Gereksiz Tekrar Edilen Total PSA Testleri; Minimum Retest İnterval ve RCV ile Değerlendirme

Unnecessary Repeated Total PSA Tests; Evaluation with Minimum Retest Interval and Reference Change Value

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ÖZET

Amaç: Bu çalışmanın amacı, minimum retest intervale göre gereksiz tekrarlanan total prostat spesifik antijen (tPSA) testlerini belirlemek ve ardışık ölçüm sonuçları arasındaki değişimi RCV ile değerlendirmektir.

Gereç ve Yöntem: Klinik Biyokimya ve Laboratuvar Tıbbı Derneği raporuna göre, tPSA testi istenen hastalarda ilk sonucun yüksek olması durumunda eğilimi görmek için tPSA testinin 6 haftada bir kez tekrarlanması önerilmektedir. Hastanemizde Mart 2015 - 2017 arasında istemi yapılan tPSA test sonuçları retrospektif olarak değerlendirildi. Ardışık iki tPSA istemi arasındaki süre <6 hafta ve ilk istenen tPSA test ölçüm sonucu >2,5 ng/mL olan istemler uygunsuz tPSA test istemi olarak değerlendirildi. RCV hesaplandı.

Bulgular: tPSA test sayısı 1794, ardışık istenen tPSA sayısı 427 (% 12,5) idi. Ardışık istenen tPSA testlerinin %46,37'sinde (198/427) ilk ölçülen tPSA test sonucu >2,5 ng/mL idi ve bu testlerin %49'u(97/198) gereksiz istemdi. RCV %51,45 olarak hesaplandı. Gereksiz tekrarlanan tPSA testlerinin % 82,5'inde(80/97) iki sonuç arasındaki değişim RCV'den küçüktü. Ardışık iki ölçüm sonucu arasındaki değişimi <RCV olan istem sıklığı uygun olarak istenen tPSA testlerinde uygunsuz istenen tPSA test istemlerine göre anlamlı olarak azdı (p=0,002).

Sonuç: Gereksiz tekrar edilen testlerde RCV'ye göre ardışık iki sonuç arasında anlamlı fark bulunmaması test istemlerinin kılavuzlara uygun yapılmasının önemini ortaya koymaktadır. Yaptığımız çalışmanın gereksiz test istemlerinin azaltılması konusunda farkındalık yaratacağını düşünüyoruz.

Anahtar Kelimeler: Sağlık hizmeti maliyetleri; maliyet azaltıcılar; prostat spesifik antijen; laboratuvar belirteçleri

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ABSTRACT

Objective: The aim of study was to determine unnecessary repeated total prostate specific antigen(tPSA) according to minimum retest interval and to evaluate the change between consecutive measurement results with RCV.

Material and Methods: According to report of Association for Clinical Biochemistry and Laboratory Medicine, when first result is raised, it is recommended to repeat tPSA once in 6 weeks to assess the trend. tPSA test results which were requested between March 2015 and 2017 in our hospital were evaluated retrospectively. If tPSA was>2.5 ng/mL and this test was repeated in less than 6 weeks, it was determined as unnecessary repeated test. RCV was calculated.

Results: The number of tPSA was 1794 and number of consecutive tPSA requested was 427 (12.5%). The first tPSA result was>2.5 ng/mL in 46.4% (198/427) of consecutive tPSA tests, 49% of these tests(97/198) were unnecessary. RCV was calculated as 51.45%. In 82.5% (80/97) of unnecessary repeated tPSA, the change between two results was smaller than RCV. Number of consecutive tests which changed below RCV was significantly lower in appropriately requested tPSA tests than unnecessary repeated tPSA (p=0,002).

Conclusion: Absence of significant difference between two consecutive results in unnecessary repeated test according to RCV suggests the importance of test requesting according to guidelines. We believe that our work will raise awareness about reducing unnecessary requests.

Key Words: Health Care Costs; cost Savings; prostate specific antigen; laboratory Markers

INTRODUCTION

Laboratory costs are one of the fastest growing area of health care cost. Not only the developments in education and technology cause a natural increase in the test requests but also unnecessary tests have an important role in the increase in laboratory use (1). Unnecessary tests also trigger unnecessary test request cascade. As a result, the total labor and cost of the laboratories increase and patient care is affected negatively.

One of the most important reasons for unnecessary test requests is inappropriately repeated tests (2). Guidelines mention minimum retest intervals depending on physiological and analytical properties, biological half-life, follow-up and treatment requirements, and evidence value criteria. The guideline prepared in 2013 under the auspices of the Association for Clinical Biochemistry and Laboratory Medicine (ACB) provides minimum retest interval recommendations for laboratory testing (3).

The concept of reference change value (RCV) was first defined by Harris and Yasaka in 1983 to have an objective interpretation of the difference between consecutive test results in patient follow-up (4). This concept, also known as critical difference, provides theoretical and practical evaluation to determine whether the change in consecutive test results requires medical attention (5, 6). Test results have their own natural variations. The sources of these variations are the intra-individual and inter-individual differences specific to the analyte. For the analyte whose individual intra-biological variation is lower than the inter-individual biological variation, the test results may be within the reference range although there is a significant difference between the consecutive test results. The lower the individuality index the greater the individuality of the analyte. The use of the reference interval for interpretation of the test result is limited depending on the natural variation of the analyte.

According to the report prepared under the auspices of the ACB, it is recommended to repeat total prostate specific antigen (tPSA) test once in 6 weeks to assess the trend,

when first result is raised. In addition to this recommendation, different follow-up intervals are recommended in patients with androgen deficiency and those who receive replacement therapy (3).

The aim of our study is to determine the unnecessary repeated tPSA tests according to the minimum retest interval and to evaluate the change between the consecutive tPSA test results with RCV.

MATERIAL AND METHODS

The tPSA test results of the patients between the ages of 40 and 70 years who were admitted to ... State Hospital urology clinic with lower urinary tract symptoms during March 1, 2015 – March 31, 2017 were evaluated retrospectively. Patients diagnosed with prostate cancer or receiving androgen replacement therapy and those who had urinary tract infection findings at the time of tPSA test measurement were excluded from the study. More than one performed tPSA test for a patient was defined as a repeated tPSA test. In the repeated tPSA tests, the time between two consecutive test requests was determined. The percentage of change between consecutive test results was calculated. The cut-off value of tPSA test was accepted as 2.5 ng / mL (10). If the tPSA test result was above 2.5 ng/mL and this test was repeated in less than 6 weeks, it was determined as unnecessary repeated test.

The tPSA test is performed by the electrochemiluminescence method in Roche Cobas e601 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) at Central Laboratory. Two levels of internal quality control material are used for the tPSA test. We calculated the coefficient of variation of the internal quality control results using with formulae; analytical coefficient of variation (CVanalytical)= Standard Deviation × 100 / laboratory mean of internal quality control. The intra-individual coefficient of variation (CVintraindividual) of the tPSA test is 18.1% (11). We calculated the RCV value for the tPSA test with formulae; $RCV=21/2\times Z\times\sqrt{}$ (CVanalytical2+CVintraindividual2) by using the internal quality control standard deviation and CVanalytical values (12). Z value is 1,96 for 95% probability ($p < 0.05$) (12). Pearson's chi-square analysis was used while the smallest theoretical frequency was above 25 (calculated as 26,94). Descriptive statistics and chi-square analysis were done using SPSS 22.0 (SPSS Inc, Chicago, IL, USA) program. The p value below 0.05 was considered statistically significant.

RESULTS

SD and CV values of tPSA test internal quality control are shown in Table 1. The tPSA RCV value was calculated as 51.5%. During 2015 - 2017, the number of tPSA tests requested from urology outpatient clinic was 1794. The frequency of consecutive tPSA tests was 12.5% (427/1794). The first measured tPSA test result was above 2.5 ng/mL in 46.4% (198/427) of consecutive tPSA tests, 49% of these tests (97/198) were unnecessary repeated tPSA test. In 82.5% (80/97) of unnecessary repeated tPSA tests, the change between the two measurements was smaller than the calculated RCV value (Table 2). The number of consecutive tests which changed below RCV was significantly lower in appropriately requested tPSA tests than unnecessary repeated tPSA tests ($p = 0.002$). In 60.7% (259/427) of consecutive tPSA tests, the change between two measurements was below RCV.

Table1. Standard deviation and coefficient of variation of the total PSA test internal quality control

		Level 1		Level 2	
Years	**Months**	**SD**	**CV**	**SD**	**CV**
2015	March	0,21	5,62	2,55	6,33
	April	0,16	4,44	1,42	3,63
	May	0,18	4,63	1,98	4,89
	June	0,07	1,84	1,63	4,04
	July	0,17	4,25	1,56	3,82
	August	0,12	3,17	1,69	4,17
	September	0,09	2,21	0,73	1,82
	October	0,06	1,54	10,78	29,14
	November	0,06	1,61	1,00	2,47
	December	0,16	4,10	1,17	2,92
2016	January	0,07	1,67	0,96	2,33
	February	0,05	1,31	0,52	1,26
	March	0,14	3,57	1,47	3,99
	April	0,11	3,01	1,27	3,68
	May	0,17	4,00	1,58	4,39
	June	0,10	2,50	0,87	2,25
	July	0,14	3,31	1,10	2,85
	August	0,15	3,65	1,18	3,02
	September	0,14	3,51	2,05	5,50
	October	0,17	4,36	1,21	3,31
	November	0,19	5,02	1,27	3,35
	December	0,12	3,03	1,82	5,01
2017	January	0,15	3,74	2,17	5,68
	February	0,20	4,89	2,15	5,73
	March	0,21	5,62	2,55	6,33
	Mean	0,13	3,37	1,84	4,82

SD: Standard deviation
CV: Coefficient of variation

Table 2. Distribution of tPSA test number of consecutive requested and first result above 2.5 ng/mL according to reference change value

The interval between the two test request in the consecutive tPSA tests with >2.5 ng /mL of the first result	<RCV	>RCV	Total
< 6 week (unnecessary repeated tPSA tests)	80	17	97
> 6 week (appropriately requested tPSA tests)	63	38	101
Total	143	55	198

DISCUSSION

The use of laboratories has been increasing in recent years, above those attributable to technological developments and population aging. Laboratory tests are estimated to constitute 4% of annual health care costs (1, 13). Although the tests are used for many important purposes for the benefit of the patient such as diagnosis, treatment and follow-up, a significant portion of the requested tests are unnecessary repeated tests (14). Researches have shown that a large percentage of laboratory tests (up to 42%) can be considered as waste (15-17). In our study, 49% of the tPSA tests, which were consecutively ordered and the first result above 2.5 ng/mL, were unnecessarily repeated. Kwork et al. (2) found that 21.2% of the tests which were requested consecutively within one year were unnecessary requests in a group of tests and this ratio was found to be 20.5% for the tPSA test while minimum retest interval was accepted as 12 weeks. The reason of higher rate in our study may be due to a specific

group. Khalifa et al. (18) reported unnecessary test rates as 25.9%. Bridges et al. (19) found that 7.7% of laboratory tests were unnecessary. Hueth et al. (20) found 1849 of 4242 repeated tests (44%) as unnecessary repeated test according to minimum retest intervals.

Unnecessary tests can be requested for many reasons. Experience, perceived medical and legal risks, hospital processes, patient-related factors such as cultural beliefs, anxiety effects clinicians' test-requesting habits (21, 22). In the studies conducted, it has been shown that there are serious variations between the number of test requests of physicians (23). Deficient habits, lack of experience, inadequate use of protocols and guidelines, lack of awareness about health care system and costs increase the number of unnecessary tests (21, 22). According to the obtained data, 25- 75% of the tests are not supported by guidance or expert recommendations (24).

Laboratory test results are a value distribution rather than a single value. The change in the serial results of a patient may be due to the improvement or worsening of the health status of the patient as well as from the pre-analytical, analytical and biological variation (25). Therefore, the use of RCV is recommended for evaluating the clinical significance of changes between serial test results. The tPSA test has a high $CV_{intraindividual}$ and interindividual coefficient of variation ($CV_{interindividual}$) values so the individuality index is low ($CV_{intraindividual}$: 18.1%, $CV_{interindividual}$: 72.4%, individuality index: 0.25) (11, 26). In our study, we found that the change between the consecutive test results was smaller than the calculated RCV value in 82.5% (80/97) of unnecessary repeated tPSA tests. The number of consecutive tests which changed below RCV was significantly lower in the appropriately requested tPSA tests than unnecessary repeated tPSA tests ($p = 0.002$). This suggests that there was no significant change between the two measurement results in most of the unnecessary tPSA tests according to the recommended minimum retest intervals. We have obtained similar results in our previous study for unnecessary repeated cholesterol tests (27). Prevention from tests requested in shorter interval than minimum retest intervals can be provided by laboratory information system software (28). While minimum retest intervals are standard for some tests, it varies according to specific clinical conditions for most tests (3). In these tests, it is difficult to determine the minimum retest interval according to the guideline using only patient information in the laboratory information system without detailed clinical query and evaluation. Therefore, we conclude that it is even more important for laboratory specialists to evaluate unnecessary tests and share the results with clinicians in order to raise awareness on this issue.

In our study, we have revealed our unnecessary repeated tPSA tests quantitatively. Evaluation of the change between consecutive test results in unnecessary repeated tPSA tests with the calculated RCV value for our laboratory has point the situation up. The fact that there is no significant difference between the consecutive measurement results in most tests repeated unnecessarily reveals the importance of making the request in accordance with the guideline recommendations.

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