; four patients were diagnosed as having metastasis from unknown primary tumour. The mean serum prostate-specific acid (PSA) level was 795ug/ml and this had ranged from 3ug/ml to 6,500ug/ml. The histopathology examinations of all the patients prostate biopsies had been reported as showing poorly differentiated or undifferentiated carcinomas. The mean survival of the patients was 16.1 months but this had ranged from 1 month to 84 months. All of the patients died as a sequel of disease progression. Astiqueta et al. [37] made the ensuing conclusions: Advanced carcinoma of the prostate gland is an uncommon condition in young adults; The presentation of advanced carcinoma of the prostate in the young adult is atypical, as metastases may mimic other diseases; The course of the disease is indolent and the prognosis is poor; With regard to patients with risk-factors, serum PSA testing should be commenced before 50 years.

Weitzner et al. [38] in 1980 reported a 27-year-old man who was diagnosed as having adenocarcinoma of the prostate gland. Weitzner et al. [38] reported that the patient initially responded to radiotherapy treatment but subsequently developed metastasis and died 13 months following histological diagnosis of the disease. Weitzner et al. [38] reported that at the time of their reported case, 4 cases of adenocarcinoma in men younger than 30 years had previously been reported and 3 of the previously 4 reported cases had presented with lower urinary tract symptoms and bone pain and they died four, five and twelve months later; the other patient was alive and asymptomatic thirty-one months after diagnosis of his disease following a routine physical examination finding.

Shimada et al. [39] in 1980 reported a case of carcinoma of the prostate gland in an 11-year-old boy. The patient's clinical findings had been characterized by the finding of a mass in the prostatic region, extensive osteoblastic bone metastasis, and normal serum acid phosphatase. Pathological examination of the autopsy specimen did show an undifferentiated tumour which was considered to have probably originated from the outer gland of the prostate. Metastases were found in the bones, liver, lungs, and the lymph nodes. Light and electron microscopic studies did reveal un-differentiated neoplastic cell, which was in contrast to the usual adenocarcinoma which tends to be found in older men. Immunohistochemistry studies revealed negative staining for acid phosphatase within the tumour cells. Shimada et al. [39] were of the opinion that probably the tumour had originated from immature basal cells of the prostate gland. Shimada et al. [39] stated that their review of the literature in 1980 did show 15 reported cases of carcinoma of the prostate gland in individuals who were younger than

21 years and that the reported cases were also characterized by an undifferentiated appearance of the tumour cells and normal serum PSA.

Summary

The number of cases of carcinoma of the prostate gland that is being reported globally is increasing perhaps because of the increasing numbers of serum PSA testing. The number of cases of carcinoma of the prostate gland being reported is also increasing. Between 2011 and 2013, 474 cases of carcinoma of the prostate gland (1.06%) had been reported in males in the United Kingdom whose ages had ranged between 0 years and 49 years out of a total of 44,833 cases of carcinoma of the prostate gland reported in all age groups. With regard to the large number cases of carcinoma of the prostate gland that are diagnosed when the disease is at low-grade and low-stage (in the low-risk group), the long term biochemical-free and cancer specific survival rates have been high. On the other hand cases of younger men whose carcinomas of the prostate that had been diagnosed at high stages the prognosis had tended to be worse in comparison with carcinomas of the prostate that had been diagnosed at higher stages in older men. Detection of carcinoma in men at a younger age would on the whole be associated with detection of low-risk tumours that would hopefully lead to longer term survival pursuant to radical prostatectomy which should encourage clinicians to be vigilant in setting up strategies that would help detect carcinoma of the prostate at an earlier age. Considering the fact that higher staged / advanced staged carcinomas diagnosed in the younger age group tend to have poor prognosis, there is need for academic urologists and oncologists to set up a large multi-centre trial relating to advanced staged carcinomas of the prostate gland in young men in order to identify new treatments including possibly new chemotherapy regimens that would help improve the prognosis of such tumours.

Conclusions

More and more cases of carcinoma of the prostate gland are now being diagnosed in the younger age group. In some cases of carcinoma involving the younger men there had been a family history of the disease. A large number of cases of carcinoma of the prostate gland diagnosed in the younger age had been tumours of low-grade and low-stage which had tended to be associated with good prognosis in the long term. However, carcinomas of the prostate gland that had been diagnosed in younger men as higher staged/advanced tumours had tended to be associated with poorer long-term prognosis in comparison with similar higher-staged tumours in older men. Perhaps early detection of carcinoma of prostate in younger men by means of serum PSA testing of men with a family history of carcinoma of prostate and or other malignancies might help detect more prostate carcinomas at a lower stage which would enable clinicians guide the men regarding all the treatment options to enable the patients opt for the best treatment of choice including active surveillance and curative treatments of choice. Younger men who are diagnosed with high-staged/advanced carcinomas of the prostate should be encouraged to enter a multi-centre trial that would identify treatment options that would hopefully improve the long-term survival of their type of disease.

Conflict of Interest: None

References

1. Venyo A, Baiden-Amissah K, Benatar B, Ahmed K. Mixed primary small cell carcinoma of the prostate and primary adenocarcinoma of the prostate: A report of two cases and review of the literature on small cell carcinoma of prostate. WebMedCentral Urology 2012; 3(2):WMC003170
2. Venyo AKG. A Review of the Literature on Primary Leiomyosarcoma of the Prostate Gland. Advances in Urology. 2015: 2015, Article ID 485786, 15 pages http://dx.doi.org/0.1155/2015/485786
3. Venyo AKG. A Review of the Literature on Primary Rhabdomyosarcoma of the Prostate Gland. Journal of Medical Science and Technology 2016; 5(1): 69 – 89
4. Venyo AKG. Lymphoepithelioma-like Carcinoma of the Prostate Gland: A Review of the Literature. Scientifica Volume 2016: 2016; Article ID 1876218, 7 pages. URL: http://dx.doi.org/10.1155/2016/1876218
5. Venyo A K G. Primary Synovial Sarcoma of the Prostate Gland: A Review of the Literature. Journal of Cancer and Tumor International (JCTI) 2016; 3(1): 1- 21. DOI::10.9734/JCTI/2016/19541.www.sciencedomain.org/ abstract12381.
6. Venyo AKG. A Review on Primary Angiosarcoma of the Prostate Gland: An Update. Journal of Cancer and Tumor International (JTCI) 2016; 3(1): 1 – 21. URL: DOI:

10.9734/JCTI/2016/21431.www.sciencedomain.org/ abstract12629.
7. Venyo AKG. Sarcomatoid Carcinoma (Carcinosarcoma) of the Prostate Gland: A Review of the Literature. Journal of Cancer and Tumor International (JCTI) 2015; 2(3): 128 – 143.
8. Yokoyama H, Saito T, Yamagishi T, Ogawa T, Kurizaki Y, Kato H, Ishizuka O, Mishizawa O. A case of advanced prostate fibrosarcoma that reacted well to chemotherapy Hinyokika Kiyo 2014 Sep; 60(9): 451 – 452.
9. Petrakis G, Koletsa T, Karavasilis V, Raillis G, Bobos M, Karkavelas G, Kostopoulos I. Primary prostatic lymphoma with components of both diffuse large B-cell lymphoma (DLBCL) and MALT lymphoma. Hippokratia 2012 Jan-Mar; 16(1): 86 – 89.
10. Venyo A K G. Squamous Cell Carcinoma of the Prostate Gland: A Review of the Literature. Journal of Medical Science and Technology 2015; 4(3): 261 – 272.
11. Prostate Cancer Statistics | World Cancer Research Fund International www.wcrf.org/cancer-facts...cancers/prostate-cancer-statistics
12. GLOBOCAN Cancer Fact Sheets: Prostate Cancer – IARC. Prostate Cancer Estimated Incidence, Mortality and Prevalence World Wide in 2012: URL: globocan.iarc.fr/old/Fact Sheets/cancers/prostate-new-asp
13. Prostate cancer research statistics | Cancer Research UK URL: www.**cancerresearchuk**.org/health.../**cancer**...**cancer**.../**prostate-cancer**]
14. Data were provided by the office for National Statistics by request on July 2015 by Cancer Research UK which is available at their website and similar data can be found from: http://www.ons.gov.uk/ons/rel/vsob1/cancer-statistics-registrations--england--series-mb1-/index.html
15. Data were provided by ISD Scotland on request made in April 2014 by Cancer Research UK and made available on Cancer Research UK website . Similar data can be found from: http://www.isdscotland.org/Health-Topics/Cancer/Publications/index.asp
16. Data were provided by the Welsh Cancer Intelligence and Surveillance Unit on request by Cancer Research UK in March 2015 which was made available at the Cancer Research UK website. Similar data can be found from: http://www.wales.nhs.uk/sites3/page.cfm?orgid=242&pid=59080
17. Data were provided by the Northern Ireland Cancer Registry on request in March 2015 by Cancer Research UK which was made available at the Cancer Research UK website. Similar data can be found from: http://www.qub.ac.uk/research-centres/nicr/
18. Chodak G W, Kim E D. Prostate Cancer Treatment & Management:Approach-Medscape URL: http://emedicine.medscape.com/article/1967731-treatment Accessed September 30 2016
19. Guideline Thompson I, Thrasher J B, Aus G, Burnett A L, Guideline for the management of clinically localized prostate cancer. 2007 update. J Urol. 2007 Jun; 177(6):2106 - 2131
20. PDQ Adult Treatment Editorial Board. Prostate Cancer Treatment (PDQ®) National Cancer Institute Available at: http://www.cancer.gov/cancertopics/pdq/treatment/prostate/HealthProfessional/page4.July 5,2016 Accessed September 29, 2016
21. Salinas CA, Tsodikov A, Ishak-Howard M, Cooney KA. Prostate cancer in young men: an important clinical entity. Nature Reviews Urology 2014 May 13; 11: 317 – 323. DOI: 10.1038/nrurol.2014.91
22. Lin DW, Porter M, Montgomery B. Treatment and survival outcomes in young men diagnosed with prostate cancer: a population based cohort study. Cancer 2009 Jul 1; 115(13): 2863 – 2871. DOI: 10.1002/cncr.24324
23. Sakr WA, Haas GP, Cassin BF, Pontes JE, Crissman JD. The frequency of carcinoma and intraepithelial neoplasia of the prostate in young male patients The Journal of Urology 1993; 10(2 Pt. 1): 379-385
24. Kotsis SV, Spencer SL, Pevser PA, Montie JE, Cooney K A. Early onset of prostate cancer: predictors of clinical grade. J Urol. 2002 Apr; 167(4): 1659 – 1663
25. Khan MA, Ham M, Partin AW, Epstein JI, Walsh PC. Long-term cancer control of radical prostatectomy in men younger than 50 years of age: update 2003. Urology 2003 Jul; 62(1): 86 – 91 discussion 91 - 92
26. Rosser CJ, Chichakli R, Levy LB, Kuban DA, Smith LG, Pisters L L. Biochemical disease-free survival in men younger than 60 years with prostatic cancer treated with external beam radiation. J Urol. 2002 Aug; 168(2): 536 – 541.
27. Smith CV, Bauer JJ, Connelly RR, Seay T, Kane C, Foley J, Thrasher JB, Kusuda L, Moul JW.

Prostate cancer in men age 50 years or younger: a review of the Department of Defense Center for Prostate Disease Research multicentre prostate cancer database. J Urol. 2000 Dec; 164(6): 1964 - 1967

28. Loeb S, Hernandez DJ, Mangold LA, Humphreys EB, Agro M, Walsh PC, Partin AW, Han M. Progression after radical prostatectomy for men in their thirties compared with older men. B J U Int 2008 Jun; 101(12): 1503 – 1506. DOI: 10.1111/j.1464-410X.2008.07500.x. Epub 2008 Mar 13.
29. Freedland SJ, Presti JC Jr, Kane CJ, Arons WJ, Terris MK, Dorey F, Amling CL, SEARCH Database Study Group Do younger men have better biochemical outcomes after radical prostatectomy? Urology 2004 Mar; 63(3): 518 – 522
30. Rouprêt M, Fromont G, Bitker MO, Gatteqno B, Vallancien G, Cusseno O. Outcome after radical prostatectomy in young men with or without a family history of prostate cancer. Urology 2006 May; 67(5): 1028 – 103
31. Edwards SM, Kote-Jarai Z, Meitz J, Hamoudi R, Hope Q, Osin P, Jackson R, Southgate C, Singh R, Falconer A, Dearnaley DP, Arden Jones A, Murkin A, Dowe A, Kelly J, Williams S, Oram R, Stevens M, Teare DM, Ponder BA, Gayther S A, Easton DF, Eeles RA, Cancer Research UK /British Prostate Group UK Familial Prostate Cancer Study Collaborators; British Association of Urological Surgeons Section of Oncology. Two percent of men with early-onset prostate cancer harbour germ line mutations in BRCA2 gene. Am J Hum Genet2003 Jan; 72(1): 1 – 12. Epub. 2002 Dec 9
32. Tomokazu K, Mizuki O, Jun M, Taeko M, Akira J, Koji K, Hiroyuki N, Shiro H, Hideyuki A. Prognostic impact of young age on stage IV prostate cancer treated with primary androgen deprivation therapy. International Journal of Urology: Official Journal of the Japanese Urological Association 2014 Jun; 21(6): 578 - 583
33. Tang P, Sun L, Uhlman M A, Robertson C N, Polascik T J, Albaia D M, Donatucci C F, Moul J W. Initial prostate specific antigen 1.5 ng/ml or greater in men 50 years old or younger predicts higher prostate cancer risk. The Journal of Urology 2010 Mar; 183(3): 946 – 950
34. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Adamovich E. Permanent interstitial brachytherapy in younger patients with clinically organ-confined prostate cancer. Urology 2004 Oct; 64(4): 754 - 759
35. Madan R, Singh L, Haresh KP, Rath GK. Metastatic Adenocarcinoma of the Prostate in a 28-Year-Old Male: The outcome is poor in young patients? Indian Journal of Palliative Care 2015 May – Aug; 21(2): 242 – 244. DOI: 10.4103/0973-1075.156510
36. D'Aprile M, Santini D, Di Cosimo S, Gravante G, Vicenzi B, Spoto S, Costantino S, Rabitti C, Tonini G. Atypical case of metastatic undifferentiated prostate carcinoma in a 36 years old man: clinical report and literature review. Clin Ter 2000 Sep-Oct; 151(5): 371 - 374
37. Astiqueta J C, Abad M A, Morante C, Pow-Sang M R, Destefano V, Montes J. Characteristics of metastatic prostate cancer occurring in patients under 50 years of age. Actas Urol Esp. 2010 Apr; 34(4): 327 - 332
38. Weitzner S, Sarikaya H, Furness TD. Adenocarcinoma of prostate in a twenty-seven-year-man Urology 1980 Sep; 16(3): 286 - 288
39. Shimada H, Misiqi K, Sasaki Y, Lizuka A, Nishihira H. Carcinoma of prostate in childhood and adolescence: report of a case and review of the literature. Cancer 1980 Dec 1; 46(11): 2534 – 2542