CERVICAL SCREENING WITH LUVIVA MACHINE FOR EARLY DETECTION OF CERVICAL DYSPLASIA: EXPERIENCE FROM EKITI STATE, NIGERIA

Sunday O. Omoya[1], Abimbola M. Obimakinde[2], Olusola B. Fasubaa[3], Olufolakemi G. Olomojobi[3], Omolola O. Alao[4], Olasunkanmi O. Alabi[3], Olajumoke O. Atanda-Owoeye[3]

[1]Department of Obstetrics and Gynaecology, State Specialist Hospital, IkereEkiti, Ekiti State.
[2]Department of Family Medicine, EkitiState University Teaching Hospital, Ado Ekiti, Ekiti State. State Ministry of Health, Ado Ekiti, Ekiti State.
[3]Department of Obstetrics and Gynaecology, Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State.

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ABSTRACT:

Background: Cervical cancer is a preventable and potentially curable cancer when detected early, yet it continues to be among the leading causes of cancer death in developing countries. Screening for cervical dysplasia is critical for early detection in order to reverse this trend. Several traditional screening methods such as pap smear test, HPV-DNA screening test, visual inspection with acetic acid or lugol iodine are in vogue with different specificity and sensitivity. LuViva advanced cervical scan is a new automated screening tool that has great promise for the detection of the disease in its earliest form both in developing and developed countries.

Objective: This study was designed to describe our experience with the use of LuViva advanced cervical scan as a primary screening tool for cervical dysplasia.

Method: This is a descriptive cross-sectional study, whose data was obtained from the free health screening for civil servants in Ekiti State conducted between 11th and 21st February, 2014. Screening for Cervical dysplasia was conducted using the LuViva advanced cervical scan for women 40 years old and above. The result was automatically recorded and transferred to an Excel sheet for analysis.

Result: A total sum of 254 patients was screened during the study period. Only one patient had a prior pap smear done. The automated self-reporting LuViva scan presented the result of the benign changes on the cervix as low risk in 143 patients (56.3%), moderate risk in 52 patients (15%) and high risk in 59 patients (11.5%). The machine further classified the dysplastic changes of the low, moderate and high risk categories as Atypical glandular cell (AGC), Atypical glandular cell favouring neoplasia (AGC-FN), Atypical glandular cell of undetermined significance(AG-US), Atypical squamous cell of undetermined significance (ASC-US),

Corresspondence*: Dr S. O. Omoya, Department of Obstetrics and Gynaecology, State Specialist Hospital, Ikere-Ekiti.*
Email address: sundayomoya@yahoo.co.uk Tel +234(0)8030637978

Atypical squamous cell where high grade cannot be excluded (ASC-H) and Low grade squamous Intraepithelial lesion (LSIL). The proportion of moderate and high risk AGC (31.2%) was just slightly lower than the moderate and high risk of ASC-US (35.2%) while a higher percentage of43.9% in low grade squamous intraepithelial lesion was recorded among the patients.

Conclusion: Our experience suggests that there is a place for the use of luViva scan in the primary screening for cervical dysplasia and there is a correlation between LuViva scan high risk result and histological diagnosis of cervical dysplasia.

INTRODUCTION

Cervical cancer is a curable disease when detected early as it usually begins slowly with recognizable dysplastic changes which progresses gradually over 10-20 years, yet it remains the commonest genital tract malignancy worldwide.[1] Globally there are 471,000 cases of cervical cancer diagnosis annually and about 233,000 deaths yearly, of which 85% of these deaths occur in low and middle-income countries.[2-4] It is the second most common female cancer and the second leading cause of cancer death in women globally.[5-6] Most women with dysplasia have no symptom, therefore screening tests are very important.

There are many modalities of screening for dysplasia which significantly reduce the disease burden. These include Pap smear test which could be the traditional Cytology, Automated Cytology or Liquid base Cytology.[2-3] Human papilloma virus (HPV-DNA) testing, Visual inspection with acetic acid (VIA), Visual inspection with acetic acid and magnification (VIAM), Visual inspection with lugol iodine (VILI) and Cervicography are also other modalities of screening.[2,3]

However the Pap test, which is the gold standard is not a perfectly reliable measure because between 15% to 25% of Pap smear test are false-negative results and as many as 25% of invasive cervical cancer cases escape early detection because of sampling errors.[4-7]New technologies continue to emerge in a bid to ensure effective screening for cervical dysplasia, one of these is the LuViva advanced cervical scan.[4,7,8]

LuViva is designed as a fast, painless, non-invasive test that has the potential to significantly improve the early detection of cervical dysplasia.[4,7,8] It identifies and quickly analyze light reflected from the cervix using a combination of fluorescence and reflectance spectroscopy to scan the cervix distinguishing between normal and diseased tissue by detecting biochemical and morphological changes at the cellular level.[4,7,8]

The LuViva Scan is a point-of-care device that can detect cervical disease up to two years earlier than Pap test, HPV test, colposcopy and biopsy, eliminating the high number of unnecessary, painful and costly testing of conventional tissue sample methods.[4,7,8] It is therefore a cost effective screening method. A study using LuViva machine reduced the number of unnecessary biopsy by about 40%.[4]The test is effective on women of all ages.[4]

The LuViva scan identified 100% of all cervical disease cases in a blinded clinical study, also correctly identified 44% of women who had a previous abnormal Pap test and who were determined to be false positives as part of the study.[8]The machine is positioned to address the

tremendous unmet need in developed countries to reduce the high number of false positive results created by conventional testing but even present greater opportunity in the developing world to detect disease where the infrastructure to support conventional laboratory-based testing may be lacking or inadequate.[4,7,8,9]

A study conducted on 55 women who had positive Pap tests concluded that there is high sensitivity, specificity and high negative predictive value of LuViva.[10]The scan offers the potential of a cost effective test that provides an immediate result while detecting significantly more of moderate and high grade dysplasia and significantly reducing the need for additional testing for benign and CIN I lesions.[4,7,9] Test results are immediately reported as one of three levels; low, moderate or high which helps the physician decide whether a colposcopy examination and biopsy is indicated.[9]LuViva effectively triages women at risk for cervical cancer, especially those with ASC-US or LSIL Paps or with evidence of high risk HPV.[10]

The LuViva scan detects cervical dysplasia with sensitivity of greater than 90% compared with 76% sensitivity for the current standard of care methods and can be used effectively in primary screening considering the limitation of routine pap test.[4]This study presents our experience with the use of LuViva advanced cervical scan as a primary screening tool for cervical dysplasia.

MATERIALS AND METHODS

This is a descriptive cross-sectional study,whose data was obtained from the free health screening for civil servants at the Ekiti State Government secretariat between 11th and 21st of February, 2014. The intervention included screening for metabolic diseases such as hypertension, and diabetes mellitus and cancers of the prostate, colon, breast and the cervix. Screening for cervical dysplasia, which is the precursor of cervical cancer was conducted using the LuViva advanced cervical scan (Guided Therapeutics Inc. GA, USA. 2012). The screening was done in a designated examination room in the data bank of the state ministry of health.

The study population consisted of female civil servants from the various ministries who were 40 years and above, who were not menstruating at the time of the screening and who consented for the test. Age limits was imposed because of limited resources. Eligible patients were referred from the various screening points for cervical screening. The procedure was explained to the patients on arrival, basic information was obtained and they were prepared for the procedure.

The scan was conducted by a team that consisted of a consultant Gynaecologist, consultant family physician, a resident in Obstetrics and Gynaecology, and medical officers from the state ministry of health. The team was trained on the use of the LuViva scan prior to the screening. The patients involved in the training were not included in the final analysis. Confidentiality and privacy was ensured in the screening room and the result was discussed with each patient before she exits the room. The scan was used as a primary screening tool. Almost all the patients had not had any cervical screening prior to the exercise. This was indicated as 'test result not available' option on the relevant cytology input dialog on the machine.

The LuViva scan produced results for each patient based on 8 distinct categories as follows; Negative, Benign changes, Atypical glandular cell (AGC), AGC-favour neoplasm, AGC-undetermined significance (AGC-US), Atypical

squamous cell-where high grade could not be excluded (ASH-H) Atypical squamous cell of undetermined significance ASC-US) and Low grade squamous intraepithelial lesion (LSIL). The only exception was the patient who had a previous Pap smear result that was inputted into the LuViva scan. She had a solitary result output. The risk for dysplasia was assessed as low, moderate or high risk. Patients adjudged as high risk for dysplasia were referred to the State Specialist Hospital, Ikere Ekiti for colposcopy and biopsy. Moderate and low risk patients were given appointments ranging from 6-12 months and 3 years respectively for follow up screening.

The result that was automatically generated by the scan was printed out. The printed result was transferred to an Excel sheet in which the result was stored and analyzed. The data is presented in frequency tables, percentages and charts. The output was assessed to reveal our experience with the LuViva scan as primary screening tool for cervical dysplasia.

Ethical approval for the study was obtained from the state ministry of health ethical committee.

RESULTS

A total of 254 patients were screened during the study period. Eligible age was limited to 40 years and above due to limited resources. Four patients below the age of 40 years however got involved in the screening. This is shown in Table 1. Only one patient had prior Pap smear done before the exercise (Table 2).

The LuViva scan presented result as low, moderate or high risk for all the various categories of the cytological classification in all the patients except the patient with a prior Pap smear result that had a single result presented under the Negative for dysplasia column. The result for this patient with Pap smear result which was Negative for intraepithelial lesion or malignancy was described as low risk on LuViva scanning.

Analysis of the result showed low, moderate or high risk for Negative finding for dysplasia, as shown in Table 3A, with 17 patients (6.7%) having high risk. Also, the result for Benign changes were presented as low, moderate or high risk, with 29 patients (11.5%) having high risk (Table 3B). The same pattern was observed in all the other 6 categories as shown in Table 3C.

The result of each patient was summarized using highest risk on screening for the various parameters. Low risk was adjudged in 143 patients (56.3%), moderate risk in 52 patients (20.5%) and high risk in 59 patients (23.2%). This was further sub classified using the age distribution and presented in Figure 1.

High risk for atypical glandular cells was observed in 40 patients (15.8%) and atypical glandular cells of undetermined significance were observed in 42 patients (16.6%). All the patients with high risk for AGC-favouring neoplasm were also stated as high risk of AG-undetermined significance(Figure 2).

Forty five patients (17.8%) were shown to have high risk for atypical squamous cell of undetermined significance (ASC-US). These patients were observed to be a subset of the total number of 53 patients (20.9) with high risk for atypical squamous cell – where high grade could not be excluded (ASC-H), who were also a subset of the total number of 59 patients (23.3%) with high risk for low grade squamous intraepithelial lesion. This was presented in Figure 3.

Preliminary report on the result of histology of colposcopy directed biopsy of the patients

adjudged as high risk (only nineteen presently available) showed 2 patients with CIN1, 8 patients with CIN II and 9 patients with CIN III (a patient with Carcinoma Insitu). Other histology results are being awaited and the follow up appointments for other patients would create sufficient data for analysis.

DISCUSSION

This study describes our experience with the use of LuViva advanced cervical scan as a primary tool in cervical screening for predicting the risk of cervical dysplasia. No previous documentation of the use of the scan as a primary tool has been done in Nigeria or in the West African subcontinent. Previous studies using the Luviva scan machine were conducted on patients with abnormal pap smear. A multicenter pivoted study involving 1607 patients showed a sensitivity of 91% in the detection of CINII+ compared to 76% for standard of care with pap smear[12]. Bentley et al (2014) also observed a sensitivity of 100% in the detection of high grade dysplasia in patients referred on account of abnormal pap smear result.

The result of this study showed low risk in 143 patients (56.3%), moderate risk in 52 patients (20.5%) and high risk in 59 patients (23.2%). This is at variance with the findings of Bentley et al (2014) where 23.6%, 12.7% and 63% were observed for low, moderate and high risk respectively. This is understandable because the 55 patients in their study were referred on account of abnormal pap smear result compared to a primary screening tool undertaken in this study.[10]In their study, all the patients with high grade cervical dysplasia were correctly identified as high grade risk on Luviva scan. In this study, all the patients classified as high risk (59 patients) were sent for histological diagnosis and nineteen (19) of them came back with results while the rest of them are yet to present for followup. This however further highlight the low level of health seeking behavior of people in this locality considering the population involved with their level of literacy and the opportunity that early detection of cervical dysplasia offers in the prevention and treatment of cervical cancer. This is further reflected in the fact that only a patient (0.39%) among female civil servants who presented for the exercise has had a documented pap smear before the screening exercise. The nineteen histology results available so far for moderate to high risk patients in the study showed 2 patients with CIN I, 8 patients with CIN II and 9 patients with CIN III. Among the patients with histology report, the ability of the machine to recognize CIN II and CIN III is about 89%. Though the sample size is small, the result is consistent with those of Bentley et al 2014 whose patients had previous abnormal results. The LuViva scan result for various cytological classification showed a distribution for negative for dysplasia in the range of low, moderate to high risk, with 17 patients (6.7%) showing high risk. The same is applicable to the results for benign changes which also had 29 patients (11.4%) showing high risk for dysplasia. The analysis showed high risk for atypical glandular cells occurring in 40 patients (15.8%). There was no discrimination between high risk for atypical cells which favours neoplasm [41 patients (16.2%)] and high risk for atypical glandular cells with undetermined significance [42 patients (16.6%)]. There was also no discrimination between atypical squamous cell, where high grade could not be excluded (ASC-H) and low grade squamous intra epithelial

lesion 53(20.9%) and 59 (23.3%) respectively. The pattern showed the patients with high risk for ASC-H observed to be subset of patients with high risk for LSIL. There was also a similar distribution for the low and moderate risk between the two categories (148(58.5%), 52(20.6%) and 142(56.1%), 52(20.6%) respectively). The results were therefore adjudged not to be specific on the cytological classification demonstrated.

The automated classification of the dysplastic changes of the low, moderate and high risk categories as AGC, AGC-FN, AG-US, ASC-US, ASC-H and LSIL may be useful for follow up when used as primary screening and also to study the dynamics of the disease. The proportion of moderate and high risk AGC (31.2%) is just slightly lower than the moderate and high risk of ASC-US(35.2%) while a higher percentage of low grade squamous intraepithelial lesion of 43.9% was recorded among the patients. It appears that the proportion of glandular dysplasia of the cervix in the study is probably higher than expected and the prediction of glandular cell carcinoma of the cervix may be on the increase in the future. This is an area that will need further evaluation for clarification in the near future.

There is definitely a place for the use of LuViva advanced scan as a primary tool for cervical screening for dysplasia. It is however important to exercise caution with the interpretation of the cytological classification. Patients with high risk for cervical dysplasia may be recommended for further assessment with colposcopy and biopsywhile those with moderate and low risk can be repeated at six - twelve months and 3 years interval respectively and final judgment made depending on the results and presentation. Further studies into the use of the LuViva advanced cervical scan in the primary screening for cervical dysplasia are recommended.

Tables: 1 Age Distribution

Age (years)	Frequency
<40	4
40-44	61
45-49	98
50-54	50
55-59	36
>60	5
Total	254

Table 2: Prior Pap Smear

YES	**1(0.39%)**
NO	**253(99.61%)**
TOTAL	**254(100%)**

Table 3: Analysis Of Result Of Luviva Machine

Table 3a Parameter 1: Negative

LOW	221(87.0%)
MODERATE	16(6.3%)
HIGH	17(6.7%)
TOTAL	254(100%)

Table 3b Parameter 2: Benign Changes

LOW	186(73.5%)
MODERATE	38(15.0%)
HIGH	29(11.5%)
TOTAL	253(100%)

Table 3c Parameter 3: Dysplastic Changes

	AGC	AGC-FN	AG-US	ASC-US	ASC-H	LSIL
LOW	174(68.8)	173(68.4)	172(68.0)	164(64.8)	148(58.5)	142(56.1)
MODERATE	39(15.4)	39(15.4)	39(15.4)	44(17.4)	52(20.6)	52(20.6)
HIGH	40(15.8)	41(16.2)	42(16.6)	45(17.8)	53(20.9)	59(23.3)
TOTAL	253	253	253	253	253	253

Figure 1: Categorization On Highest On Risk On Screenin Within The Age Group

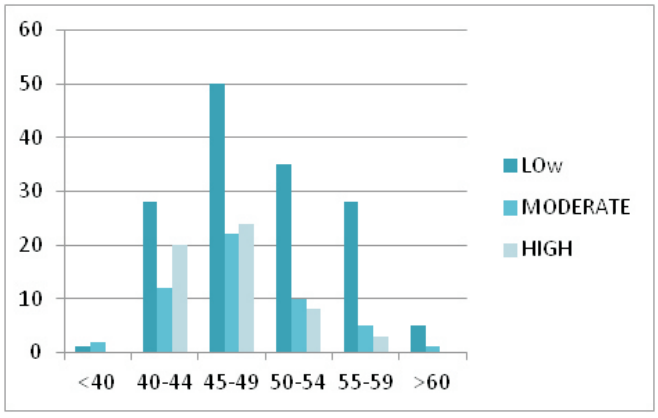


Figure 2: Distribution Of Glandular Cells Dysplasia

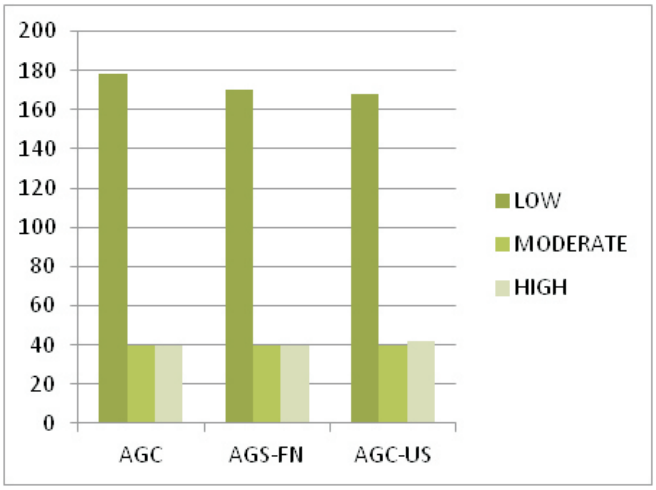
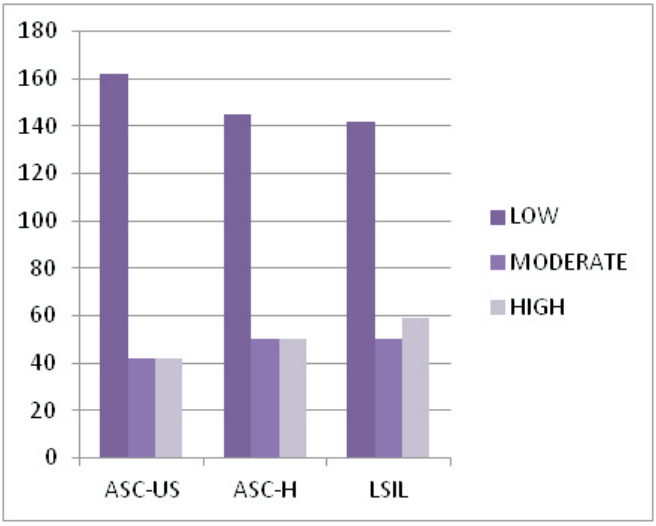


Figure 3: Distribution Of Squamous Cell Dyspasia



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