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Significance of Serum Prostate Specific Antigen with Histopathological Grading in Men with Prostate Adenocarcinoma at Makassar, Indonesia

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Abstract

Prostate adenocarcinoma is the second most common malignancy in men after lung cancer worldwide. In Makassar, South Sulawesi, prostate adenocarcinoma cases increased significantly, from 2017, 2018 and 2019 respectively, the cases reached 31, 43 and 51 cases. Although not specific, Prostate Specific Antigen (PSA) is the first-line test in the screening of prostate adenocarcinoma. Gleason grading is one of the most powerful predictors of biological behavior and when combined PSA with Gleason score and clinical stage. It improves the prediction of the pathological stage for prostate carcinoma. The aim of this study was to determine the association between serum PSA concentration and the new (2016 modified) This was a retrospective study of the correlation between age of patients, serum PSA and grade group of Gleason score of patients diagnosed as Prostate Adenocarcinoma with HE staining at Anatomical Pathology Laboratory, Faculty of Medicine, Hasanuddin University. The age of patients and the serum PSA values were retrieved from laboratory files. Histological slides of appropriate cases were reviewed to confirm the Gleason score and group grade. There were 27 cases fulfilled criteria, from September 2020 to November 2021. The data obtained were subjected to statistical analysis to look for associations and correlations serum PSA and group grade of prostate adenocarcinoma.

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This study showed that there was a significant correlation between serum PSA level with histopathological grading based on Gleason score of prostate adenocarcinoma ($p<0,05$).

Keywords: Serum PSA; Gleason score; histopathological grading; prostate adenocarcinoma.

1. Introduction

Globally, prostate adenocarcinoma is the second most common malignancy in men after lung cancer. The number of new cases in 2018 reached 1,276,106 people with a mortality rate of 358,989 people (3.8% of all cancer deaths in men) [1]. In Asia, the average incidence of prostate adenocarcinoma is 7.2 per 100,000 men per year. In Indonesia, the number of prostate adenocarcinoma sufferers in three educational center hospitals (Jakarta, Surabaya and Bandung) for the last 8 years was 1,102 patients with an average age of 67.18 years based on data from the Ministry of Health of the Republic of Indonesia (National Guidelines for Prostate adenocarcinoma Medical Services 2017). The province that has the highest prevalence of prostate adenocarcinoma is D.I. Yogyakarta, Bali, North Sulawesi, and South Sulawesi, which is 0.5% [2]. In Makassar, prostate adenocarcinoma cases showed a significant increase. Based on data from the Anatomical Pathology Laboratory in Makassar, there was a significant increase from year to year, namely in 2017 (31 cases), 2018 (43 cases) and 2019 (51 cases). Prostate adenocarcinoma incidence increases with age, but only 1 in 350 men under the age of 50 years will be diagnosed with prostate adenocarcinoma. The development of prostate adenocarcinoma is usually accompanied by a rise in the concentration of serine protease prostate-specific antigen (PSA). Screening with serum PSA has led to an increasing number of prostate adenocarcinoma diagnoses, especially in younger men and at an earlier cancer stage [3] . PSA screening may increase the detection of prostate cancer (7 more per 1000 men (95% confidence interval 1 to 15 more) at 10 years), particularly of localised can- cer (7 more per 1000 men (2 to 15 more)). But the data show no difference in prostate cancer mortality [4]. There is strong evidence that PSA testing reduces prostate cancer mortality.1–3 However, PSA has a high false-positive rate translating into unnecessary prostate biopsies and overdiagnosis of low-risk cancers, resulting in potential overtreatment [5]. PSA is a 34-kilodalton glycoprotein secreted by prostatic epithelial cells, unless they are extremely poorly differentiated. The test has a high sensitivity, but rather low specivicity, it is rapid and inexpensive and is minimally invasive [6,7]. Histopathological diagnosis of prostate adenocarcinoma can be established by transrectal ultrasound-guided (TRUS) biopsy after an abnormal finding in digital rectal examination or finding an augmentation in prostate specific antigen (PSA) level [8]. The degree of prostate malignancy currently uses a new scoring system that is simpler and more accurate in providing histopathologic features of prostate malignancy. It has been recommended by the World Health Organization (WHO) in 2016, that the degree of prostate malignancy uses grading groups. Based on the International Society of Urological Pathology Consensus, grading groups using the Gleason scoring system and the latest modifications in 2015 [9,10]. This study aims to determine correlation of serum PSA with grade group of patient with prostatic adenocarcinoma in Makassar, South Sulawesi of Indomesia.

2. Methods

This was a retrospective study to determine the correlation serum PSA and group grade of gleason score in

men with prostate adenocarcinoma. The sample of this study was the cases of prostate adenocarcinoma diagnosed at Anatomical Pathology Laboratory, Hasanuddin University, from September 2020 to November 2021. This study was conducted by searched the data of patient in database of Anatomical Pathology Laboratory, Faculty of Medicine, Hasanuddin University. There were 27 cases fulfilled include and exclude criterias. After collecting data, we followed with evaluation of all histopatological slide involving a senior pathologist to make sure that group grade suitable with the lastest criteria released by WHO released in 2016. The data collected and result of slide evaluation then analysed with SPSS 20 programm. Chi square correlation used to analysed serum PSA and grade group of gleason score with significance was set at $p<0,05$.

3. Results

In this study, 27 samples which was fulfilied inclusion criterias (diagnosed as prostate adenocarcinoma and had PSA serum data), avalaible from data based of Anatomical Pathology Laboratory of Hasanuddin University Hospital Makassar September 2020 to November 2021. The general characteristics of sample are described in table 1 as follow:

Table 1: Samples Characteristics.

Age (years old)	**Number**	**Persentage (%)**
≤50	3	11,1
51-60	6	22,2
61-70	7	25,9
71-80	9	33,3
≥80	2	7,4
PSA Value		
<4	3	11,1
4-9,9	2	7,4
10-19,9	1	3,7
20-100	4	14,8
>100	17	63,0
Grade Group		
1	4	14,8
2	2	7,4
3	4	14,8
4	7	26,0
5	10	37,0

Correlation PSA serum and Grade Group of Gleason Score described in tabel 2 as follow:

Table 2: Correlation PSA serum and Grade Group of Gleason Score.

PSA (	**Grade Group**				
	1	**2**	**3**	**4**	**5**
<4	1 (3,7)	0	0	1 (3,7)	1 (3,7)
4-9,9	0	0	0	1 (3,7)	1 (3,7)
10,0-19,9	0	0	0	0	1 (3,7)
20,0-100,0	1 (3,7)	1 (3,7)	0	0	2 (7,4)
>100,0	2 (7,4)	1 (3,7)	4 (14,8)	5 (18,51)	5 (18,51)

Chi Square: 0,0137 (p<0,05)

4. Discussion

Based on data on table 1, we found that case prostate adenocarcinoma tend to increase with the age of patient. Of 27 cases, 9 (33%) cases occur in 71-80 years old patient. Although in some literature stated that Prostate adenocarcinoma more common up to 50 years old, but in this study we found 3 cases (11,1%) occured on under 50 years old. The case up 80 years old declined compare with 70-80 years old, its may be correlated with life expectancy of Indonesian population, where in 2019 its 73,3 years. This finding similar with Globogan data that prostate adenocarcinoma incidence increases with age. Although only 1 in 350 men under the age of 50 years will be diagnosed with prostate adenocarcinoma the incidence rate increases up to 1 in every 52 men for ages 50 to 59 years. The incidence rate is nearly 60% in men over the age of 65 years [1]. Many prostate adenocarcinomas are detected on the basis of elevated plasmatic levels of prostate-specific antigen (PSA > 4ng/mL), a glycoprotein normally expressed by prostate tissue. So PSA is an important parameter checked routinely on patien with prostate problem, although its not spesific for prostate adenocarcinoma. In some cases, men without cancer have also been found with elevated PSA. There are some factor that maight raise serum PSA levels include prostate enlargement such benign prostate hyperplasia (BPH), older age, prostatitis,ejaculation, riding a bicycle, certain urologic procedures and certain medicine like testosterone [11,12] . Due to this condition a tissue biopsy is the standard of care to confirm cancers presence[6].

The range of PSA level in this study was enough wide, from less than 4 ng/mL to up to 100 ng/mL. Interestingly, there were 3 cases which PSA level under 4 ng/mL (11,1%). This finding suitable with study by Tikkinen at all, they found that About 15% of men with a normal PSA result will subsequently be diagnosed with prostate cancer; with about 2% of men with a normal PSA result diagnosed with advanced cancer (that is, false negative results of PSA screening) [4]. The chance of having prostate cancer goes up as the PSA level goes up, but there is no set cutoff point that can tell for sure if a man does or doesn't have prostate cancer. Many doctors use a PSA cutoff point of 4 ng/mL or higher when deciding if a man might need further testing, while others might recommend it starting at a lower level, such as 2.5 or 3. Most men without prostate cancer have PSA levels under 4 ng/mL of blood. When prostate cancer develops, the PSA level often goes above 4. Still, a level below 4 is not a guarantee that a man doesn't have cancer. About 15% of men with a PSA below 4 will

have prostate cancer if a biopsy is done. Men with a PSA level between 4 and 10 (often called the "borderline range") have about a 1 in 4 chance of having prostate cancer. If the PSA is more than 10, the chance of having prostate cancer is over 50% [12]. Same with the other cancer, histopatologic evaluation is gold standart to confim definitive diagnosis. According to table 1, mostly sample of this study include in grade group 5 (37,0%) and grade group 4 (26,0%). Grade Group 5 (Gleason scores 9–10), histopathologic finding include lacks gland formation/necrosis with or without poorly formed/fused/cribriform glands, meanwhile Grade Group 4 (Gleason score 8), signed by poorly formed/fused/cribriform glands or predominantly well-formed glands with a lesser component lacking glands or predominantly lacking glands with a lesser component of well-formed glands [13]. Correlation of serum PSA and grade group of Gleason score showed in table 2. Based on the table 2, sample with serum PSA level less than 4, distributed into three grade group that grade group 1, 4 dan 5. At the same time, serum PSA level up to 100 ng/mL can be found in all grade group although mostly in grade group 4 and 5. With Chi square analyze, we found that there was a significant correlation between serum PSA level and histopathological grading based on Gleason score ($p<0,05$). The different result had been published by Ikenna at all in their study on black men with symptomatic prostate adenocarcinoma in Nigeria, they found that Gleason score may not be confidently predicted by the serum PSA. Higher serum PSA does not correlate with higher Gleason score and vice versa [14]. On the other hand, L Adebayo at all in their study revealed a weak positive correlation between the serum PSA value, the Gleason group grade system and 4 tiers grading of prostate cancer [3]. Okolo at all in their study found that there was a positive correlation between serum PSA and Gleason grade, as well as between serum PSA and Gleason score in Nigerian African men with prostate cancer [6]. The weakness of this study was limitation of samples and there are many cases without pre-biopsy serum PSA data.

5. Conclusion

This study shows that in patients with prostatic adenocarcinoma, there is a statistically significant correlation between serum PSA levels with Grade Group of Gleason score that newly introduced (2016) by WHO. For further study, we recommend additional large and multicenter studies involving all anatomical pathologic center in Indonesia, so we have national data in correlation serum PSA and Grade Group of adenocarcinoma prostate patients that will be useful for epidemiologic and clinical approach.

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