RESEARCH ARTICLE

Management of Precancerous Cervical Lesions in Iran: A Cost Minimizing Study

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Abstract

Background: Cervical cancer is a common, preventable and manageable disease in women worldwide. Objectives: This study was conducted to determine the cost of follow-up for suspicious precancerous cervical lesions within a screening program using Pap smear or HPV DNA test through the decision tree. Materials and Methods: Patient follow-up processes were determined using standard guidelines and consultation with specialists to design a decision tree model. Costs of treatment in both public and private sectors were identified according to the national tariffs in 2010 and determined based on decision tree and provided services (visits to specialists, colposcopy, and conization) with two modalities: Pap smear and HPV DNA test. The number of patients and the mean cost of treatment in each sector were calculated. The prevalence of lesions and HPV were obtained from literature to estimate the cost of treatment for each woman in the population. Results: Follow-up costs were determined using seven processes for Pap smear and 11 processes for HPV DNA test. The total cost of using Pap smear and HPV DNA process for each woman in the population was 36.1$ and 174 $ respectively. Conclusions: The follow-up process for patients with suspicious cervical lesions needs to be included in the existing screening program. HPV DNA test is currently more expensive than Pap smear, it is suggested that we manage precancerous cervical lesions with this latter test.

Keywords: Cost minimization - Pap smear - HPV DNA testing - decision tree - Iran

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Introduction

Cervical cancer is the fourth most common cancer in women. According to Globocan (Ferlay et al., 2013), the incidence and mortality rates of cervical cancer were 14 and 6.8 per 100000 worldwide. 80% of cervical cancers occur in developing countries (Ferlay et al., 2013). Unlike other cancers, due to its long preclinical period, cervical cancer is preventable. Cervical screening programs have been able to reduce the incidence and mortality rate of cervical cancer. In the U.S, for instance, the incidence rate of the disease decreased from 44 per 100,000 in 1974 to 5.7 per 100,000 in 2010 (Ries et al., 2002). The Pap smear is regarded as the best cancer prevention method and has been used as the main and most effective screening method in many countries (Mählck et al., 1994). However, human papillomavirus (HPV) has been detected in 93% of cervical cancer cases and is thus known as a major risk factor for the disease (Bosch et al., 1993). Since the virus has rarely been absent in samples of patients with cervical cancer (Walboomers et al., 1999), different strategies to apply new detection method for HPV have been developed in health care settings (Gakidou et al., 2008). Moreover, recent studies have shown HPV DNA test to be more sensitive than Pap smear in diagnosing the disease (Malloy et al., 2000; Wang et al., 2013).

According to The Cancer in Five Continents book, age adjusted incidence rate(ASR) in Golestan province of Iran was5.4 per 100000 (Forman et al., 2013). Gynecologic cancers in Iran are about 7.8% of total female cancers (Arab et al., 2014). Iran and other Muslim countries like Turkey are known as the low incidence cervical cancer areas in the world (Sengul et al., 2014). The prevalence of HPV in cervical cancer patients in Iran were 76% and 7% among healthy women (Khorasanizadeh et al., 2013). The current national screening program in Iran includes Pap smear test, and HPV DNA test is performed outside the program. Meanwhile, due to the low incidence rate of cervical cancer in Iran, the screening programs do not embrace patient follow-up after Pap smear sampling and the follow-up process is not free of charge. We Should kept in mind that management of precancerous lesion is important to reduce incidence of cancer (Pity et al., 2012). The present study used the cost minimization approach to calculate the follow-up costs of patients with precancerous lesions through Pap smear and HPV DNA tests since the

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management of lesions is important, its findings can help policymakers to choose the best method of follow-up and embedding it in the existing screening program. It is noteworthy that every screening method employs its relevant treatment and the follow-up methods are based on the type of lesions. These methods can be followed within a number of processes, each of which provides patients with specific services and at particular costs. According to limited resources and the role of management of abnormal lesions, the purpose of this study was to determine the cost of treatment of precancerous lesions of cervix and to compare the cost of two methods for follow-up of these lesions using decision tree model.

Materials and Methods

The study was performed from health system perspective. A decision tree for management of cervical lesions was constructed using international guidelines (Partridge et al., 2010). Then we modified the tree according to Iran practice by a panel of gynecologists (Figure1 and 2). We identified the list of services in tree including number of visits, type of intervention, diagnostic tests, and treatment of suspicious lesions. The cost of each service was determined in public and private sector based on the Book of Diagnostic and Treatment Service Tariffs in Public and Private Sectors in 2010 (Treatment., 2010). We used Tehran's cancer registry database reported by the Cancer Research Center of Cancer Institute of Iran to determine the distribution of patient visits to the public and private sectors. The proportion of patients that received diagnostic and treatment service was then computed for both public and private sectors. Finally, the costs were measured based on the proportion of services in public and private sectors.

The data about prevalence of lesions (LSIL and HSIL) in the population, Prevalence of HPV and the probability of regression and progression of lesions and HPV in the natural history of disease were obtained from literature.

A cohort of 100 women with age 35 years was entered into the model and their total screening cost was estimated using the above assumptions.

All cost estimates were converted to 2010 international dollars.

In patients diagnosed with high-grade squamous intraepithelial lesion (HSIL), we considered one specialist visit since the treatment continued after hospitalization of the patients and the cost of the next visit was included in the conization process. However two visits were accounted for the provision of other services. After performing conization patients back to the routine screening.

In order to calculate the treatment cost based on the type of lesion and patient's follow-up, different processes were designed for positive/negative lesions. If the patient's test was negative therefore that case entered into the routine screening. Considering that only low-grade squamous intraepithelial lesion (LSIL) and HSIL lesions precede to cervical squamous cell carcinoma, the costs of other lesions were not calculated in this study. In the screening process through HPV DNA test, the lesions were followed up with cytology triage and Pap smear test.

Results

Calculating the costs of services provided by the public and private sectors

Based on Tehran's cancer registry database, during 1998-2001, 923 and 938 cervical cancer patients had attended the city's treatment and diagnostic centers, respectively. Patients visiting private and public sector diagnostic centers comprised 40% and 60% of all subjects, respectively (Table 1). With conization being a therapeutic method, the proportion of patients referring to public and private treatment centers was calculated as 84% and 16%, respectively (Table 2). Afterward, tariffs of public and private screening were multiplied by the calculated coefficient and the mean costs were computed.

Prevalence of HSIL, LSIL and HPV and percentage of regression and progression of lesions

The prevalence of lesions and HPV were obtained from Iranian literature (Table 3) (Afrakhteh et al., 2007; Khodakarami et al., 2012) and the percentage of regression and progression of lesions and the sensitivity and specificity of tests were obtained from national and international literature according to the natural history of disease (Andrae et al., 2008; Behtash et al., 2008; Tanprasertkul and Sritipsukno, 2010).

Calculating the cost of follow-up processes using the Pap smear or HPV DNA method

In the processes, patients were followed for 18-36 months after lesions were detected. In the Pap smear method the follow-up involved three processes (Figure1).

Table 1. The Mean Cost of Screening Services Based on Referred to Governmental or Private Services

Services	Governmental Tariff ($)	Patient Referred to Governmental Sector (%)	Private Tariff($)	Patient Referred to Private Sector (%)	Mean Cost($)
Pap smear	2	60	5	40	3
Colposcopy	12	60	29	40	18
Biopsy	13	60	34	40	22
HPV DNA	70	60	153	40	103
Visit	4	60	11	40	7

Table 2. The Mean Cost of Conization Based on Referred to Governmental or Private Services

Services	Governmental Tariff ($)	Patient Referred to Governmental Sector (%)	Private Tariff($)	Patient Referred to Private Sector (%)	Mean Cost($)
Conization	308	84	1538	16	504
Laboratory	11	60	26	40	17
Total cost	318	-	1563	-	521

Table 3. Prevalence of HSIL, LSIL and HPV

Prevalence	Percent	Reference
LSIL	0.0021	Afrakhteh et al
HSIL	0.0012	Afrakhteh et al
HPV	0.051	Khodakarami et al

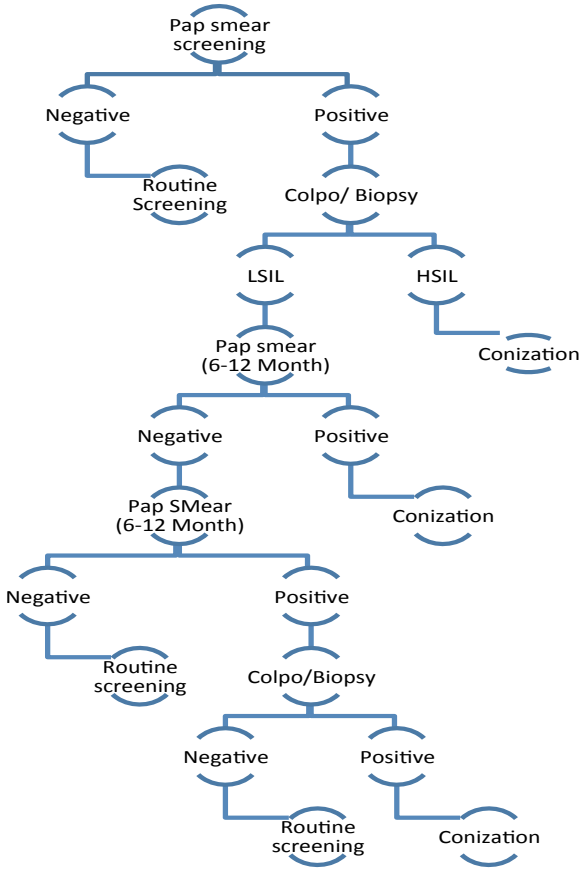

Figure 1. Management of Precancerous Lesions with Pap smear Process

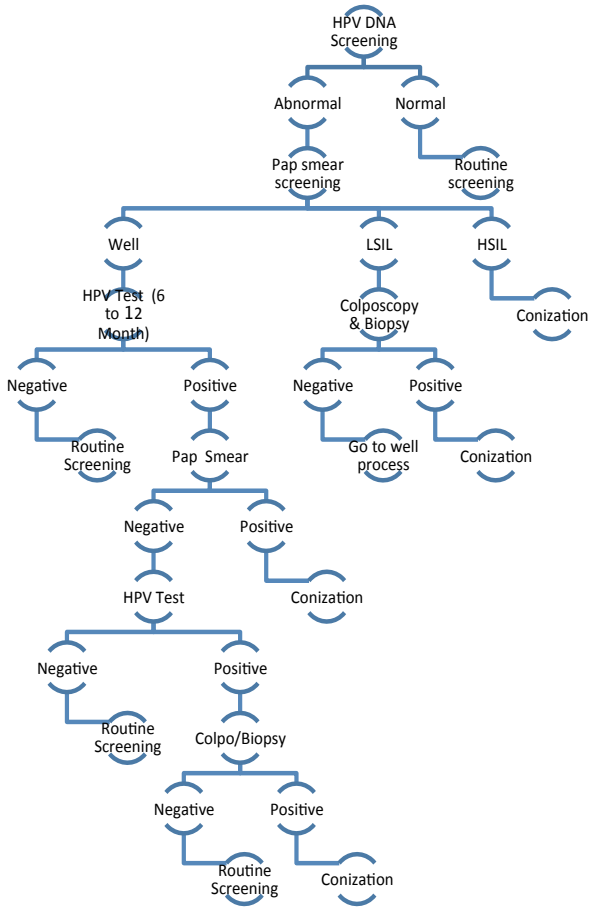

Figure 2. Management of Precancerous Lesions with HPV DNA Testing Process

Patients with positive HPV DNA test results in the course of follow-up underwent cytology. Cytology results may be normal or may indicate LSIL or HSIL and involved eleven processes (Figure 2).

According to the Table 3and decision tree, the total cost of management of lesions with Pap smear methods based on prevalence rate and natural history of disease in Iranian population was 36.1$ per woman.

The total cost of management of lesions based on prevalence rate of HPV and other lesions and the natural history of disease in Iranian population was 174$ per woman.

Discussion

Our findings showed that patient follow-up through screening with Pap smear were less expensive than using HPV DNA test. To the best of our knowledge, this was the first study to design the decision tree to calculate the costs of follow-up for lesions diagnosed in screening programs in Iran. Due to decrease incidence and mortality rate of cancer in countries implementing screening programs, the importance of an organized screening program is undeniable (Franco et al., 2001; Chawla et al., 2014). In Finland, for instance, the incidence and mortality rate of cancer was reduced by 80% during 1963-90 following the adoption of an organized screening program (Anttila et al., 1999).

Since screening program in Iran lasts only up to the time of taking cytology, cervical lesions are not followed up systematically and the patients are supposed to follow up their suspicious lesions (who may not actually feel compelled to do so). Therefore, embracing an organized screening program in the country will reduce the incidence of precancerous lesions and lead to earlier diagnosis of the disease. According to the national cancer registry, ASR for cervical cancer had an increasing trend during 2005-2008 (1.86, 2.12, 2.47, and 2.61, respectively). Although the rate decreased to 2.17 in 2009, this reduction was mainly caused by changes in cervical tumor coding and the actual incidence of the disease did not decrease in 2009 (Center for Disease Control and prevention Noncomunicable Diseases Unit Cancer Office, 2012). In 2010 in Iran 7.3% of GDP per Capita was spent in health expenditure. This means that, 777.3$ out of 6575$ of GDP per Capita allocated to health programs (World, 2012), It seems that adding the cost of follow-up (36.1$ or 174$ per woman) to the screening program's cost, would have more advantages than spending money on cancer treatment even in a low incidence country.

The present study sought to not only highlight the significance of lesion follow-up, but also estimates the treatment costs of precancerous lesions and thus help policy makers to decide the best follow-up method in the existing screening program. This study indicated that patient follow-up was less expensive with Pap smear than with HPV DNA test. However, factors other than expenses have to be considered when selecting a follow-up method:

While we calculated follow-up costs based on the tariffs reported by the Ministry of Health and Medical Education, many studies have suggested the cost price

of services to be much higher (Doshmangir, 2011). On the other hand, as the HPV DNA test has not yet been incorporated in Iran's screening program, the test seems expensive compared to countries where it is routinely performed. Research on the cost-effectiveness of various screening methods revealed HPV DNA test to be twice as expensive as Pap smear in different countries (Andres-Gamboa et al., 2008; Berkhof et al., 2010; Chow et al., 201; Chuck, 2010; de Kok et al., 2012), while, the difference between the costs of these two tests is considerable in Iran.

There are inexpensive kits to detect HPV DNA which used in low-income countries to reduce the costs of HPV DNA test (Shi et al., 2011; Saxena et al., 2012). Since the HPV DNA test imposes lower underlying costs compared to the Pap smear (Kuhn et al., 2000), this method can be applied in cervical cancer screening in Iran. On the other hands, as the HPV DNA test is a preferable method for diagnosis of precancerous lesions, policymakers should focus on techniques to reduce the costs of this test (Wang et al., 2013). Global recommendations have also emphasized on the importance of the above-mentioned point in revising screening programs in developing countries (Sankaranarayanan et al., 2001). Besides The Food and Drug Administration(FDA) is currently approved the HPV Test for primary cervical cancer screening in women aged 25 years or older (R 2014).

Sensitivity and specificity of lesion follow-up methods should also be taken into account. Due to the higher sensitivity of HPV DNA testing compared to the Pap smear, the large number of patients with cervical cancer were diagnosed thus it can reduce the incidence and mortality rate of the disease. Furthermore this test imposed additional diagnostic, treatment, and psychological costs. Meanwhile, the higher specificity of Pap smear compared to HPV DNA test makes more healthy people involved in the diagnostic process and likewise increases the costs (Malloy et al., 2000).

Furthermore, despite the high cost of screening with HPV DNA test, the higher sensitivity of this method in diagnosis of actual patients decreases a proportion of unnecessary colposcopies. Besides, high negative predictive value of this method prolongs the intervals between screening sessions. These two factors can largely reduce the costs (Burr et al., 2007).

Another superiority of HPV DNA test, which can be performed as self-sampling, over Pap smear is its acceptability (Dzuba et al., 2002; Nabandith et al., 2012). Cost-effectiveness of lesion follow-up methods should also be evaluated by economic studies through which a better framework can be created for decision-making in this regard (Chalkidou et al., 2014). Moreover, policymakers should bear other issues, such as equity, accessibility, and acceptability of methods, in mind.

This study mainly had some limitations due to the lack of information. First, we calculated direct costs. Therefore the indirect and psychological costs of patients following their diagnosed pre-cancerous lesions were not considered in our study. Second, we used available data from Teheran population based cancer registry's data from 1998 to 2001 to estimate proportion of patients who referred to governmental and private sectors which was relatively old. third, to show the trend of cervical cancer in Iran, we used ASR from national cancer registry which is mainly pathology based and these statistics might be underestimated (Zendehdel et al., 2010).

In conclusion, the follow-up process for patients with suspicious cervical lesions needs to be included in the existing screening program. HPV DNA test is currently more expensive than Pap smear, it is suggested that to manage precancerous cervical lesions with Pap smear test.

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