A Dissertation on

CLINICAL PRESENTATIONS, MANAGEMENT OPTIONS AND OUTCOME IN CARCINOMA OF VULVA

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BONAFIDE CERTIFICATE

This is to certify that Dr.D.AMUDHAN, bonafide student of M.Ch., Surgical Oncology in the Department of Surgical Oncology, Government Royapettah Hospital, Chennai – 600 014 has done this dissertation on "**CLINICAL PRESENTATIONS, MANAGEMENT OPTIONS AND OUTCOME IN CARCINOMA OF VULVA"** under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamil Nadu Dr.M.G.R. Medical University, Chennai for M.Ch., Surgical Oncology Examination to be held in August 2012.

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CLINICAL PRESENTATIONS, MANAGEMENT OPTIONS AND OUTCOME IN CARCINOMA OF VULVA

ABSTRACT

OBJECTIVE: Carcinoma of the vulva is a relatively rare disease accounting for 0.3% of all cancers affecting females and 1.3% of all gynecological malignancies in Chennai. Aim of the present study is to analyze the clinical presentations, treatment options, morbidity, failure pattern and survival for invasive carcinoma of vulva treated in our institution during a period of eight years and to compare our results with other published series.

MATERIALS AND METHODS: Retrospective analysis of case records of 35 patients who underwent surgery for invasive carcinoma of the vulva from 2004 to 2011 in the Department of Surgical Oncology, Government Royapettah Hospital, Chennai.

RESULTS: The mean and median age was 52.5 years and 55 years respectively (range 21-72). Labia majora was the predominant site of disease (80%). Twenty eight patients underwent Radical Vulvectomy with Nodal Dissection, 2 underwent Hemivulvectomy with Nodal Dissection, 2 underwent Simple Vulvectomy, 2 underwent Wide Local Excision and 1 underwent Wide Local Excision with Nodal Dissection. Lymphadenectomy was not done in 4 patients. With a median follow up of 26 months (range 2-67 months), 8 patients (22.9%) developed recurrence, of which one is systemic, 4 regional and 3 local. The estimated 5 year Overall Survival (OS) and Disease Free Survival (DFS) for all cases in our series using Kaplan-Meier analysis was 85.1% and 65.4% respectively. On univariate analysis using log rank test, advanced stage, lymph node positivity and lymph node positivity with extracapsular spread (ECS) significantly affected estimated 5 year overall survival.

CONCLUSION: Carcinoma vulva, a relatively rare disease should better be managed in dedicated cancer centers where treatment can be tailored to individual patients with multidisciplinary cooperation. The median age in our series was 55 years which is well below the western world. Extracapsular nodal spread was observed as the strongest prognostic factor for survival in our series like other international series. Since there has been a dearth of reports about this disease from our country as well as other developing countries we urge the need for more studies from various centers and probably well designed multicentric studies keeping in mind the low prevalence of this disease.

Key Words: *Carcinoma Vulva; morbidity; recurrence; survival.*

INTRODUCTION

Carcinoma vulva is a relatively rare disease accounting for 4% of all gynecological malignancies in United States[1]. It constitutes 0.3% of all cancers affecting females and 1.3% of all gynecological malignancies in Chennai[2]. The vulva is the anatomic area immediately external to the vagina. It includes the labia and the perineum. The inguinofemoral nodes are the sites of regional spread. Tumor involvement of pelvic lymph nodes is considered distant metastasis.

Cases should be classified as carcinoma of the vulva when the primary site of the growth is in the vulva. Tumors present on the vulva as secondary growths from extragenital site should be excluded. TNM stages are based on clinical and/or pathological classification[3]. FIGO (Fédération Internationale de Gynécologie et d'Obstétrique) uses surgical/pathologic staging for carcinoma of vulva[4]. Stage should be assigned at the time of definitive surgical treatment or prior to radiation or chemotherapy if either of these is the initial mode of therapy. The stage cannot be changed on the basis of disease progression or recurrence or on the basis of response to initial radiation or chemotherapy that precedes primary tumor resection.

Carcinoma of the vulva mainly affects the elderly population, although it is becoming increasingly common in younger women[5.] Most patients in developing countries such as India present with advanced loco-regional disease for various

socio-economic reasons, including lack of awareness, resulting in poorer outcomes and posing management challenges[6]. Most of our patients have hesitancy to have examination of the external genitalia which may also be an important factor for advanced disease at presentation.

Most of the literature on carcinoma of vulva is from the western world. There is a striking paucity of literature related to this subject from the developing countries. Due to the tumor rarity, large prospective randomized trials to guide management are few in this disease. The purpose of this analysis is to know the demographic pattern of invasive carcinoma of vulva in our patients, post operative complications and outcome following surgery which will be of immense help in the understanding of this relatively rare disease so as to plan continued evaluation and future studies to improve our multimodal treatment option to reduce morbidity without oncological compromise and also to compare our results with other international series.

AIM OF THE STUDY

1. To study the various methods of clinical presentation

2. To study management options

3. To analyze the outcome

MATERIALS AND METHODS

A retrospective analysis of all patients who underwent surgery for invasive carcinoma of the vulva in our Department of Surgical Oncology, Government Royapettah Hospital during a period of 8 years between 2004 and 2011 was carried out. All patients were treated with curative intent, and followed up regularly. The preoperative evaluation consisted of complete clinical examination including detailed gynecological examination, routine blood and urine examination, chest radiography, US (Ultrasonogram) abdomen and pelvis. CECT (Contrast Enhanced Computed Tomography) abdomen and pelvis including the groin was done as indicated. Selected patients were additionally evaluated with examination under anesthesia (EUA) and Cystoscopy. Histopathological documentation of the primary lesion was done for all cases preoperatively.

Of those 35 patients, 28 underwent Radical Vulvectomy (RV) with nodal dissection, 2 underwent Hemivulvectomy with nodal dissection, 2 underwent Simple Vulvectomy (SV), 2 underwent Wide Local Excision (WLE) alone and 1 underwent Wide Local Excision with nodal dissection.

In this series, except a few variations in surgical practice to assess the lymphatic spread in the earlier periods, all patients were treated with same concept. During RV, the primary lesion was removed with a minimum of 1 cm margin of

normal tissue in all directions with the incision extending down to the inferior fascia of the urogenital diaphragm. Bilateral labia majora and minora including the clitoris were included in the surgical specimen. Each inguinofemoral node dissection was performed using separate incisions from the vulva incision.

Three patients received pre-operative EBRT (External Beam Radiation Therapy - 50GY in 25 fractions) and one patient received pre operative concurrent Chemo-RT using Cisplatin and 5-fluorouracil (5-FU) as chemotherapeutic agents. All other patients underwent upfront surgery. After surgery, patients with margin positivity, involvement of more than 1 node and presence of extracapsular disease even in 1 node were given adjuvant EBRT.

Patients were followed up monthly in the first year, 2 monthly in the second year, 3 monthly in the third year, 6 monthly for fourth and fifth years and yearly thereafter. Follow-up included clinical examination at each visit, yearly chest x-ray and, CECT abdomen with pelvis and other investigations as indicated.

The demographic pattern, clinical presentation, management options, postoperative complications, failure pattern and survival were analyzed. Survival analysis was done using Kaplan Meier method with SPSS 17® (SPSS Inc, USA) for Windows Software. The log-rank test was used in the univariate analysis to identify the potentially important prognostic variables. P-value of less than 0.05

was considered to be statistically significant. Results were compared with published data available in the literature.

RESULTS AND ANALYSIS

Over this 8 year period, 35 patients with invasive carcinoma of the vulva were treated with surgery in our Department. Preoperative radiation was given for 3 patients because of large inguinal nodal enlargement. One young patient received preoperative chemoradiation because of extensive local disease with involvement of distal urethra. In the remaining 31 patients, upfront surgery was done. Till date no sentinel lymph node procedure was performed for carcinoma of the vulva in our Department. Human Papilloma Virus (HPV) status was also not evaluated.

The mean age of the patients in our series was 52.5 years with a range of 23 – 73 years. The median age at presentation was 55 years. Of those 35 patients, 22 patients were less than 60 years (62.9%). Ten patients (28.6%) were less than 50 years (Table-1). Most of our patients were between 50 to70 years (25/35=71.4%).

TABLE 1

AGE GROUP

Age Group in years	Frequency
20-29	2
30-39	2
40-49	6
50-59	12
60-69	12
70-79	1
Total	35

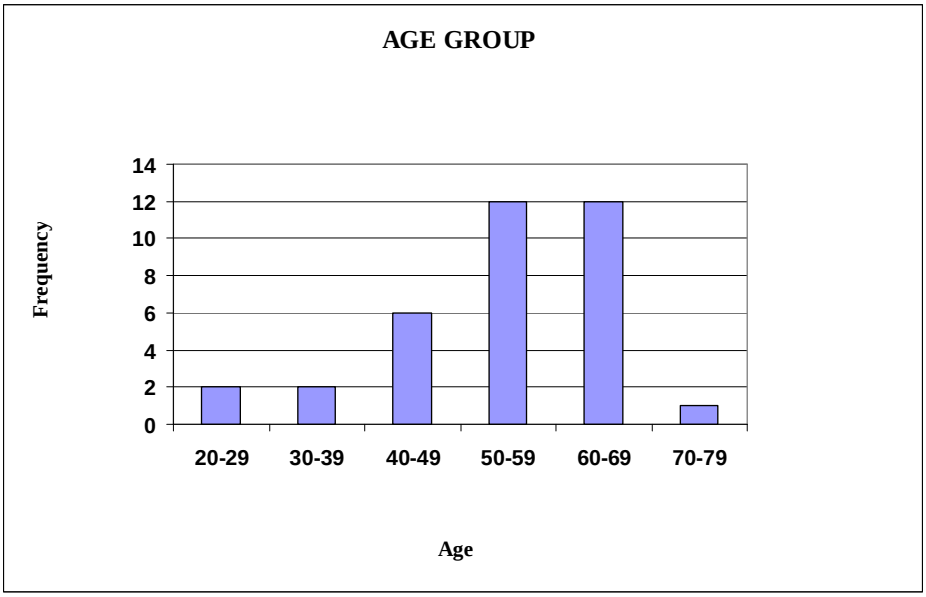
Almost all of our patients were referred from various centers. All of our patients were symptomatic. Some patients presented with more than one symptom. Thirty two (91.4%) of the patients presented with ulcer over external genitalia, 26 (74.3%) of the patients presented with pruritus vulvae, 8 patients (22.9%) presented with pain and 6 (17.1%) patients presented with other complaints like discharge, swelling (Table-2).

TABLE 2

CLINICAL PRESENTATION

Symptom	Frequency	Percentage (%)
Ulcer	32/35	91.4%
Pruritus	26/35	74.3%
Pain	8/35	22.9%
Others	6/35	17.1%

Labia majora was the predominant site of disease in 80% of our patients and labia minora in 14.3%. Clitoris was the predominant site in 5.7% of the patients. Right side of the vulva was predominantly affected in 60% of the patients and the left side in 11.4%. In 28.6 % of the patients the disease was bilateral and hence laterality cannot be fixed. The details of the site and side of involvement are given below in table-3 &4.


AGE GROUP
Frequency
14
12
10
8
6
4
2
0
20-29
30-39
40-49
50-59
60-69
70-79
Age

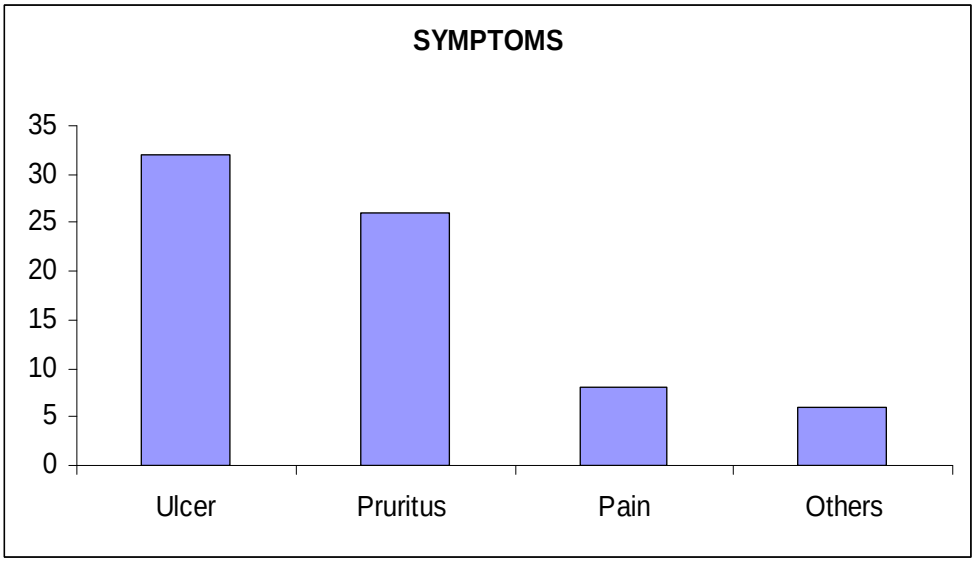

SYMPTOMS
35
30
25
20
15
10
5
0
Ulcer
Pruritus
Pain
Others

TABLE 3

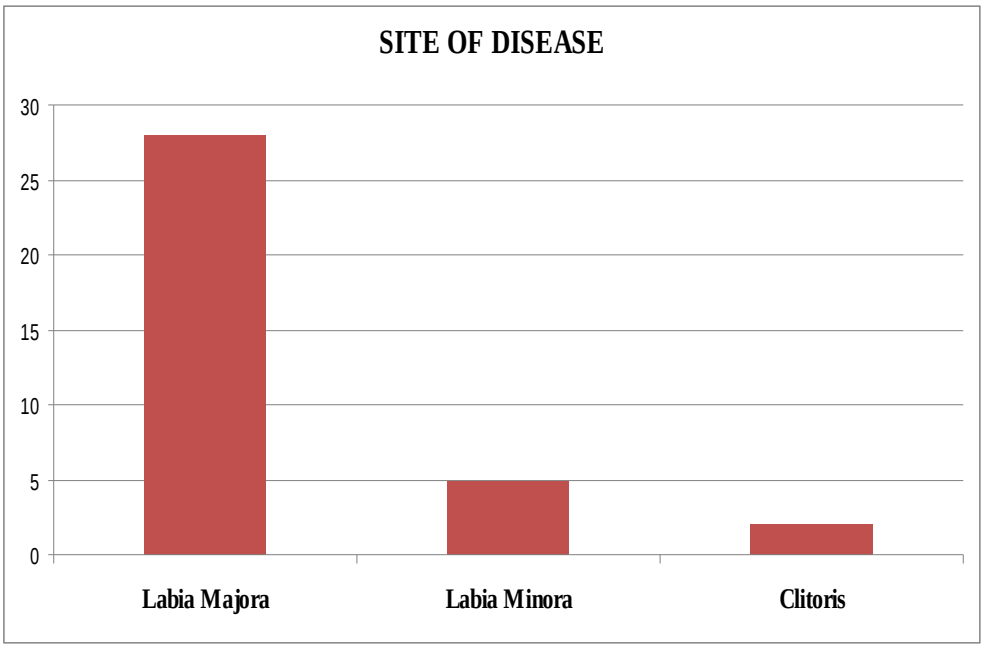
PREDOMINANT SITE OF INVOLVEMENT

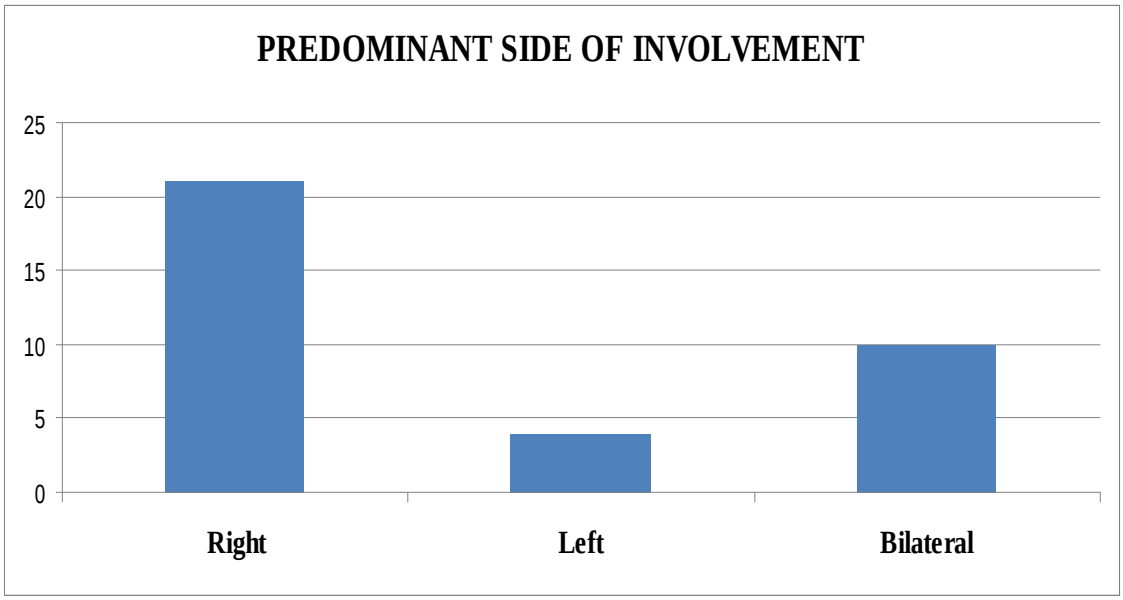
Site	Frequency	Percentage (%)
Labia Majora	28/35	80%
Labia Minora	5/35	14.3%
Clitoris	2/35	5.7%

TABLE 4

PREDOMINANT SIDE OF INVOLVEMENT

Side	Frequency	Percentage (%)
Right	21	60%
Left	4	11.4%
Bilateral	10	28.6%


SITE OF DISEASE
30
25
20
15
10
5
0
Labia Majora
Labia Minora
Clitoris


PREDOMINANT SIDE OF INVOLVEMENT
25
20
15
10
5
0
Right
Left
Bilateral

Of those 35 patients, 28 underwent Radical Vulvectomy (RV) with nodal dissection, 2 underwent Hemivulvectomy with nodal dissection, 2 underwent Simple Vulvectomy (SV), 2 underwent Wide Local Excision (WLE) alone and 1 underwent Wide Local Excision with nodal dissection.

In our center, Radical Vulvectomy was done using three separate incisions, one for the radical vulvectomy and one for each groin dissection. Primary lesion was removed with a minimum of 1 cm margin of normal tissue in all directions with the incision extending down to the inferior fascia of the urogenital diaphragm. Both labia majora and minora including the clitoris were included in the surgical specimen. In Wide Local Excision, the primary lesion was excised with a minimum of 1 cm margin of normal tissue in all directions, with the incision extending down to the inferior fascia of the urogenital diaphragm, preserving the other uninvolved part of vulva.

Unlike radical vulvectomy, Simple vulvectomy does not require an incision all the way to the perineal fascia. The skin and subcutaneous tissues, labia majora, labia minora and clitoris of the vulva are removed enbloc with the tumor.

Inguinofemoral block dissection was performed through a transverse incision below the inguinal ligament, following the standard method without any modification. After doing standard complete inguinofemoral block dissection,

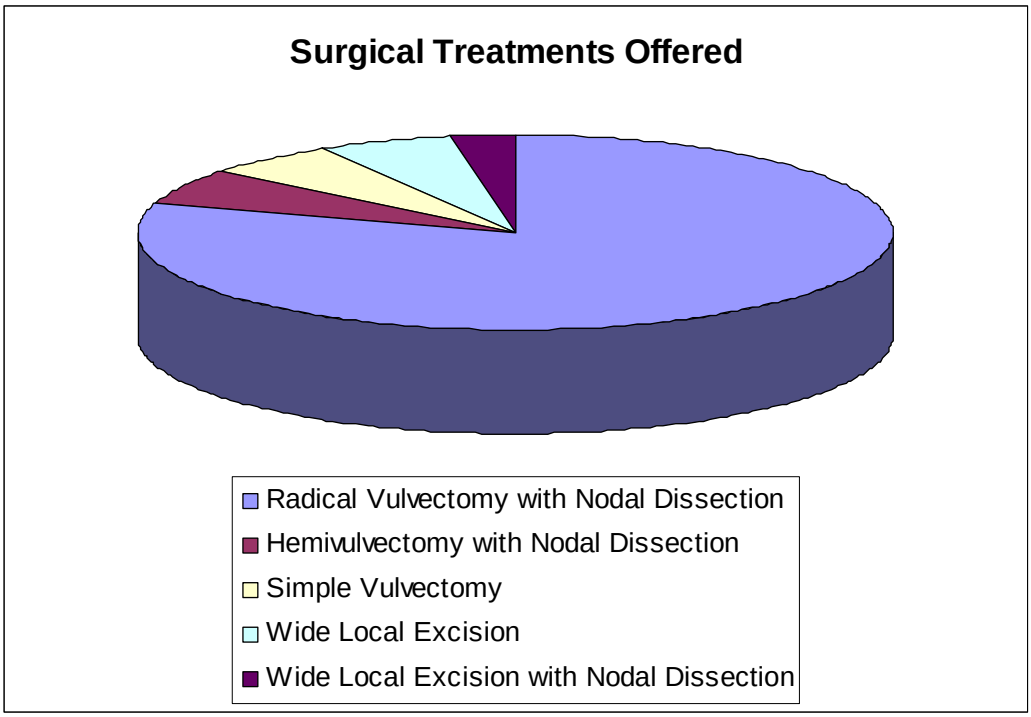
sartorius transposition was done for all patients to protect the femoral vessels in the event of subsequent wound breakdown. The practice of saphenous vein preservation was not followed in our institution. In our institution, iliac nodal dissection was not practiced from the year 2005. Before that period, iliac node dissection was done if the inguinal nodes were positive by frozen section analysis. The various surgical procedures performed were given below in table-5.

TABLE 5

SURGICAL TREATMENTS OFFERED

Surgical treatment	Frequency	Percentage (%)
Radical Vulvectomy with Nodal Dissection	28/35	80%
Hemivulvectomy with Nodal Dissection	2/35	5.7%
Simple Vulvectomy	2/35	5.7%
Wide Local Excision	2/35	5.7%
Wide Local Excision with Nodal Dissection	1/35	2.9%

Generally in our institution, no reconstructive procedures were done for the post vulvectomy area. In one of our patient, bilateral gracilis myocutaneous flap was done for reconstruction of the primary area since the patient had removal of


Surgical Treatments Offered
Radical Vulvectomy with Nodal Dissection
Hemivulvectomy with Nodal Dissection
Simple Vulvectomy
Wide Local Excision
Wide Local Excision with Nodal Dissection

lower part of vagina for adequate clearance. In all other patients, wounds were closed primarily without any flap (Table-6).

TABLE 6

TYPE OF RECONSTRUCTION FOR THE LOCAL AREA

Type of Reconstruction	Frequency	Percentage (%)
Flap (Bilateral Gracilis Myocutaneous flap)	1/35	2.9%
Primary Closure	34/35	97.1%

In general, primary closure of the inguinal wound was done following inguinofemoral block dissection in our center. However, depending upon the clinical status of inguinal nodes and the need for sacrifice of skin, decision whether to use flaps or primary closure was made. Of those 31 patients who underwent nodal dissection, Tensor fascia lata myocutaneous flap (TFL flap) reconstruction was done in 4 patients for whom primary closure alone was deemed to be inappropriate. In all other patients, groin wound was closed primarily (table-7). One of our patient needed tensor fascia lata myocutaneous flap (TFL flap) reconstruction when ilioinguinal block dissection was done for regional recurrence in the right inguinal region, 5months after simple vulvectomy.

TABLE 7

TYPE OF RECONSTRUCTION AFTER NODAL DISSECTION

Type of Reconstruction	Frequency	Percentage (%)
Flap (Tensor Fascia Lata Myocutaneous Flap)	4/31	12.9%
Primary Closure	27/31	87.1%

Overall, in 4 of 35 patients, inguinal lymph node dissection was not performed (Table-8). Of these, one patient (27 year old) who presented with multiple verrucous lesions, who underwent simple vulvectomy alone, developed nodal recurrence on right inguinal region 5 months after the primary surgery. She was treated with right ilioinguinal block dissection with TFL flap reconstruction followed by adjuvant RT because of the involvement of multiple nodes. After that she was on follow-up for another 21 months and defaulted subsequent follow-up. The remaining 3 patients had well lateralized disease with stromal invasion less than 1 mm and hence node dissection was not done. These 3 patients are on regular follow-up and they did not develop any recurrence till date. In two of our patients, right inguinofemoral block dissection alone was done with right hemivulvectomy

without nodal dissection on opposite side for well lateralised lesion on labia majora on the right side since the nodes were negative on frozen section examination. Other than this, 4 cases underwent unilateral nodal block dissection.

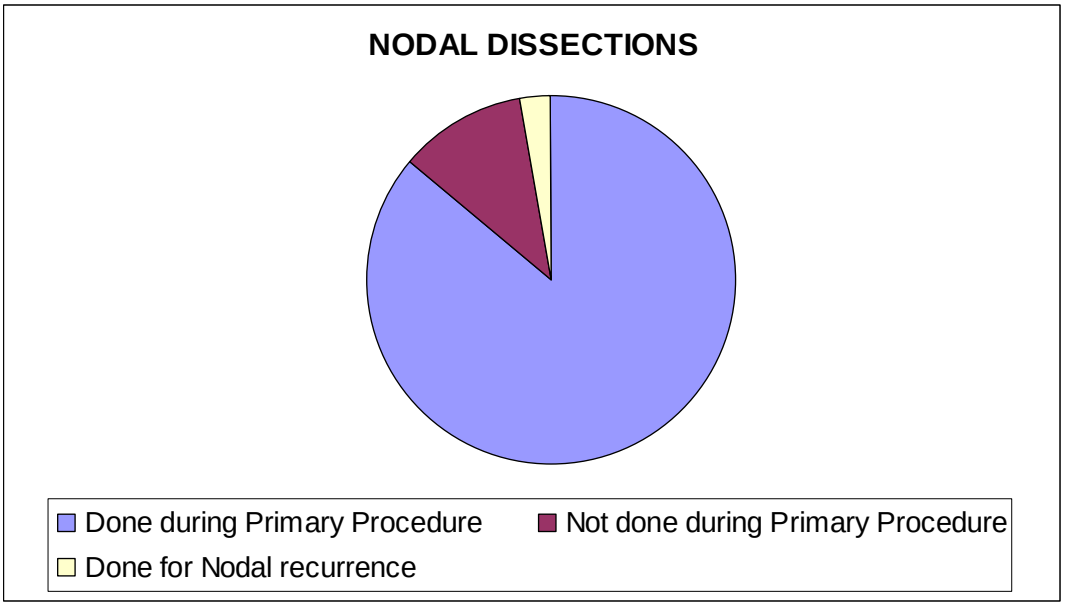
TABLE 8

NODAL DISSECTIONS

Node Dissection	No of Patients
Done During Primary Procedure	31
Not Done During Primary Procedure	4
Done for Nodal Recurrence	1

Post Operative Histopathology

Squamous Cell Carcinoma (SCC) is the most frequent form of cancer of the vulva. All patients in our series were affected with SCC. Except 3 (2 had positive margin, 1 had close margin), R0 resection was achieved in all patients (Table-9). The nodes were found positive in 45.2% (14/31) of the patients those underwent nodal dissection and negative in 54.8% (17/31) of the patients (Table-10). Of the node negative patients, 3 developed recurrence (1 local, 1 regional, 1 systemic). Of the node positive patients, 4 developed recurrence (2 local, 2 regional). Of the 4 patients who had nodal positivity with extra capsular spread, 3 died and 1 patient


NODAL DISSECTIONS
Done during Primary Procedure
Not done during Primary Procedure
Done for Nodal recurrence

defaulted follow-up 14 months following surgery. The average node retrieval per inguinofemoral block dissection in our series was 8.5 which remained well above the recommended optimum number (6 nodes) [3].

TABLE 9

MARGIN STATUS FOLLOWING SURGERY

Margin Status	Frequency	Percentage (%)	Adjuvant Treatment	Recurrence
Negative	32	91.4%	Depending upon nodal status	8
Positive and Close Margin	3	8.6%	**1st Patient→** no adjuvant treatment (received Pre op. RT) **2nd Patient→** (1/4th margin was positive) defaulted RT **3rd Patient→** (Close margin) no adjuvant treatment (received Pre op. RT)	Nil Nil Nil

TABLE 10

NODAL STATUS FOLLOWING SURGERY

Nodal Status	Frequency	Percentage (%)	Current Status
Node Positive with ECS	4	11.4%	3 dead 1 defaulted follow-up
Node Positive without ECS	10	28.6%	1 dead 2 defaulted follow-up 1 alive with disease 6 alive
Node Negative	17	48.6%	1 defaulted follow-up 2 alive with disease 14 alive
Node Dissection not done	4	11.4%	1 defaulted follow-up 3 alive

ECS - Extra Capsular Spread

In our series, 36.4% of patients with clinically suspicious nodes had negative findings at lymphadenectomy and 35% of patients with clinically negative nodes had inguinal lymph node metastases (Table-11).

TABLE 11

CORRELATION OF CLINICAL FINDINGS WITH HISTOPATHOLOGY

Nodal Status	Clinical	Histopathology	Both Clinical & HPE
Positive	11/31	14/31	7
Negative	20/31	17/31	13

Clinically positive, HPE positive →7

Clinically positive but HPE negative→4

Clinically negative but HPE positive →7

Clinically negative, HPE negative →13

Since 1988, the Federation International of Gynecologists and Obstetricians (FIGO) have recommended the adoption of surgical-staging system in carcinoma of vulva due to the clinical difficulties in diagnosing inguinal nodal metastasis. After surgery our patients were fixed into various stages, according to FIGO-2009 Staging System[4, 7] (Tables-12).

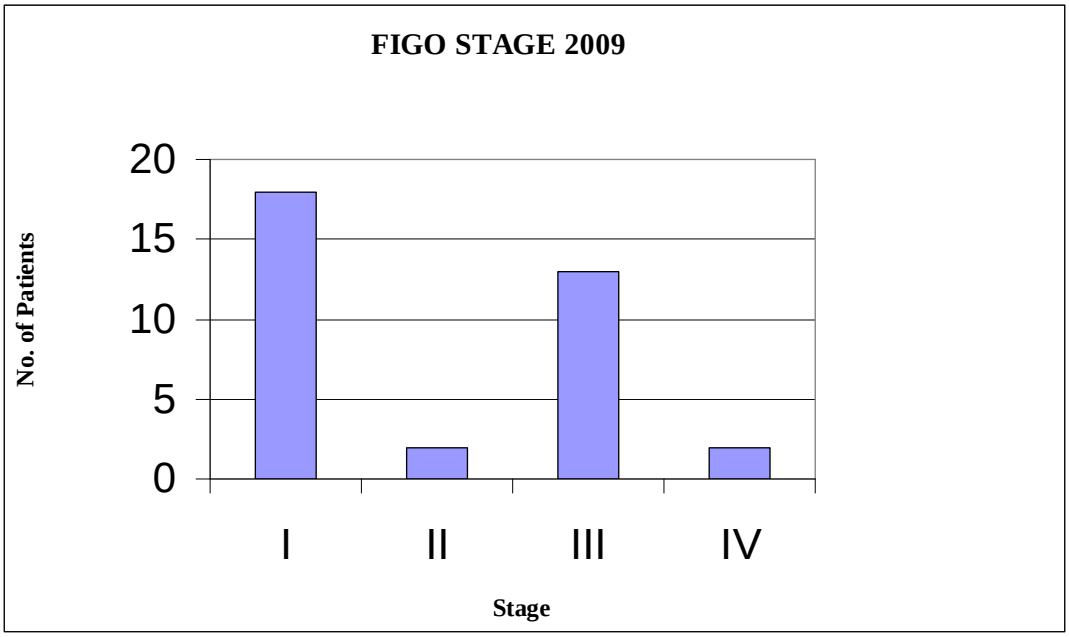
TABLE 12

DISTRIBUTION OF CASES ACCORDING TO FIGO STAGE (2009)

FIGO stage	No of patients
I	18
II	2
III	13
IV	2

Post Operative Complications

No peri-operative mortality occurred in our series. Post operative complications noted in our series were mainly due to nodal block dissection. Majority of cases developed some amount of seroma after nodal block dissection. Seroma requiring repeated aspirations was observed in 58.1% (18/31) of cases. Skin flap necrosis (45.2 %) with wound gaping was the most worrisome complication observed in our series following nodal dissection which increased the


FIGO STAGE 2009
No. of Patients
20
15
10
5
0
I
II
III
IV
Stage

duration of hospital stay. The skin flap necrosis was salvaged with removal of the necrosed part and secondary suturing in some cases and split skin graft after making the wound to granulate well in few cases which caused delay in starting adjuvant RT in indicated cases. We had necrosis of the pedicled flaps used for reconstruction in 2 patients. In a 62 year old female following vulvectomy, the primary wound was reconstructed with bilateral Gracilis myocutaneous flap who already had received pre operative EBRT. She developed flap necrosis which necessitated removal of flap on both sides. Post operatively patient had posterior margin positivity and nodal involvement with extracapsular spread and she died after 20 months. Another 48 year old female who received TFL flap for the reconstruction of inguinal wound following nodal dissection, developed necrosis of the distal part of the flap which was managed conservatively with removal of necrosed part alone. She also developed deep venous thrombosis (DVT) in the immediate post operative period which was managed successfully. Two patients developed wound infection that was treated with appropriate antibiotics. The major late complication was found to be lymphedema of legs which occurred in almost all cases to certain extent but not producing significant problem. We did not observe recurrent lymphangitis in any of the cases during follow-up. The post operative complications occurred in our patients were given below in table-13.

TABLE 13

POST OPERATIVE COMPLICATIONS *

Complication	Frequency	Percentage (%)
Seroma requiring repeated aspiration	18/31	58.1%
Necrosis of Skin Flaps Following Node Dissection	14/31	45.2%
Wound Infection	2/35	5.7%
Necrosis of Pedicled Flap (TFL, Gracilis)	2	5.7%
Deep Venous Thrombosis	1	2.9%

***Some patients had more than one complication**

Adjuvant Therapy

Adjuvant radiation therapy (EBRT) was given to patients with two or more metastatic nodes, margin positive patients and for patients with extracapsular nodal extension irrespective of number of nodes. Patients with negative lymph nodes,

clear resection margins and single node involvement without extracapsular spread were followed expectantly with no adjuvant therapy. Twelve patients were candidates for adjuvant RT, of which 5 defaulted therapy (Table-14). Of those 5 defaulters, two patients with nodal positivity remained disease free for 36, 41 months respectively and defaulted further follow up. One with margin positivity, with negative nodes was found disease free till last follow up (67 months). One with extracapsular nodal disease, developed regional recurrence and died in spite of giving RT. One patient with retroviral positivity who underwent wide local excision remained disease free till last follow up (39 months).

Table 14

Treatment Groups

Treatment Needed	No of patients	Percentage (%)
Surgery alone	19	54.3%
Surgery + Adjuvant RT	12 (5 defaulted)	34.3%
Preop RT/chemo-RT + Surgery	4	11.4

Pattern of Recurrence

At a median follow up of 26 months (range 2-67 months), 8 patients 22.9% (8/35) developed recurrence, of which one is systemic, 4 regional and 3 local. Of the 4 patients with regional recurrence, 2 developed nodal disease and the other two developed soft tissue recurrence. Of the 2 with nodal disease, the patient who had mobile node was treated with Right Ilioinguinal Block Dissection with TFL (Tensor Fascia Lata) flap reconstruction followed by 50GY EBRT in 25 fractions as adjuvant since she had multiple positive nodes. The other one who presented with fixed nodal mass was treated initially with 50 GY EBRT and then another 16 GY EBRT because of poor response to initial therapy. She was put on chemotherapy for residual disease. She received 1 cycle of chemotherapy with Cisplatin and 5-Fluorouracil (CDDP & 5FU) and defaulted further therapy. Of the two patients with soft tissue disease, one patient was a defaulter of adjuvant RT and she developed ulcer left inguinal region 6 months after primary surgery and was given 60 GY EBRT and finally succumbed to disease and died 4 months later. The other one developed soft tissue recurrence in right inguinal region 3 months after primary surgery and was salvaged with chemoradiation and she is on regular follow up till date without disease.

Of the 3 patients with local recurrence, 1 developed recurrence 33 months after surgery. She was planned for RT, but defaulted therapy. At the last follow-up (13 months after the development of recurrence) she was alive with the disease. One patient developed recurrence 21 months after primary surgery, and chemotherapy was planned since she already received 50 GY EBRT as adjuvant therapy. She received 1 cycle of chemotherapy with Cisplatin and 5-fluorouracil (5-FU). Further chemotherapy was deferred because of poor general condition, and she died after 4 months. The other one developed recurrence in the periurethral region 21 months after primary surgery and defaulted therapy. In our series only one patient developed systemic metastases involving lung and humerus and was treated with local RT to bone and systemic chemotherapy with Cisplatin and 5-fluorouracil (5-FU). Of these 8 patients, 3 were stage I, 4 were stage III, 1 was stage II (FIGO-2009). The details of the pattern of recurrence are given below (table-15).

Of the 8 patients, 5 developed recurrence within 1 year of surgery. One patient developed recurrence within 2 year (21 months) and the other 2 patients within 3 years (31, 33 months). An interesting observation that, all the regional and systemic recurrences occurred within 1year of primary surgery in our series (4 regional and 1systemic). All 3 local recurrences occurred 1 year after primary surgery (21, 31, 33 months). The exact reason for this observation was unknown. Since the number of patients was low, any meaningful conclusion could not be made.

TABLE 15

PATTERN OF RECURRENCE

Recurrence Site	Time to recurrence (months)	Age in years	Lymph node status	Stage	Adjuvant treatment	Status
Regional	5	27	Not known	I	Nil	Defaulted follow-up
Regional	4	45	Positive (single node)	III	Nil	Dead
Local	33	55	Negative	I	Nil	Alive with disease
Local	31	48	Positive	III	RT	Alive with disease
Regional	6	50	Positive with ECS	III	Defaulted RT	Dead
Local	21	54	Positive with ECS	III	RT	Dead
Systemic	8	23	Negative	II	Nil	Alive with disease
Regional	3	45	Negative	I	Nil	Alive

ECS – Extra Capsular Spread

Survival Analysis

Of those 35 patients, 4 (11.4%) died during follow-up and 5 (14.3%) defaulted regular follow-up. Of the remaining 26 patients, 3 patients were alive with disease and remaining 23 patients were on regular follow-up and were disease

free. The mean follow-up period for those 5 patients defaulted follow-up was 26 months (range 13 – 41 months). The estimated 5 year Overall Survival (OS) and Disease Free Survival (DFS) for all cases in our series using Kaplan-Meier analysis was 85.1% and 65.4% respectively. On univariate analysis using log rank test, advanced stage, lymph node positivity and lymph node positivity with extracapsular spread (ECS) have emerged as important prognostic factors that significantly affected estimated 5 year overall survival. The important observation was that the estimated 5 year OS for patients with nodal positivity with extracapsular spread was significantly less than patients with nodal positivity without extracapsular spread (P=0.015) and it was more significant when compared with node negative patients (P=0.000). This highlights the importance of extracapsular nodal spread as an important prognostic factor for survival. Since the numbers of patients were low, multivariate analysis was not done.

At the same time, on univariate analysis using log rank test, advanced stage, lymph node positivity did not affect the DFS to a statistically significant level. In our series, the only factor that affected the DFS to a statistically significant level was extracapsular nodal spread (Table-16). The DFS for patients with nodal positivity without ECS (estimated 2 year DFS 63.5%, 3 year DFS 47.6%) was less when compared to patients with node negativity (estimated 2 year DFS 87.1%, 3 year DFS 74.6%) but it was not significant (P=0.245). The DFS for patients with

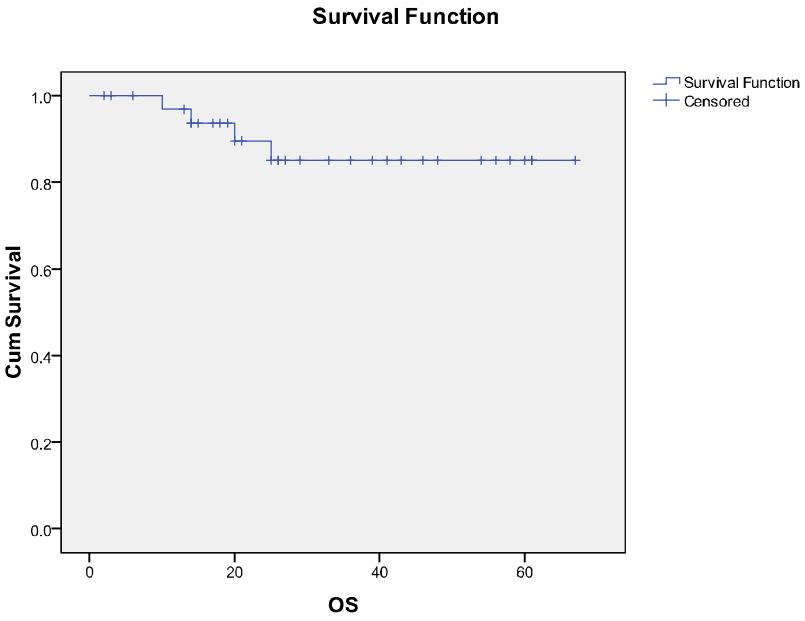
nodal positivity with extracapsular spread was significantly less when compared with patients with nodal positivity without extracapsular spread (P=0.023) and patients with node negativity (P=0.011).

TABLE 16

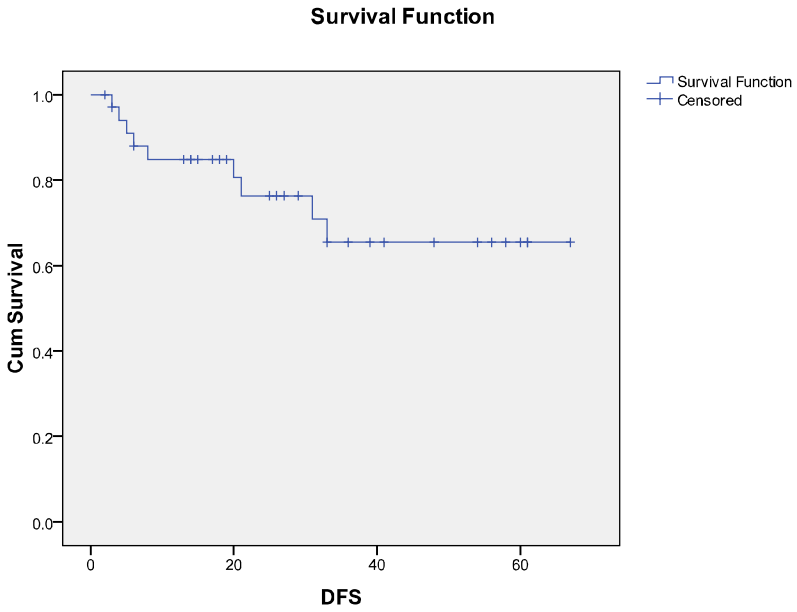
DISEASE FREE SURVIVAL

Lymphnode Status	**Estimated 5 year DFS**
Nodal Positivity with ECS	0%
Nodal Positivity without ECS	66.7%
Node Negative	74.6%

Kaplan Meier Curve -Overall Survival for all Cases



Kaplan Meier Curve -Disease Free Survival for all Cases



REVIEW OF LITERATURE

Carcinoma of vulva is an uncommon disease affecting the elderly population. Despite its infrequency, vulvar cancer remains an important female disease, because of its significant impact on sexuality. Over the past decade, numerous advances have been made in the management of vulvar cancer, with a trend toward more conservative surgery. Early detection and biopsy of any abnormal vulvar lesions are imperative to achieve diagnosis of vulvar cancer in the early stages and to improve subsequent morbidity and survival.

Regarding anatomy[8], the vulva includes the mons pubis, labia majora, labia minora, clitoris, vestibule, vestibular bulb and the greater vestibular glands. The

arterial blood supply is derived from the superficial and deep external pudendal branches of the femoral artery and the internal pudendal artery on each side. Venous drainage of the vulval skin is via external pudendal veins to the long saphenous vein. Venous drainage of the clitoris is via deep dorsal veins to the internal pudendal vein and superficial dorsal veins to the external pudendal and long saphenous veins.

The mons pubis is the rounded hair-bearing area of skin over the pubic symphysis and adjacent pubic bone. It is formed by a mass of subcutaneous adipose connective tissue. The labia majora are two prominent, longitudinal folds of skin that extend back from the mons pubis to the perineum. They form the lateral boundaries of the vulva. Each labium has an external, pigmented surface covered with hairs and a smooth, pink internal surface with large sebaceous follicles. The labia are thicker anteriorly, where they join to form the anterior commissure. Posteriorly they do not join, but instead merge into neighbouring skin, ending near and almost parallel to each other. The connecting skin between them forms the posterior commissure that overlies the perineal body and is the posterior limit of the vulva.

The labia minora are two small cutaneous folds, devoid of fat, that lie between the labia majora. They extend from the clitoris obliquely down flanking

the vaginal orifice. Anteriorly, each labium minus bifurcates. The upper layer of each side passes above the clitoris to form the prepuce, which overhangs the glans of the clitoris. The lower layer of each side passes below the clitoris to form the frenulum of the clitoris. The vestibule is the cavity that lies between the labia minora. It contains the vaginal and external urethral orifices and the openings of the two greater vestibular (Bartholin's) glands and of numerous lesser vestibular glands.

The clitoris is an erectile structure partially enclosed by the anterior bifurcated ends of the labia minora. It has a root, body and glans. The body can be palpated through the skin. It contains two corpora cavernosa, composed of erectile tissue and enclosed in dense fibrous tissue, and separated medially by an incomplete fibrous pectiniform septum. The fibrous tissue forms a suspensory ligament that is attached superiorly to the pubic symphysis. Each corpus cavernosum is attached to its ischiopubic ramus by crus that extend from the root of the clitoris. The glans clitoris is a small round tubercle of spongy erectile tissue at the end of the body and connected to the bulbs of the vestibule by thin bands of erectile tissue.

Perineal membrane (previously the inferior fascia of the urogenital diaphragm) is a triangular membrane, attached laterally to the periosteum of the

ischiopubic rami and its apex is attached to the arcuate ligament of the pubis. The posterior border is fused with the deep part of the perineal body and is continuous with the fascia over the deep transverse perinei. It is crossed by the urethra, 2–3 cm behind the inferior border of the symphysis pubis; the vagina, centrally; the ducts of Bartholin's glands, posterolateral to the urethral orifice; the deep dorsal vessels and dorsal nerves of the clitoris, behind the pubic arch in the midline; the posterior labial vessels and nerves, anterior to the transverse perinei.

The femoral triangle is a depressed, intermuscular space in the anteromedial aspect of the proximal thigh. The inguinal ligament constitutes the base of the femoral triangle's inverted triangular outline. Its lateral boundary is the medial margin of sartorius. Its medial boundary is the medial margin of adductor longus. Its distal extremity, the apex, is where sartorius overlaps adductor longus. Its floor is provided laterally by iliacus and psoas major, medially by pectineus and adductor longus. Its roof is the overlying fascia lata. The femoral vessels, passing from midbase to apex, are in the deepest part of the triangle. Lying lateral to the artery and outside the femoral sheath is the femoral nerve, which, on entering the femoral triangle divides into multiple branches. The triangle also contains fat and lymph nodes.

The tensor fascia lata (TFL) originates from the anterior superior iliac spine. It inserts into the fascia lata and is supplied by the lateral femoral circumflex artery. It can be used as a myocutaneous flap for the reconstruction of inguinal wounds following inguinofemoral lymphadenectomy where there is significant skin loss. It is a Type-I flap based on a single vascular pedicle (ascending branch of the lateral circumflex femoral artery). The flaps are easily made long enough to reach and close the large area created during inguinofemoral lymphadenectomy in few cases.

Gracilis myocutaneous flap is a Type-II flap based on dominant and minor vascular pedicles. The gracilis flap can be harvested as either a muscle or musculocutaneous flap. The dominant pedicle is the ascending branch of the medial circumflex femoral artery. The minor pedicles are the first and second branches of the superficial femoral artery. The muscle is innervated by the anterior branch of the obturator nerve which enters it on its deep surface, superior to the vascular pedicle. It can be used in the reconstruction of post vulvectomy area in selected cases.

Regarding lymphatic drainage, a meshwork of connecting vessels join to form three or four collecting trunks around the mons pubis which drain to superficial inguinal nodes lying on the cribriform fascia covering the femoral

artery and vein; these nodes drain through the cribriform fascia to the deep inguinal nodes lying medial to the femoral vein. The deep inguinal nodes drain via the femoral canal to the pelvic nodes. The last of the deep inguinal nodes lies under the inguinal ligament within the femoral canal and is often called Cloquet's node. Lymph vessels from the clitoris and labia minora drain to deep inguinal nodes and direct clitoral efferents may pass to the internal iliac node. Direct spread to the deep nodal groups without metastasis to the superficial group has been documented using lymphatic mapping. This type of direct spread is uncommon and represents fewer than 5% of cases. Despite the extensive anastomosis of lymphatics, metastasis of vulvar carcinoma to contralateral nodes is uncommon in patients with well lateralized T1 lesions.

The vulvar lymphatics run anteriorly through the labia majora, turn laterally at the mons pubis, and drain primarily into the superficial inguinal lymph nodes. Elegant lymphatic dye studies by Parry-Jones[9] demonstrated that vulvar lymphatic channels do not extend lateral to the labiocrural folds and generally do not cross the midline unless the site of dye injection is at the clitoris or perineal body.

Vulvar cancer spreads by the following routes:

- Direct extension, to involve adjacent structures such as the vagina, urethra, and anus

- Lymphatic embolization to the regional inguinal and femoral lymph nodes
- Hematogenous spread to distant sites, including the lungs, liver, and bone

Haematogenous spread and spread by direct extension are both infrequent.

Two different pathways for Squamous Cell Carcinoma (SCC) of the vulva have been put forth[10]. The first pathway is triggered by infection with a high-risk-type Human Papilloma Virus (HPV). Integration of the HPV DNA into the host genome leads to the development of a typical Vulvar Intraepithelial Neoplasia (VIN), accompanied with over expression of p14ARF and p16INK4A. This lesion subsequently forms a warty or basaloid type SCC. The second pathway is HPV-independent where keratinizing SCC develops within a background of lichen sclerosus (LS) through a differentiated VIN. It has a different set of genetic alterations than those in the first pathway, including p53 mutations, Allelic Imbalances (AI), and Microsatellite Instability (MSI). Characteristics of the warty / basaloid type and the keratinizing type of SCC of the vulva are shown in Table – 17.

TABLE 17

TWO DIFFERENT TYPES OF VULVAR SCC

Variables	Warty or Basaloid type	Keratinizing type
Frequency	20%–35%	65%–80%
Age	Younger 55 (35–65) Years	Older 77 (55–85) Years
Precursor	Warty or Basaloid VIN	Lichen Sclerosus Differentiated VIN
Molecular characteristics	HPV Integration	p53 Mutation
Prognosis	Better	Worse

About 70% of vulvar squamous carcinomas arise primarily on labia. Disease more commonly occurs on the labia majora; however, it may appear on the labia minora, clitoris and perineum. The disease is localized and well demarcated; although it can occasionally be so extensive that the primary location cannot be determined[11].

More than 90% of invasive vulvar cancers are squamous cell carcinomas[12]. The other histopathologic types are as follows:

- Bartholin's gland carcinoma
- Primary mammary adenocarcinoma
- Malignant melanoma
- Vulvar sarcoma
- Paget's disease
- Basal cell carcinoma

Diagnosis of vulvar carcinoma is often delayed. Women neglect to seek treatment for a considerable period of time from the onset of symptoms[11]. In many cases, a biopsy of the lesion is not performed until the problem fails to respond to numerous topical therapies. A biopsy should be performed when any discrete lesion of the vulva is discovered. The most common presentation is a pruritic lesion of the vulva or a mass detected by the patient herself. However, early vulvar cancer may be asymptomatic and recognized only with careful inspection of the vulva. More advanced vulvar carcinomas present with bleeding, pain, or discharge.

During the past 20 years, a number of significant advances have been made in the management of carcinoma of vulva, reflecting a paradigm shift towards a

more conservative surgical approach without compromised survival and with markedly decreased physical and psychological morbidity. Great effort has been devoted to decreasing the morbidity of surgery for vulvar carcinoma. They are as follows[13]:

- Individualization of treatment for invasive carcinoma of vulva
- The use of separate incisions for lymphadenectomy to improve wound healing
- Elimination of routine pelvic lymphadenectomy
- Omission of lymphadenectomy for patients with T_1 tumors with <1 mm of stromal invasion
- Vulvar conservation for patients with unifocal tumors
- Omission of the contralateral groin dissection in patients with lateral T_1 lesions and negative ipsilateral nodes
- The use of postoperative radiation therapy to decrease the incidence of recurrence in patients with multiple positive groin nodes
- The use of preoperative radiation therapy in patients with advanced disease

In the early part of the 20th century, patients commonly presented with advanced disease, and surgical techniques were poorly developed; thus, the 5-year

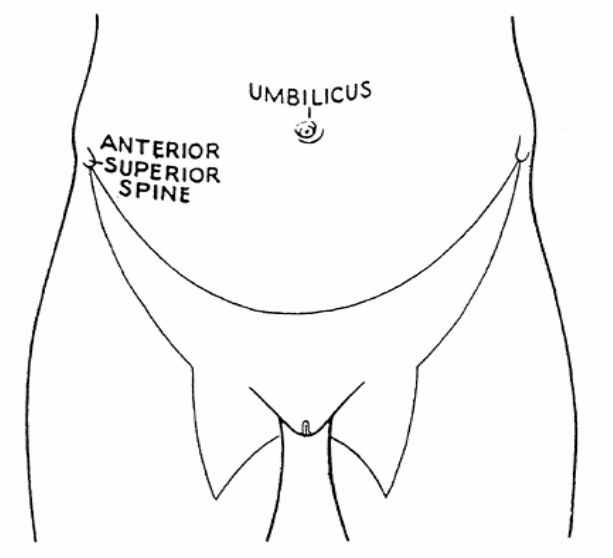
survival rate for vulvar cancer was 20% to 25%. Taussig, in the United States, and Way, in Great Britain, pioneered the radical en bloc dissection for vulvar cancer[14, 15]. Since the early part of the 20th century, the traditional surgery has been a radical resection of the primary lesion with a bilateral groin node dissection performed through a single incision. This operation involves radical removal of the entire vulva, the mons pubis, the inguinofemoral lymph nodes, and often the pelvic lymph nodes. A large surgical defect is created that is generally closed under tension with a high subsequent breakdown rate and marked disfigurement of the genital area. Although this technique was later modified to remove less skin, the primary wound breakdown rate exceeded 50%.

Fred Taussig collected a large series of vulvar cancer cases from 1911-1940[14]. He initially started his series with a radical excision of the primary tumor with an en bloc dissection of the inguinal lymph nodes. Later, he modified his technique for patients with small lesions in an attempt to decrease operative morbidity. He used separate incisions for the groin dissection and the vulvar excision. This less radical operation for small lesions was not routinely used until Hacker reported his experience 1981[16]. The report by Hacker and colleagues in 1981 consisted of 100 patients in whom three separate incisions were used to perform the bilateral inguinofemoral lymphadenectomy and radical vulvectomy, leaving a bridge of tissue between the incisions and sparing the mons pubis. Major groin wound breakdown occurred in 14 patients, which was a considerable

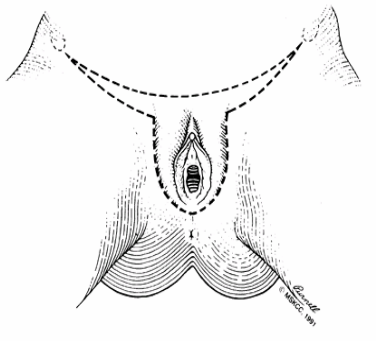
reduction from the 50% or higher groin wound breakdown rate generally seen with the en bloc excision.

Although a number of modifications have been described, the basic incisions for radical vulvectomy and bilateral lymphadenectomy can be described as being based on either a butterfly or longhorn approach[17]. The butterfly incisions use convex wings over the groins and around the anus to facilitate closure of the defect. The longhorn incisions were developed to limit skin resection over the groin in an attempt to reduce wound breakdown.

BUTTERFLY INCISION FOR EN BLOC RADICAL RESECTION

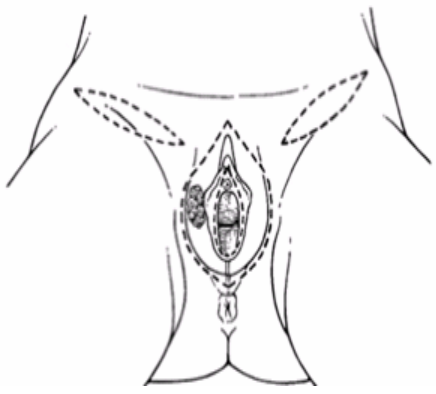


MODIFIED SKIN-SPARING LONGHORN INCISION FOR EN BLOC RADICAL RESECTION



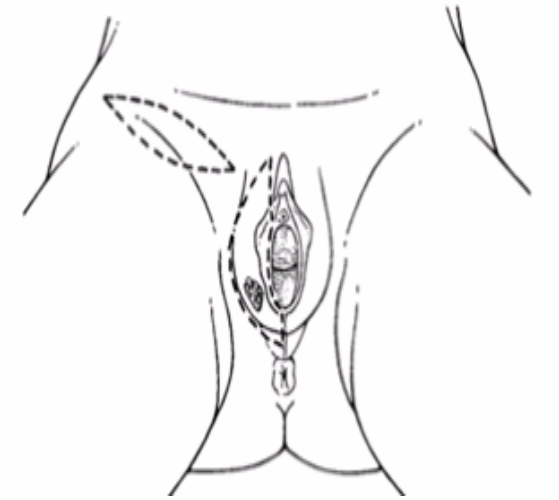
Oncologically no significant difference was noted between radical excisions of the primary tumor with an en bloc dissection of the inguinal lymph nodes through single incision and triple incision with the advantage of reduced wound morbidity in the triple incision method. After this observation, surgery for vulvar carcinoma was done using triple incision technique. Then as a continuing trend towards reducing the wound morbidity; radical wide local excisions of the vulvar carcinomas were carried out sparing the uninvolved normal vulva without oncological compromise.

THREE SEPARATE INCISIONS



Unilateral lesions (defined as 1cm or more from the midline) present another variation for therapy[11]. Homesley et al in GOG study confirmed the low incidence of contralateral node involvement, making ipsilateral inguinal lymphadenectomy a rational initial approach[18] .

UNILATERAL LYMPHADENECTOMY FOR A WELL-LATERALIZED LESION



The following table [12](Table-18) shows an overview of five studies, which registered the percentage of inguinofemoral lymph node metastases related to depth of invasion ≤ 1mm in patients with T1 (≤ 2cm) tumors. In all the five studies, there was no lymphnode involvement when the stromal invasion was ≤ 1mm in patients with T1 (≤ 2cm) tumors. Hence it is obvious that lymphadenectomy can be avoided for T1 tumors with stromal invasion ≤ 1mm.

Table 18

LYMPHNODE METASTASIS IN T1 TUMORS WITH STROMAL INVASION ≤ 1mm

Study	Number of Patients with Stromal invasion ≤ 1mm	Number of Patients with Positive Nodes who had Stromal invasion ≤ 1mm	Percentage
Binder et al.[19]	7	0	0%
Ross and Ehrmann[20]	17	0	0%
Hoffman et al.[21]	24	0	0%
Hacker et al.[22]	34	0	0%
Andreasson and Nyboe[23]	8	0	0%

The International Society for the Study of Vulvovaginal Diseases (ISSVD) had proposed this pathologic definition of microinvasive carcinoma of vulva:

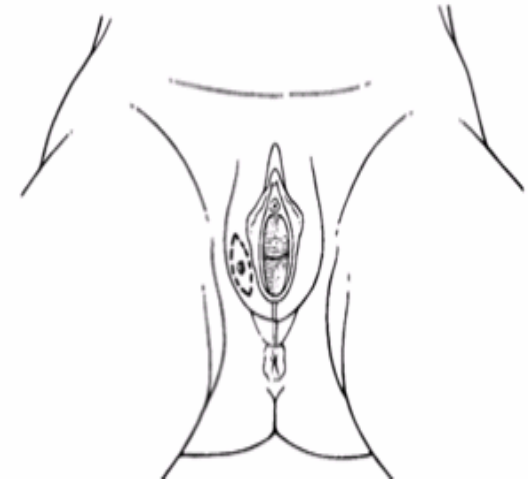
* SCC having diameter of 2cm or less (as measured in fresh state)

* Depth of invasion of 1mm or less (measured from the epithelial–stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion)

* No vascular space invasion

These lesions do not need inguinal lymphadenectomy of any type as stated above.

EARLY LESION WITH LYMPHADENECTOMY OMITTED



Like the changing concepts for surgery for vulvar cancers, concept of nodal dissection has also undergone several changes, ranging from radical removal of ilioinguinal nodes via single incision to sentinel node biopsy which can avoid nodal block dissection if sentinel node is negative, thus avoiding the potential

morbidity of lymph node block dissection. The concept relies on the presumption that the sentinel lymph node is the initial site of metastatic disease and that the histology of the sentinel lymph node reflects the histology of the rest of the lymph nodes in the basin.

In 1979, the International Federation of Gynecology and Obstetrics (FIGO) approved a clinical classification for invasive squamous cell carcinoma of the vulva. That was based on an analysis of tumor (T) by size and location; node (N) status by palpation; distant metastases (M) as assessed by general and pelvic examination; evaluation of the bladder or rectum, or both; and radiologic investigation. Most patients with invasive carcinoma of the vulva were treated surgically, and it was recognized through a number of studies that there were substantial discrepancies between the clinical assessment of the inguinal lymph node status and the surgical pathologic findings. The prognostic importance of the lymph node status is significant, yet the accuracy of the clinical assessment of the lymph nodes is limited. Microscopic metastases may be present in nodes that are not clinically suspicious, and suspicious nodes may be enlarged because of inflammation only. When compared with surgical staging, the percentage of error in clinical staging increases from 18% for stage I disease to 44% for stage IV disease[13].

These factors led the Cancer Committee of the International Federation of Gynecology and Obstetrics (FIGO) in 1988 to introduce a surgical staging system for vulvar cancer. That system was based on well-established surgical-pathologic prognostic criteria. Hacker concluded that the term microinvasive vulvar cancer should be reserved for tumors with a depth of invasion ≤ 1mm, because of the negligible risk on lymph node metastases. In 1995, stage I was divided into A and B based on a depth of invasion less or greater than 1 mm. Another revision was made in the year 2009, giving consideration to the number of nodes involved and extracapsular nodal involvement. Over the years the UICC (International Union for Cancer Control), AJCC (American Joint Committee on Cancer), and FIGO have modified their staging systems for gynecological cancers so that all 3 systems are virtually identical. It is inevitable that changes will, of necessity; occur as more data and information emerge regarding molecular markers and mechanisms, as will a more precise understanding of the actual genetic factors and aberrations involved in cancer etiology and pathogenesis. An increasing awareness of prognostic scoring systems and the incentive to adopt them is already evident and will play a major role in future classification systems. The recent FIGO (Table-19) and TNM staging are given below.

TABLE 19

FIGO STAGING FOR CARCINOMA OF VULVA (2009)

Stage	Description
I	Tumor confined to the vulva
IA	Lesions 2 cm or less in size, confined to the vulva or perineum and with stromal invasion 1.0 mm or less *
IB	Lesions more than 2 cm in size *or* any size with stromal invasion more than 1.0 mm, confined to the vulva or perineum
II	Tumor of any size with extension to adjacent perineal structures (lower 1/3 urethra, lower 1/3 vagina, anus) with negative nodes
III	Tumor of any size with or without extension to adjacent perineal structures (lower 1/3 urethra, lower 1/3 vagina, anus) with positive inguinofemoral nodes
IIIA	1-2 lymph node metastasis(es) (<5 mm) One lymph node metastasis 5 mm or greater
IIIB	Three or more lymph node metastases (<5 mm) Two or more lymph node metastases 5 mm or greater
IIIC	Lymph node metastasis with extracapsular spread
IVA	Tumor of any size with extension to any of the following: upper 2/3 of urethra, upper 2/3 vagina, bladder mucosa, rectal mucosa, or fixed to pelvic bone Fixed or ulcerated regional lymph node metastasis
IVB	Distant metastasis (including pelvic lymph node metastasis)

* *Note:* The depth of invasion is defined as the measurement of the tumor from the epithelial–stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.

TNM stages are based on clinical and/or pathological classification but the FIGO stages are based on surgical staging[3].

TNM Classification for Vulvar Cancer -7th Edition

T = Tumor

T1a- Tumor confined to vulva/perineum, ≤ 2cm in size, and depth of invasion ≤ 1mm

T1b- Tumor confined to vulva/perineum, > 2cm in size, or depth of invasion > 1mm

T2- Tumor extension to lower ⅓ urethra, lower ⅓ vagina or anus

T3- Tumor extension to upper ⅔ urethra, upper ⅔ vagina, bladder or rectal mucosa, or fixed to the pelvic bone

N = Nodes

N0- No lymph nodes involved

N1a- 1 – 2 inguinofemoral lymph node metastasis each < 5mm

N1b- 1 inguinofemoral lymph node metastasis ≥ 5mm

N2a - ≥ 3 inguinofemoral lymph node metastases each < 5mm

N2b- ≥ 2 inguinofemoral lymph node metastases ≥ 5mm

N2c- Inguinofemoral lymph node metastases with extracapsular spread

N3- Fixed or ulcerated inguinofemoral lymph nodes

M = Metastasis

M0- No distant metastases

M1- Any distant metastases

Radiation therapy, frequently with concurrent chemotherapy, is gaining an increasingly important role in the management of patients with vulvar cancer. The indications for radiation therapy for patients with primary vulvar cancer are still evolving. At present, radiation seems to be clearly indicated in the following situations[13]:

- Preoperatively, in patients with advanced disease who would otherwise require pelvic exenteration or suffer loss of anal or urethral sphincteric function
- Postoperatively, to treat the pelvic lymph nodes and groin of patients with two or more microscopically positive or one grossly positive groin node with extracapsular spread
- Postoperatively, to help prevent local recurrences in patients with involved or close surgical margins

Unfortunately, reports of chemotherapy activity in the treatment of metastatic or recurrent squamous cell carcinoma of the vulva are largely anecdotal. In the absence of reliable data specific to this cancer, clinicians often use single

agents and combination regimens that have had some activity in the treatment of cervical cancer.

DISCUSSION

The mean age of the patients in our series was 52.5 years and the median age was 55 years with a range of 23 to 73 years (2004-2011). In the 2 Indian series, Bafna et al. (1996-2000) reported that the mean age of the patients was 54.7 years with a range of 24 to 75 years and Sharma et al. (1998-2005) reported that the median age was 63 years with the range of 24 to 92 years[6, 24]. In a study from Nigeria (1998-2009), the ages ranged from 54 to 79 years with a mean of 61.2 years[25]. In Landrum et al. (1990-2005) series the median age of 175 patients at the time of primary diagnosis was 59.9 years with a range of 32 to 95 years[26]. In a study by Hampl et al. the mean age was 57 years in their most recent cohort of 102 women (05/1998 to 06/2007), of those, 41.2% (42 women) were aged 50 years or less and the youngest woman diagnosed with an invasive vulvar carcinoma was 18 years old with a history of sexual contact for three years and severe pain and dysuria for several months[5]. In our series 45.7% (16/35) of the patients were aged 50 years and below and the youngest patient diagnosed was 23 years old. In Bafna et al. series, 16 were less than 60 years (43.2%) [6]. When compared to western patients the median age in our series is low (Table-20).

Table 20

THE MEAN AND MEDIAN AGE OF PATIENTS IN VARIOUS SERIES

Series	Study Period	Total Patients	Mean Age in Years	Median Age in Years	Age Range in Years
Bafna et al[6]	1996-2000	37	54.7	60	24-80
Landrum et al[26]	1990-2005	175	-	59.9	32-95
Sharma et al[24]	1998-2005	60	-	63	24-92
Hampl et al[27]	2003-2006	127	61.4	-	-
Hampl et al[5]	1998-2007	102	57	-	18-93
Eke et al[25]	1998-2009	11	61.2	-	54-79
Present Series	**2004-2011**	**35**	**52.5**	**55**	**23-73**

Labia majora was the common site of primary lesion in our series (28/35=80%). Hampl et al. in their series of 224 patients with vulvar cancers reported that the tumor localization changed significantly from the labia to the area between the clitoris and urethra[5]. They state that area between clitoris and urethra

seems to be the most frequent tumor site (38.4%). They further state that the remarkable change of the tumor localization could be explained by the "higher susceptibility of the non-keratinizing epithelium to tiny injuries or tears facilitating HPV infection, the earlier onset of sexual non-penetrating contact in young adolescents nowadays, promiscuity and/or a more rapid progression from infection to VIN to invasive tumors without understanding how this occurs". In our series with low number of cases, such a shift in location was not observed and labia majora was the common site of involvement. In our series, 14.3% (5/35) of disease occurred in labia minora and 5.7% (2/35) of the disease occurred in clitoris.

HPV infection is now a well established cause of cervical cancer and there is growing evidence of HPV being a relevant factor in other anogenital cancers (anus, vulva, vagina and penis) and head and neck cancers. HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide[28]. Since HPV testing was not done in our series, the status of HPV in our patients could not be commented.

In a study by Shukla et al [29]the following points were noted about the prevalence of HPV infection in cancers of female genital organ. In India, 85-90% cervical cancer cases are squamous cell carcinoma and the HPV 16 is the most prevalent type among them compared to other parts of the world where the

proportion of HPV16 is much lower and ranges only upto 70% when both HPV16 and 18 are considered. In India, HPV type 16 alone in cervical cancer is 70-90% while occurrence of HPV type 18 varies from 3 to 20%. Other highrisk HPV types such as HPV 45, 33, 35, 52, 58, 59, and73 have also been reported are rare and constitute only a minor group. Interestingly, the peak of HPV infection, particularly HPV 16, appears to reach at later stage in third decade of sexual life at 26-35 years in Indian women in contrast to 18-25 years reported in western countries. Etiologically vulvar carcinomas are heterogeneous and thus the presence of HPV infection in invasive vulvar cancer cases varies. In India, no report is available on the prevalence and type distribution of HPV infection in vulvar cancer.

A report by Dhir et al.[30] provides the risk estimates for cancers in HIV-infected (Human Immunodeficiency Virus) persons in India. These authors examined HIV prevalence in persons with all types of cancer who presented at the Tata Memorial Hospital, one of the largest tertiary cancer referral medical centers in India, during 2001–2005. They used proportional incidence ratios (PIR) to assess the likelihood that specific cancer types were associated with HIV infection, comparing the cancer distribution in PHA to that in the age- and sex-specific distribution of all cancer patients seen at the same medical center in 2002. HIV infection was found in 1.2% of cancer admissions, including 166 men and 85

women. In women, Non Hodgkin Lymphoma (NHL) was increased 10-fold (n = 14), while one case of Hodgkin Lymphoma (HL) was observed (non-significant 2-fold increase). Cervical (n = 33) and vulva/vaginal cancer (n = 2) risks were both increased (4-fold and 8-fold, respectively). This report provided no data about possible risk factors such as sexual practices, smoking or chewing tobacco, or infections. In our series one patient was found to be positive for HIV. She underwent wide local excision for cancer vulva and was advised adjuvant EBRT, but defaulted. During the last follow-up (39 months) she remained disease free.

In the era of multimodality approach and organ conservation in the treatment of cancer, the radicalism of surgery was gradually getting decreased over a period of time. The traditional operative approach of radical en bloc resection of the vulva and inguinofemoral nodes through single incision underwent a drastic change after the landmark study by Hacker et al. They demonstrated that a less morbid surgical approach, operating through separate vulvar and groin incisions, achieved cure rates similar to those achieved with the traditional radical vulvectomy[16]. Since then, there has been a continuing trend towards less radical surgery. For all our cases requiring nodal dissection, separate incisions were used. Significant reduction of wound complications and very low chance of recurrence in the tissue bridge between the incisions were noted in international series[16, 31]. We follow the

same principle and we did not come across any recurrence in the tissue bridge between the incisions.

Studying the relationship between surgical margins and tumor recurrence, Heaps et al. reported no local failures in 91 patients whose closest tumor margin was 8 mm or more in the fixed specimen[32]. As per the seminal article by Heaps et al we routinely follow the practice of giving 1 cm gross margin to vulvar cancer. In our series, except 3 (2 had positive margin, 1 had close margin), R0 resection was achieved in all patients. Of these 3 patients, 2 had locally advanced disease for which preoperative EBRT was given. The other one was treated with upfront surgery.

Like treatment for the primary in carcinoma vulva, the radicalism of doing pelvic lymphadenectomy along with inguinofemoral block dissection was questioned after a landmark study by Homesley et al. In 1986, Homesley et al.[33] published results of a prospective randomized study that compared pelvic lymphadenectomy with inguinal and pelvic irradiation in patients with inguinal node metastases from carcinoma of the vulva. All patients were initially treated with radical vulvectomy and inguinofemoral lymphadenectomy. Patient randomization was done intraoperatively after frozen-section evaluation of the inguinofemoral lymph nodes. This trial was closed prematurely, after 114 eligible

patients had been entered, when interim analysis revealed a survival advantage for the radiotherapy arm (P = .03). The difference was most marked for patients with clinically positive or multiple positive groin nodes on histopathological examination. For patients with two or more positive nodes, the 2-year survival rates were 63% and 37% for the radiotherapy and pelvic lymphadenectomy groups, respectively. With the publication of this study, most practitioners abandoned routine pelvic lymphadenectomy, and postoperative radiotherapy became the standard for most patients with inguinal node metastases.

Adjuvant radiation therapy was given to patients with two or more metastatic nodes, margin positivity and extracapsular nodal extension irrespective of number of nodes[33]. Patients with negative inguinal nodes and clear resection margins were followed expectantly with no adjuvant therapy. We follow this principle.

In Bafna et al. series, the nodes were negative in 13/26 (50%) cases who had had groin lymph node dissection and all the patients with negative nodes have had no evidence of disease until their last follow-up[6]. In a series by Homesley et al. they reported that 24% of patients with clinically negative nodes had inguinal lymph node metastases and 24% of patients with suspicious but mobile nodes had negative findings at lymphadenectomy suggesting that the clinical examination is

inadequate in assessing the nodal spread[18]. For this reason, in 1988, the FIGO staging system was changed from a clinical staging system to one that incorporate the more accurate information gained from surgical assessment of regional lymph nodes. In our series also, 36.4% of patients with clinically suspicious nodes had negative findings at lymphadenectomy and 35% of patients with clinically negative nodes had inguinal lymph node metastases post surgery, which is in concordance with his view (Table-21).

TABLE 21

CLINICAL AND PATHOLOGICAL CORRELATION OF INGUINAL NODES

Series	**Inguinal nodes - clinically suspicious, negative finding at lymphadenectomy**	**Inguinalnodes - clinically negative, positive finding at lymphadenectomy**
Homesley et al[18]	24%	24%
Present series	**36.4%**	**35%**

In a series by Le et al. the total number of nodes harvested during primary surgical management was proved to be an independent predictor of both progression- free and overall survivals. It is conceivable that the more nodes that are removed, the less chance there is of missing an occult nodal metastasis, which

could affect timely treatment, thereby reducing recurrence. They propose to define optimal inguinal nodal dissection using a cut-off value of at least 10 nodes in total for patients undergoing bilateral inguinofemoral lymphadenectomy[34]. In our series the nodal yield per bilateral inguinofemoral lymphadenectomy was 17 which indicate optimal dissection.

Over the years, there has been a consistent trend toward less radicalism in the operative management of invasive squamous cell carcinoma of the vulva. Inguinal nodal dissections can be complicated by significant postoperative complications such as infections, seroma, wound breakdown, as well as chronic lymphedema of the extremities that seriously interfere with the quality of life of the patients. To limit the morbidities associated with this procedure, some authors have recommended either the use of sentinel node sampling or superficial nodal dissection with saphenous vein preservation. Recently, a number of investigators have explored the use of intraoperative lymphatic mapping to identify a sentinel node that would predict the presence or absence of regional metastases[27]. Patients without malignant deposit in sentinel node can be avoided from definitive nodal dissection thus avoiding the potential complications of lymphadenectomy. Currently, due to the lack of established long-term oncologic outcomes as well as experience with sentinel node procedures in most centers, this approach remains

experimental. None of our patient with invasive carcinoma of vulva underwent sentinel node biopsy.

Participants in a 2008 expert panel at an International Sentinel Node Society Meeting concluded that sentinel node biopsy "is a reasonable alternative to complete inguinal lymphadenectomy when performed by a skilled multidisciplinary team in well selected patients"[35]. They concluded that patients who have tumors that fulfill the following criteria are good candidates for the procedure.

1. Tumors that invade more than 1 mm
2. No obvious metastatic disease
3. Tumor diameter of less than 4 cm

Some surgeons have tried to reduce the incidence and severity of surgical complications by reducing the extent of lymph node dissections. In April 1992, the Gynecologic Oncology Group (GOG) reported the results of protocol 74[36]. A total of 121 patients with negative superficial inguinal lymph nodes were observed, and nine (7.3%) had a groin relapse. This relapse rate was compared with the long-term follow-up of 81 control patients treated with complete inguinofemoral lymphadenectomy on GOG protocol 36. Among the historical controls, there were no groin relapses. The GOG properly rejected superficial inguinal

lymphadenectomy, and most gynecologic oncologists resumed performing inguinofemoral lymphadenectomy. In 1995, Burke et al.[37] reported 4 (5%) groin recurrences in 74 patients with T1 or T2 tumors treated with wide local excision and superficial inguinal lymphadenectomy (unilateral or bilateral depending on the location of the tumor). However, a recent update of the M. D. Anderson Cancer Center experience had longer follow-up and demonstrated a higher recurrence risk of 16% at 5 years in patients treated with superficial lymphadenectomy alone[38]. It has been suggested that the procedure used in these studies did not remove medial inguinofemoral nodes that may be the primary site of drainage of some vulvar cancers[39]; for this reason, many gynecologic oncologists now recommend removal of at least the superficial and medial inguinofemoral nodes. Thus superficial inguinal lymphadenectomy alone is not recommended at present. We follow standard inguinofemoral lymphadenectomy for carcinoma of vulva.

In our series 45.2 %(14/31) of patients develop skin flap necrosis (Table-22). In Bafna et al. series, only three of 26 patients who had groin node dissection had wound healing with primary intention, remaining 23 patients (88.4%) had considerable groin wound dehiscence[6]. Zhang et al. published their retrospective analysis comparing saphenous vein sparing to saphenous vein ligation during the inguinal lymphadenectomy and its impact on the development of complications[40]. They found significant decrease in the development of short-term lower limb

phlebitis in the saphenous vein spared group; otherwise, no significant differences were noted between the two groups as regards the development of post-operative wound seroma, acute inguinal wound cellulitis, or lymphocyst formation. However, in a series by Soliman et al, they conclude that "local complications after inguinofemoral lymphadenectomy are still very high, with no single pre-, intra-, or postoperative factor that could be incriminated, and saphenous vein sparing provided no significant difference in decreasing the rate of local complications"[41]. They suggested that more trials should be done to study the efficacy sentinel lymph node detection technique in vulvar cancers so that the morbidity of inguinofemoral block dissection can be avoided in sentinel node negative patients. In our institution the practice of saphenous vein sparing was not done.

The sartorius muscle historically was transferred to the inguinal ligament to cover the exposed femoral vessels. Judson et al reported this technique is not beneficial based on a randomized control trial and it increased the risk of lymphocyst formation[42]. However we routinely practice this technique because, in situations where inguinal wound gaping occurs due to skin flap necrosis this will prevent exposure of major vessels.

TABLE 22

COMPARISON BETWEEN WOUND COMPLICATIONS

Series	Wound breakdown	Wound seroma	Wound infection
Gaarenstroom et al.[43]	11%	27%	27%
Gould et al.[44]	19.4%	13.1%	-
Soliman et al[41]	9.7%	12.5%	3.2%
Bafna et al[6]	88.4%	-	-
Present Series	**45.2%**	**58.1%**	**5.7%**

In our series, 5 (14.3%) patients defaulted follow up. However poor follow-up in Indian females due to several factors like long travelling distance, poor socio economic status and elderly age is not unusual[24]. Patients were kept on surveillance at monthly interval for one year and two monthly interval for next year, three monthly interval for next year and then six monthly for the next two years and annually thereafter until the lifespan. During the follow up, if recurrent disease was detected, patients were treated accordingly. However, in public sector hospitals like ours, despite providing free transportation train pass and other facilities, due to financial constraints, some of the patient dropout on follow-up. In a regional cancer center in South India, they report that more than 50% were compliant to treatment protocol, less than 30% default during adjuvant therapy and 20% default after the preliminary investigation[45].

At a median follow up of 26 months (range 2-67 months), 8 patients 22.9% (8/35) developed recurrence, of which one is systemic, 4 regional and 3 local. This failure pattern was almost like other reported series worldwide (Table-23). All the regional and systemic recurrences occurred within 1year of primary surgery in our series.

In a study by Woelber and colleagues[46], in multivariate analysis, lymph node status and age were the only independent prognostic factors for disease-free and overall survival. After adjusting the level of significance to 0.02%, only nodal involvement persisted as an independent prognostic factor (p=0.002). They state that, the risk for recurrent disease was 5.1 times higher for patients with unilateral lymph node involvement and 16.9 times higher for those with bilateral lymph node involvement compared to those with negative nodes.

Studying the relationship between surgical margins and tumor recurrence, Heaps et al. reported no local failures in 91 patients whose closest tumor margin (deep or at the skin surface) was 8 mm or more in the fixed specimen[32]. Accounting for specimen preparation and fixation, they suggested that 1-cm tumor-free surgical margin on the vulva results in a high rate of local control, whereas a margin <8 mm is associated with a 50% chance of recurrence. From that study 1cm surgical margin was followed by most of the surgeons worldwide.

In a study by Groenen et al[47], 93 patients underwent surgery for invasive SCC of the vulva from 2000 to 2005. With a median follow-up of 31 months (range, 2-90 months), 18 patients (23%) developed a local recurrence. The recurrence rate did not differ between patients in whom the margin was 8 mm or more and those in whom the margin was less than 8 mm, (23% and 22%, respectively). There is discordance between his observation with that of Heaps et al.

TABLE 23

FAILURE PATTERN IN FEW SERIES

Series	Recurrence in Percentage	Study Period	Median Follow-up In months
Heaps et al[32]	15.6% (21/135)	1957-1985	-
Fonseca-Moutiho et al[48]	26.8% (15/56)	1987-1997	-
Bafna et al[6]	32.4% (12/37)	1996-2000	-
Cheng et al[49]	34% (34/100)	1980-2002	-
Woelber et al [46]	13.6% (14/103)	1996-2003	36
Le et al[34]	29.3% (17/48)	1980-2004	37
Landrum et al[26]	13% (22/175)	1990-2005	54.5
Sharma et al[24]	43% (26/60)	1998-2005	23
Groenen et al[47]	23% (18/93)	2000-2005	31
Present Series	**22.9% (8/35)**	**2004-2011**	**26**

In a study by Oonk et al[50], 65 of 238 patients (27%) developed recurrent disease within a mean of 25 months (median, 21 months; range, 3 – 76 months) after the end of the primary treatment. Local recurrences occurred after a mean progression-free survival of 30 months (median, 27 months; range, 4 – 76 months)

whereas regional recurrences (skin bridge and inguinal region) developed after 8 months (median, 8 months; range, 3 – 15 months) and distant recurrences after 11 months (median, 11 months; range, 4 – 22 months). The time between primary treatment and recurrence was found to be longer for patients with local recurrences compared with those with regional and distant recurrences (P=0.0001). Stehman et al[51] noted that groin recurrences occur sooner (median time to recurrence 6 months) than vulvar recurrences (median time to recurrence 3 years). In our series also all the regional and systemic recurrences occurred within 1year of primary surgery (4 regional and 1systemic) and all three local recurrences occurred 1 year after primary surgery (21, 31, 33 months) which is in concordance with the above reported series.

The estimated 5 year Disease Free Survival (DFS) and Overall Survival (OS) in our series was 65.4% and 85.1% respectively. The 5-year overall survival was 75.9% in a series from Singapore with a mean follow-up of 39 months[52]. In the series from AIIMS (All India Institute of Medical Sciences) India, Sharma et al. reported 41% five year survival for all stages[24]. In 1991, the GOG (Gynecologic Oncology Group) reported the survival analysis of 588 patients and observed that 5-year survival in Stage I, II, III, and IV was 98, 85, 74 and 31% respectively [53]. This concludes stage as important prognostic marker. It also found out significant correlation between number of positive nodes and survival. In our series, on

univariate analysis using log rank test, advanced stage, lymph node positivity and nodal positivity with extracapsular spread significantly affected estimated 5 year overall survival. Because of the changes in FIGO staging system over a period of time, stage by stage comparison of survival between our series with other international series may not be representative. But the outcome of our patients was comparable with other reported series (Table-24).

TABLE 24

SURVIVAL IN CERTAIN SERIES

Series	**Disease Free Survival (DFS)**	**5 Year Overall Survival (OS)**
Sharma et al[24]	-	41%
Cheng et al[49]	66.5%	-
Shamini et al[52]	-	75.9%
Present Series	**65.4%**	**85.1%**

About the 2 series from India, the one from South India concludes that ‘‘no firm conclusions could be drawn given small number of patients, however it appears from the present study that bilateral involvement of the inguinal lymph nodes would carry a worse prognosis than unilateral involvement, provided multiple nodes are not involved and neoadjuvant chemotherapy appears beneficial

in selective locally advanced cases and the role of neoadjuvant chemotherapy compared to neoadjuvant radiotherapy/ chemoradiation in locally advanced tumors needs to be explored"[6]. In the other Indian series by Sharma et al. despite the majority of patients presenting in advanced stage, the 5 year overall survival was 41%.They found that FIGO stage and pathological node positivity were the two statistically significant prognostic factors for survival[24].

In a retrospective analysis of 389 cases of vulvar cancer, Raspagliesi et al. identified nodal status as the most significant prognostic factor among all tumor-related variables and proposed that certain variables related to positive nodes (such as extracapsular spread) could be critical for further risk assessment[54]. In contrast to these results, a retrospective population-based study by Rhodes et al. demonstrated an unfavorable survival for patients with positive inguinal lymph nodes only in univariate analysis; after multivariate analysis, it did not retain its prognostic significance[55]. These inconsistent findings are most likely caused by heterogeneous treatment strategies in the investigated population, as Rhodes et al. also observed that the management of vulvar cancer varied widely between different centres, many of which treated only very few patients per year.

In a study by Landrum et al. the overall survival (OS) and progression free survival (PFS) in patients with advanced vulvar cancer managed by either primary

surgery or primary chemoradiation did not show any statistical difference between these two groups. Interestingly, in that study, lymph node status was not a predictor for OS or PFS and they proposed that "complete surgical excision of inguinofemoral lymph nodes followed by adjuvant radiation resulted in improved PFS and OS compared to that of historic controls and reduced the predictive value of lymph node metastasis in that population"[56].

In our series nodal positivity with extracapsular spread was the only factor which significantly affected the estimated 5 year DFS. In 1995, van der Velden et al.[57] published a detailed study of nodal prognostic factors in 71 patients with inguinal node metastases from vulvar carcinomas. Patients with extranodal spread or more than two positive nodes received adjuvant radiotherapy to an unspecified dose. The most powerful predictor of outcome in their study was extranodal tumor extension: 28 of 44 patients (64%) with extranodal tumor died of disease versus 3 of 22 patients (14%) without this finding. Origoni et al.[58] reported similar findings in a series of 53 patients with positive nodes. In our study also lymph node involvement with extracapsular spread was observed as a significant prognostic factor for OS and DFS. Of the 4 patients with extracapsular nodal involvement, 3 died and 1 defaulted follow-up after 14 months.

Studies also suggest that, when corrected for the number of involved nodes, lymph node bilateralism and local factors such as tumor size and early involvement of adjacent structures have little impact on survival[7]. However, extracapsular nodal extension was found to be a powerful prognostic indicator. In 2009, to incorporate these findings and to improve the prognostic accuracy of FIGO staging system, another major revision was implemented (extracapsular nodal spread is now FIGO Stage IIIC) [7].

A possible limitation of our study is its retrospective and monocentric nature, but the low prevalence of vulvar cancer makes prospective studies difficult to complete. However, the decent number of patients with vulvar cancer treated in our dedicated cancer center and the uniform treatment by a highly specialized surgical team might be strengths of this study, as inter-patient variability in the treatment regimens are very low.

CONCLUSION

Carcinoma vulva, a relatively rare disease should better be managed in dedicated cancer centers where treatment can be tailored to individual patients with multidisciplinary cooperation. The median age in our series was 55 years which is well below the western world. On univariate analysis using log rank test, advanced stage, lymph node positivity and lymph node positivity with extracapsular spread (ECS) have emerged as important prognostic factors that significantly affected estimated 5 year overall survival. Extracapsular nodal spread was observed as the only prognostic factor that significantly affected both OS and DFS on univariate analysis in our series. HPV status of all vulvar cancers should be evaluated which may help to study the association of the virus with this disease and the possibility of potential prevention using vaccines.

Analyzing the epidemiological pattern, management options and outcome of these patients will pave way for the future treatment protocols, proper understanding of this disease and in the design of well controlled clinical trials regarding management of this reatively rare disease with the aim of reducing the morbidity without oncological compromise.

Since there has been a dearth of reports about this disease from our country as well as other developing countries we urge the need for more studies from

various centers and probably well designed multicentric studies keeping in mind the low prevalence of this disease. Uniform consensus should be arrived from those well controlled studies regarding organ conservation strategies and morbidity reducing approaches in nodal dissections.

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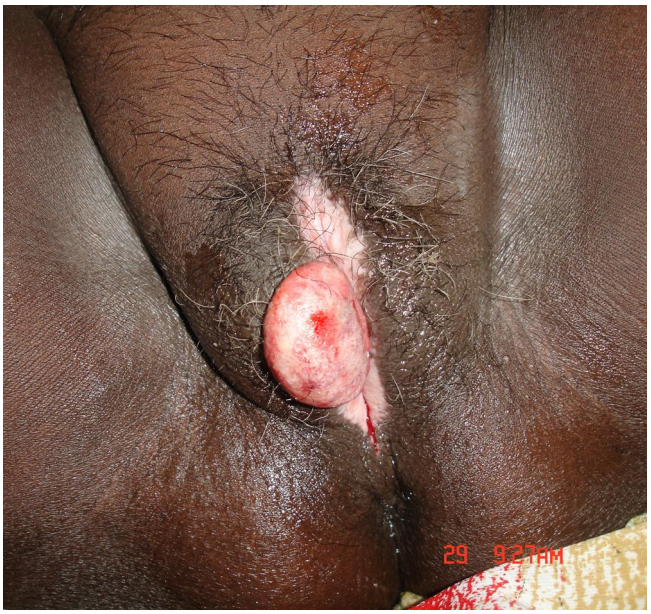
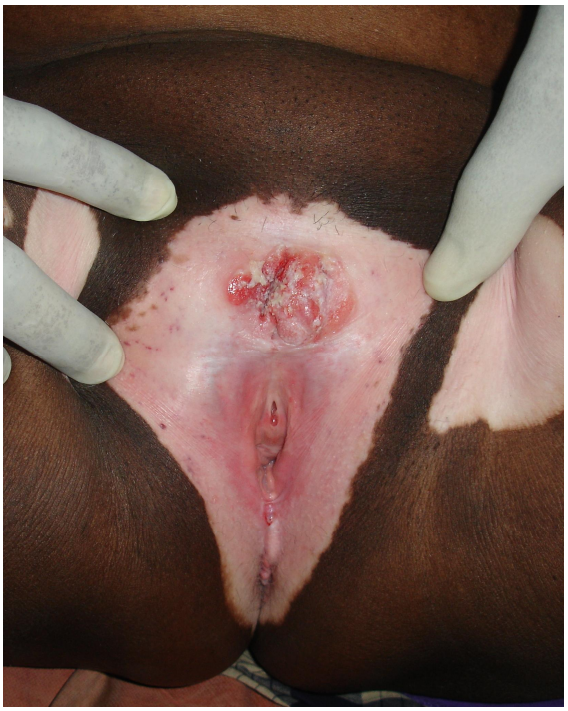
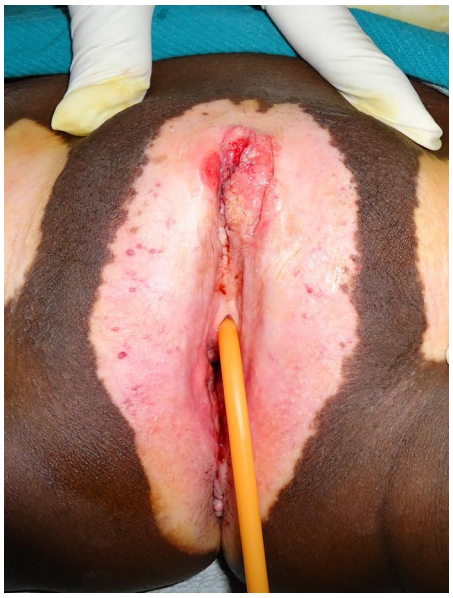
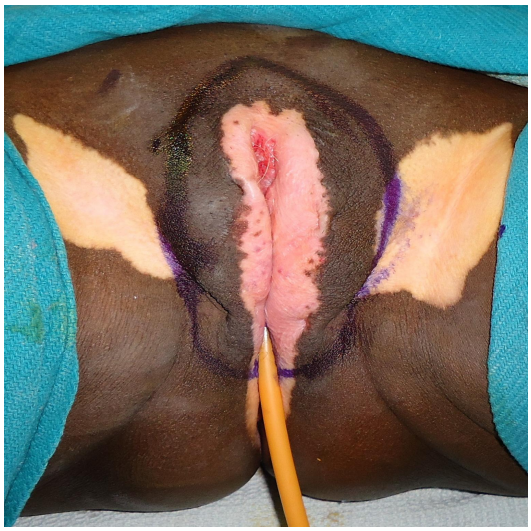
CLINICAL PHOTOGRAPH – CARCINOMA VULVA

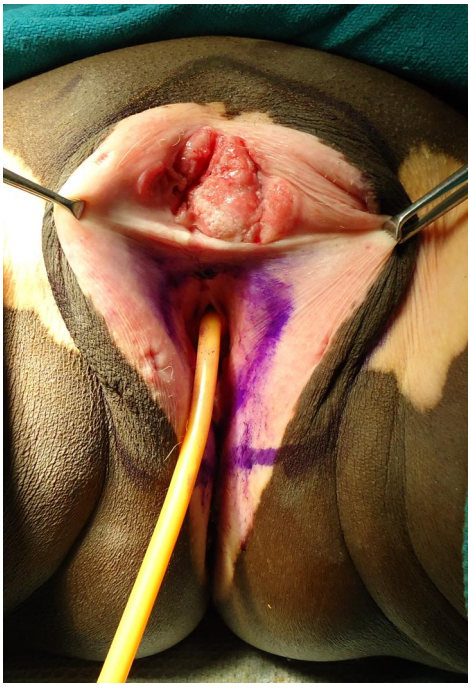


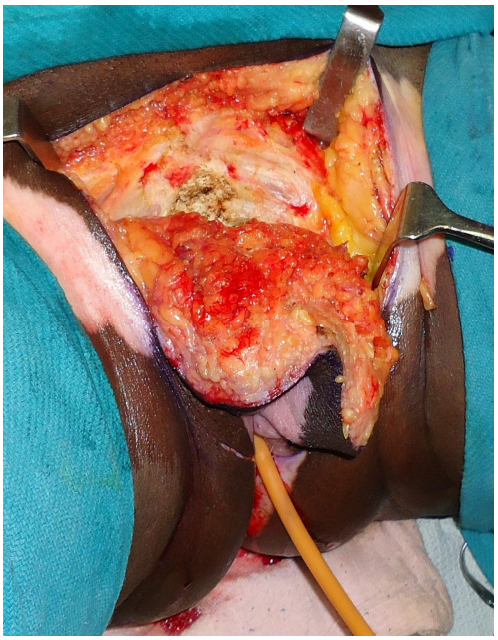


STEPS OF RADICAL VULVECTOMY - 1

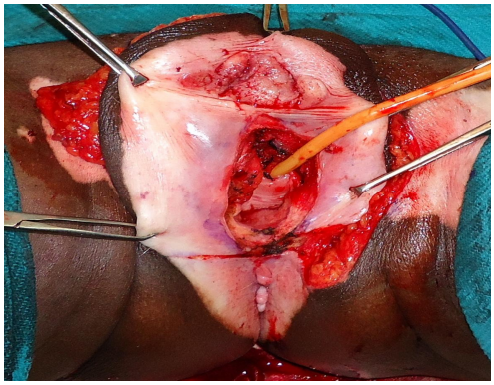


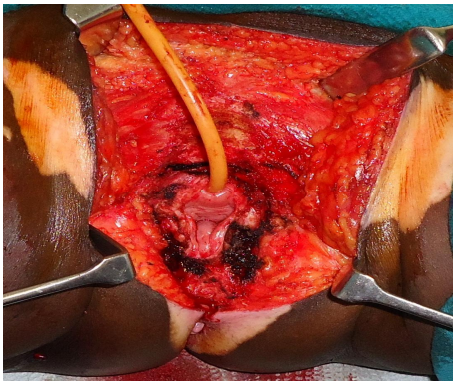


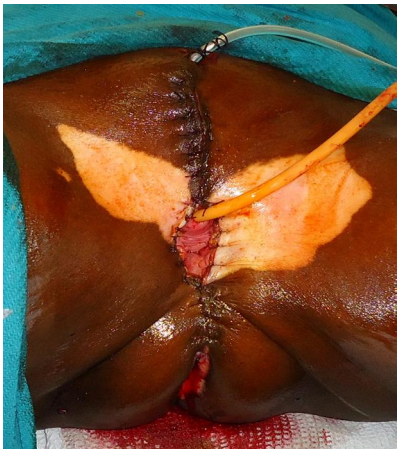


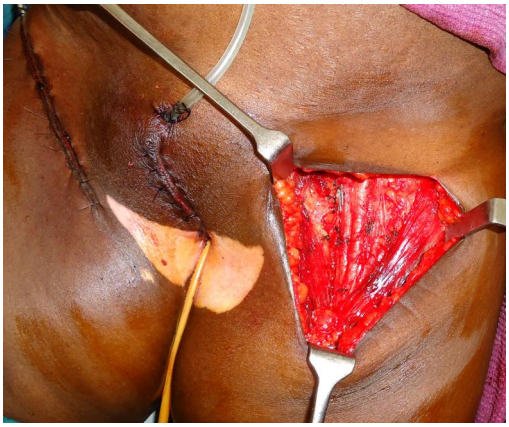


STEPS OF RADICAL VULVECTOMY - 2









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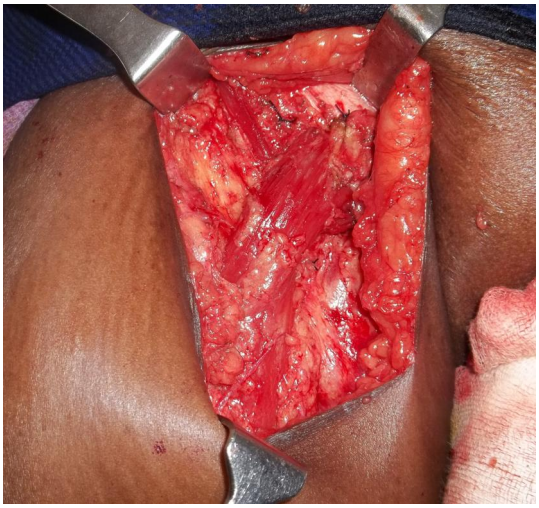
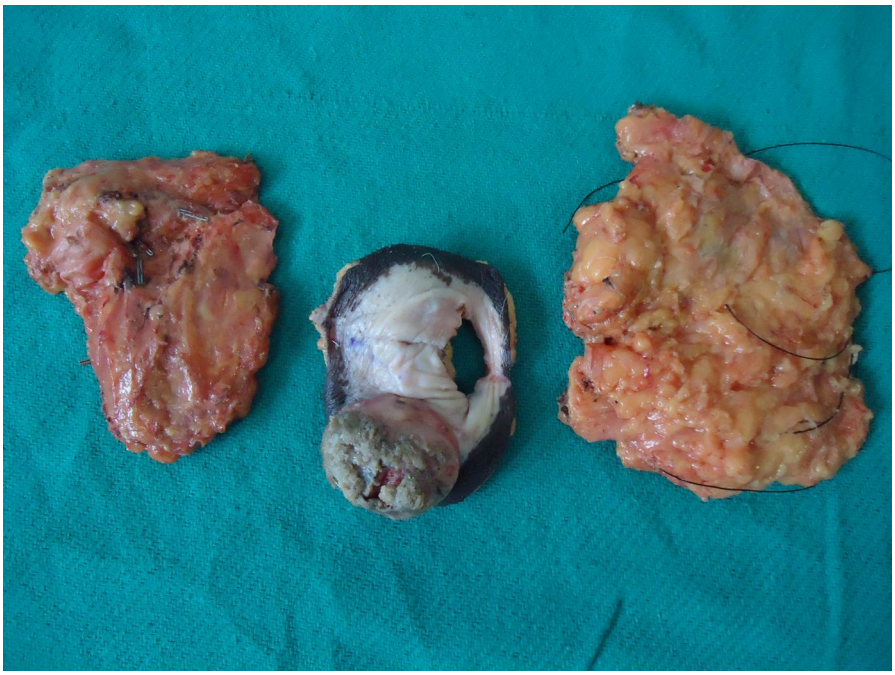


RADICAL VULVECTOMY –

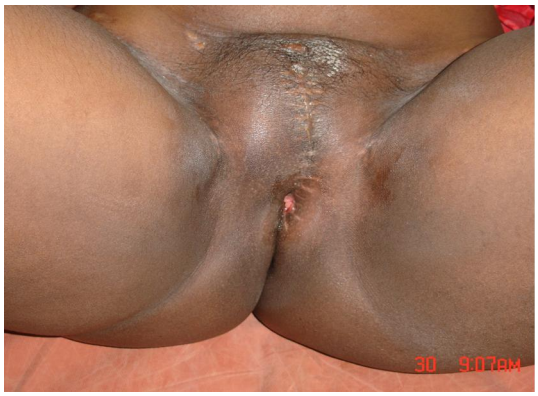
SPECIMEN PHOTOGRAPH

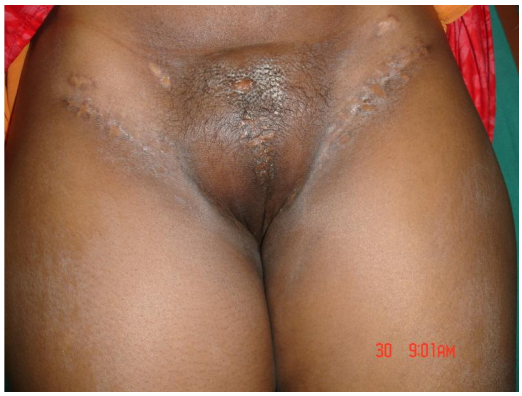


POST OPERATIVE COMPLICATION –

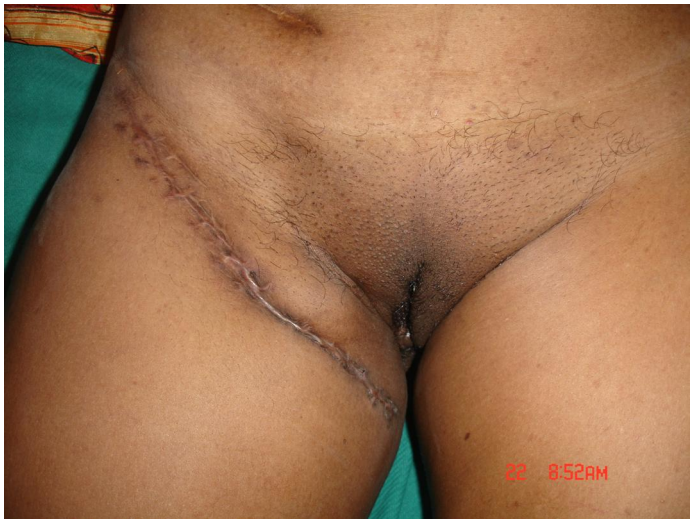
FLAP NECROSIS

RADICAL VULVECTOMY - FOLLOW-UP





HEMIVULVECTOMY - FOLLOW-UP



PROFORMA

Name: Age: Address:

Occupation: Cancer Department No:

Chief complaints:

1. Itching
2. Ulcer
3. Pain
4. Others

H/o Present illness:

H/o Past illness:

H/o Co-morbid illness:

H/o Previous Treatment:

Previous H/o Malignancy:

Personal History:

Family History:

Menstrual History:

General Examination:

Clinical Examination: Abdomen and Pelvis

PR & PV Examination

Thorough Gynecological Examination:

Examination of the Lesion:

1. Site
2. Predominant side
3. Size
4. Extent
    1. Involvement of Vagina
    2. Involvement of Urethra
    3. Involvement of Anus
5. Nodal Status

Examination of other systems:

Investigations: Confirmation of disease, Routine Investigations, Metastatic Evaluation

1. Biopsy
2. Blood Investigations
3. Chest Radiography
4. Ultrasonogram Abdomen & Pelvis
5. Others (if necessary)

Preoperative Treatment:

1. Nil
2. Pre operative EBRT
3. Pre operative Chemo-RT

Treatment: Surgery

Type of Surgery

1. Simple Vulvectomy
2. Radical Vulvectomy
3. Hemivulvectomy
4. Wide Local Excision

Nodal Block Dissection

1. Side
    a. Right
    b. Left
    c. Bilateral
2. Type
    a. Inguinofemoral
    b. Ilio-inguinal

Reconstruction with Flap

1. Flap used
2. Primary Closure without Flap

Post operative Histopathology:

1. Primary Lesion
2. Margin Status
    a. Free
    b. Close Margin
    c. Positive Margin
3. Nodal status
    a. Positive
    b. Positive with Extracapsular Spread
    c. Negative
4. Nodal Yield

    a. Total number of nodes
    b. Positive Nodes

FIGO Stage (2009):

Postoperative complications:

1. Seroma
2. Wound Infection
3. Wound Dehiscence due to necrosis
4. Others

Adjuvant Therapy:

1. EBRT
2. Chemotherapy
3. Chemo-RT

Recurrence Pattern:

1. Site
    a. Local
    b. Regional
    c. Systemic
2. Time Taken
3. Salvage of Recurrence
    a. Surgery
    b. EBRT

    c. Chemo-RT

Follow-up details:

1. Disease Free Period
2. Total Follow-up Period
3. Current Status
    a. Alive
        i. With Disease
        ii. Without Disease
    b. Dead
    c. Defaulted Follow-up

S.No	Name	Age	CD no	Itching	Ulcer	Pain	Others	DM	Retroviral status	Other cutaneous Lesion	Previous Malignancy	Family H/O malignancy	Predominant Side of involvement	Site	Size	Node involvement Clinically	Urethra	Anus	Vagina	Previous treatment	Pre operative treatment	DOS
1	Malliga Simon	40	296/04	yes	yes	yes	discharge	Nil	Negative	No	No	No	Right	Right Labia majora	3x3 cm	Right inguinal	Normal	Normal	No	Nil	Nil	1/4/2004
2	Anjalai	27	527/04	yes	yes	no	no	Nil	Negative	No	No	No	Bilateral	Bilateral Labia majora (multiple warty lesions)	multiple small lesions, largest 2x1 cm	No	Normal	Normal	No	Nil	Nil	13/05/2004
3	Rajalakshmi	30	539/04	yes	yes	no	no	Nil	Negative	No	No	No	Bilateral	Bilateral Labia majora	6x4 cm	Right inguinal 6x4 cm - fixed	Normal	Normal	No	Nil	50 GY EBRT 25 #	20/07/2004
4	Ethirajam	62	826/04	yes	yes	yes	discharge	Nil	Negative	No	No	sister had Ca. breast	Bilateral	Bilateral,lower 1/3 vagina involved	6x3 cm	Right inguinal	Yes lower1/3	Normal	yes lower1/3	Excision elsewhere 2 years back	40 GY EBRT 20 #	1/11/2004
5	Jothimani	45	607/05	yes	yes	no	no	Nil	Negative	No	No	No	Right	Right Labia majora	3x2 cm	No	Normal	Normal	No	Nil	nil	17/06/05
6	Lakshmiammal	60	704/05	yes	yes	no	no	Nil	Negative	No	No	No	Right	Right Labia majora	4X3 cm	No	Normal	Normal	No	Nil	nil	22/06/2005
7	Sundarammal	50	840/05	no	yes	no	no	Nil	Negative	No	No	No	Bilateral	Bilateral labia majora	5x5 cm	No	Normal	Normal	No	Nil	Nil	5/8/2005
8	Mangammal	65	141/06	no	yes	no	no	Nil	Negative	No	No	No	Right	Right Labia minora with Clitoris	2x2 cm	No	Normal	Normal	No	Nil	Nil	16/02/2006
9	Jayalakshmi	60	292/06	yes	yes	no	no	Nil	Negative	No	No	Maternal Uncle & Elder Brother had Ca. Esophagus	Right	Rt Labia majora, Rt labia minora, close to anus	4x3 cm	Right Inguinal	Normal	Normal	No	Topical Ointments	nil	10/4/2006
10	Annammal	60	914/06	no	yes	yes	no	Nil	Negative	No	No	No	Right	Right Labia minora	1.5x1 cm	No	Normal	Normal	No	Punch Biopsy Elsewhere	nil	26/08/2006
11	Tamilarasi	35	1026/06	yes	yes	yes	no	Nil	Negative	No	No	No	Right	Rt labia majora involving rt labia minora and clitoris	6x4cm	No	Normal	Normal	No	Nil	nil	9/9/2006
12	Abaranji	65	1032/06	yes	yes	no	no	yes	Negative	No	No	Son had Ca. Stomach	Bilateral	labia majora,minora onboth sides, clitoris	6X4 cm	No	Normal	Normal	No	Punch Biopsy Elsewhere	nil	16/09/06
13	Samiammal	55	1426/06	yes	yes	yes	no	Nil	Negative	Leukoderma	No	No	Left	Labia minora - Left	5x3	No	Normal	Normal	No	Topical Ointments	nil	8/12/2006
14	Chinnammal	55	555/07	no	yes	no	no	Nil	Negative	No	Ca.cervix IIIB	No	Right	Right labia majora	4x3 cm	No	Normal	Normal	No	known Ca. cervix IIIB treated with Radical RT 4 years back	nil	15/05/2007
15	Tamilarasi Gopal	48	1506/07	yes	yes	no	no	Nil	Negative	No	No	No	Left	Left labia majora with distal1/3 vagina	5x3 cm	Left inguinal	Normal	Normal	lower 1/3	Nil	Nil	24/11/2007
16	Gowrammal	59	1531/07	no	yes	yes	discharge	Nil	Negative	No	No	No	Right	Rightlabia majora and labia minora extending to perineal body	6x4 cm	Right inguinal	Normal	Normal	No	Nil	50 GY EBRT	8/12/2007

17	Pappammal	50	61/08	yes	yes	yes	no	Nil	Negative	No	No	No	Bilateral	Both Labia majora	4x3 cm	Bilateral inguinal	Normal	Normal	No	Nil	Nil	5/2/2008
18	Ruckmani	54	218/08	yes	yes	no	no	Nil	Negative	No	No	No	Right	Right Labia majora involving urethral meatus	4x3 cm	Bilateral inguinal	yes meatus	Normal	No	Splenectomy for Autoimmune Hemolytic Anemia 3 years back	Nil	19/02/2008
19	Vediammal	42	1060/08	no	yes	no	no	Nil	Positive	No	No	No	Right	Right Labia majora	2x3cm	No	Normal	Normal	No	Nil	Nil	5/7/2008
20	Savithri	61	1145/08	no	yes	no	bleeding	Nil	Negative	No	No	No	Right	Right labia majora involving clitoris	3x2 cm	Left inguinal	Normal	Normal	No	Nil	Nil	24/07/2008
21	Kaladevi	45	1217/08	yes	yes	yes	discharge	Nil	Negative	No	No	No	Bilateral	Bilateral labia majora with clitoris	6x3 cm	No	Normal	Normal	No	Nil	Nil	25/07/2008
22	Muniammal Deva	65	1885/08	yes	yes	no	no	Nil	Negative	No	No	Daughter had Ca. cervix	Right	Entire Right vulva extending to left side	5x3 cm	Bilateral inguinal	yes meatus	Normal	No	Nil	Nil	10/12/2008
23	Vimala	50	1922/08	yes	yes	no	no	Nil	Negative	No	No	No	Left	Left Labia majora	1x1 cm	Left inguinal	Normal	Normal	No	40 GYEBRT elsewhere , 2months before admission	Nil	19/12/2008
24	Mary	58	14/09	yes	yes	no	no	Nil	Negative	No	No	No	Right	Right labia majora	5x4cm	No	Normal	Normal	No	Nil	Nil	27/01/2009
25	Gangammal	65	364/09	yes	yes	no	no	Yes	Negative	No	No	No	Right	Right labia minora	3x2 cm	No	Normal	Normal	No	Nil	Nil	21/04/2009
26	Jayammal	60	850/09	yes	yes	no	no	Nil	Negative	No	No	No	Bilateral	Bilateral labia majora anteriorly	4x3 cm	No	Normal	Normal	No	Nil	nil	22/07/2009
27	Anila	23	956/09	no	yes	no	no	Nil	Negative	No	No	No	Right	Entire right hemivulva upper half of left hemivulva,distal urethra	6x3 cm	No	Distal urethra	Normal	No	Nil	Concurrent chemo RT, (50 GY 25 #, 3 cycles of PF chemo)	5/11/2009
28	Velankanni	45	163/10	yes	no	no	no	Nil	Negative	No	No	No	Right	Right labia minora	2x2 cm	No	Normal	Normal	No	Vaginal Hysterectomy 4 months back	Nil	15/03/2010
29	Thenammal	50	454/10	no	yes	no	no	Nil	Negative	No	No	No	Clitoris	Clitoris	2x1cm	No	Normal	Normal	No	Excision biopsy elsewhere	nil	26/05/2010
30	Thamayanthi	65	503/10	yes	no	no	swelling	Nil	Negative	No	No	No	Right	Right labia majora	2x1 cm	No	Normal	Normal	No	Excision biopsy elsewhere, vaginal hysterectomy 5 years back	nil	20/05/2010
31	Nirmala	55	783/10	yes	no	no	no	Nil	Negative	No	No	No	Left	Left labia majora with Clitoris	3x2 cm	No	Normal	Normal	No	Topical Ointments	Nil	10/8/2010
32	Therasammal	73	891/10	yes	yes	no	no	Nil	Negative	leucoderma	No	No	Right	Right labia majora	3x4cm	No	Normal	Normal	No	Nil	Nil	19/08/2010
33	Alagammal	50	471/11	yes	yes	no	no	yes	Negative	No	No	No	Clitoris	Clitoris	3x2 cm	No	Normal	Normal	No	Nil	nil	7/5/2011
34	Syriapuspam	60	806/11	yes	yes	no	no	yes	Negative	No	No	No	Right	Right labia majora	3x4cm	No	Normal	Normal	No	Nil	Nil	9/8/2011
35	Rathinam	50	1012/11	yes	yes	no	no	yes	Negative	No	No	No	Right	Right labia majora with clitoris	5x3 cm	No	Normal	Normal	No	Nil	Nil	19/09/2011

Surgery	Nodal dissection	Flap Reconstruction	Post operative complication	Post Operative HPE	Margin status	Nodal status	No of nodes positive	Nodal positivity	Nodal positivity with ECS	FIGO stage	Adjuvant RT	Adjuvant Chemotherapy	Pattern of recurrence	Treatment of recurrence	DFS in months	Total follow up period in months	Status
Wide Local Excision	Right Ilioinguinal Block Dissection	Nil	Skin flap necrosis	SCC	Free	Right inguinal 5/8 +, Right pelvic 7/7 free	5 out of 15	Positive	Positive without ECS	III	Defaulted RT	Nil	Nil	Nil	36	36	Alive & defaulted followup
Simple vulvectomy	Nil	Nil	Uneventful	SCC Gr-I	Free	Nil	NA	NA	NA	I	Nil	Nil	Right inguinal node 5 months after primary surgery	Right Ilioinguinal Block Disection with Extended TFL flap Rt inguinal regionon 05/11/2004, HPE- Right inguinal 7/10 +ve, Right pelvic 1/6 +ve, 50GY EBRT 25 # as adjuvant	5	26	Alive & defaulted follow up
Radical Vulvectomy	Right Ilioinguinal, Left inguinofemoral Block Dissection	TFL flap Rt inguinal region	Uneventful	SCC-nonkeratinizing Gr- II	Free	Right inguinal 14/14 free, Left inguinal 11/11 free, Right pelvic 7/7 free	0 out of 32	Negative	Negative	IVA	Nil	Nil	Nil	Nil	56	56	Alive
Radical Vulvectomy	Rt ilioinguinal, Lt inguinofemoral Block Dissection	Bilateral Gracilis myocutaneous flap for primary surgery, TFL flap for Rt inguinal region	Gracilis flap necrosis,on 07/11/2004 Diversion colostomy with removalof necrosed flaps	SCC Gr-II	posterior margin +ve	Rt inguinal 12/12 + with perinodal disease, Lt inguinal 1/5 +ve, Rt pelvic nodes 6/7 +ve with perinodal disease	19 out of 24	Positive	Positive with ECS	IVB	Nil	Nil	Nil	Nil	20	20	Dead
Radical Vulvectomy	Right ilioinguinal Block Dissection	Nil	Skin flap necrosis	SCC- Gr-I	Free	Right inguinal 1/8 +, Right iliac 4/4 free	1out of 12	Positive	Positive without ECS	III	Nil	Nil	Left inguinal nodes matted on 06/10/2005	50 GY EBRT,nonresponsive 16 GY EBRT, 1cycle chemo CDDP, 5FU,patient defaulted	4	14	Dead
Simple Vulvectomy	Nil	Nil	Uneventful	SCC Gr-I	Free	Nil	NA	NA	NA	I	Nil	Nil	Nil	Nil	60	60	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC Gr-II	Free	Right inguinal 2/8 +,Left inguinal 7/7 free	2 out of 15	Positive	Positive without ECS	III	50GY EBRT 25 #	Nil	Nil	Nil	58	58	Alive
Right Hemivulvectomy	Right Inguinofemoral Block Dissection	Nil	Wound infection with skin flap necrosis	SCC- small cell keratinizing	1/4th margin +ve	Right inguinal 6/6 free	0 out of 6	Negative	Negative	I	Defaulted RT (came after 15 months)	Nil	Nil	Nil	67	67	Alive
Radical Vulvectomy	Right Inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC- Gr-I	Free	Right inguinal 9/9 free	0 out of 9	Negative	Negative	I	Nil	Nil	Nil	Nil	54	54	Alive
Wide Local Excision	Nil	Nil	Uneventful	SCC- Gr-I	Free	Nil	NA	NA	NA	I	Nil	Nil	Nil	Nil	61	61	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC- Gr-I	Free	Right inguinal 7/7 free, Left inguinal 8/8 free	0 out of 15	Negative	Negative	I	Nil	Nil	Nil	Nil	48	48	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Skin flap necrosis	Verrucous Carcinoma, areas of invasion 2 mm	Free	Right inguinal 9/9 free, Left inguinal 5/5 free	0 out of 14	Negative	Negative	I	Nil	Nil	Nil	Nil	61	61	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC- Gr-I	Free,Urethra Free	Right inguinal 4/5 +,Left inguinal 7/11 +	11 out of 16	Positive	Positive without ECS	III	Defaulted RT	Nil	Nil	Nil	41	41	Alive & defaulted followup
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC-Nonkeratinizing	Free	Right inguinal 7/7 free, Left inguinal 9/9 free	0 out of 16	Negative	Negative	I	Nil	Nil	local recurrence 04/02/2010 (33 months after surgery)	brachytherapy planned, pt defaulted	33	46	Alive with Disease
Radical Vulvectomy	Left Inguinofemoral Block Dissection	TFL flap left side	Distal part of TFL flap necrosis, DVT Lt Iliac veins & CFV & PV	SCC large cell type	Free	Left inguinal 1/10 +	1 out of 10	Positive	Positive without ECS	III	60 Gy EBRT 30 #	Nil	periurethral region	Defaulted followup	31	43	Alive with Disease
Radical Vulvectomy	Bilateral Ilioinguinal Block Dissection	TFL flap rt side	perineal wound infection treared	SCC-keratinizing	Right lateral margin close	Right inguinal 3/7 +, Right iliac 4/4 free, Left inguinal 6/6 free,Left iliac 4/4 free	3 out of 21	Positive	Positive without ECS	III	Nil	Nil	Nil	Nil	25	25	Alive

Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC keratinizing large cell type	Free	Right inguinal 10/10 free, Left inguinal 2/9 +ve with perinodal disease	2 out of 19	Positive	Positive with ECS	IIIC	Defaulted RT	Nil	Ulcer Left inguinal region 6 months after primary surgery	60 GY EBRT	6	10	Dead
Radical Vulvectomy	Bilateral inguinofemoral Block Dissection	Nil	Skin flap necrosis, slough excision, SSG	SCC keratinizing	Free	Right inguinal 3/10 +ve with perinodal disease, Left inguinal 4/4 free	3 out of 14	Positive	Positive with ECS	IIIC	50GY EBRT 25 #	Nil	local recurrence 30-11-09 (21 months after primary surgery)	Chemotherapy received - PF 1 cycle	21	25	Dead
Wide Local Excision	Nil	Nil	Uneventful	SCC ,3mm invasion	Free	Nil	NA	NA	NA	I	Defaulted RT	Nil	Nil	Nil	39	39	Alive
Radical Vulvectomy	Bilateral inguinofemoral Block Dissection	Nil	Uneventful	SCC keratinizing	Free	Right inguinal 13/13 free, Left inguinal 8/8 free	0 out of 21	Negative	Negative	I	Nil	Nil	Nil	Nil	26	26	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	Basisquamous cell carcinoma	Free	Right inguinal 13/13 free, Left inguinal 6/6 free	0 out of 19	Negative	Negative	I	Nil	Nil	Clinical nodal recurrence at 13 months ,no biopsy proof	Defaulted followup	13	13	Alive & defaulted followup
Radical Vulvectomy	Bilateral inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC Gr-I, minimally invasive	Free	Right inguinal 7/7 free, left inguinal 6/6 free	0 out of 13	Negative	Negative	II	Nil	Nil	Nil	Nil	33	33	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	TFL flap Lt inguinal region	Skin flap necrosis rt side, marginal wound gap lt side	No residual tumor	Free	Right inguinal 13/13 free, Left inguinal 2/13 +ve	2 out of 26	Positive	Positive without ECS	III	Nil	Nil	Nil	Nil	19	19	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC- Gr-II	Free	Right inguinal node 7/7 free, Left inguinal 2/8 +ve with perinodal disease	2 out of 15	Positive	Positive with ECS	IIIC	50GY EBRT 25 #	Nil	Nil	Nil	14	14	Alive & defaulted followup
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC- Gr- I	Free	Right inguinal 9/9 free, Left inguinal 11/11 free	0 out of 20	Negative	Negative	I	Nil	Nil	Nil	Nil	29	29	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC Gr-I	Free	Right inguinal 2/9 +, Left inguinal 3/11 +	5 out of 20	Positive	Positive without ECS	III	60 Gy EBRT 30 #	Nil	Nil	Nil	27	27	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	Tiny residual SCC	Free	Right inguinal 3/3 free, Left inguinal 3/3 free	0 out of 6	Negative	Negative	II	Nil	3cycles of PF	Multiple metastases lung,humerus	4 cycles of chemo with PF, 20 GY RT 5# for deposit humerus medial condyle on January 2011	8	21	Alive with Disease
Right Hemivulvectomy	Right Inguinofemoral Block Dissection	Nil	Uneventful	SCC Gr-II	Free	Right inguinal 8/8 free	0 out of 8	Negative	Negative	I	Nil	Nil	soft tissue recurrence in rt inguinal region on 22-06-10,FNAC +	(Chemo-RT) 50Gy EBRT with 6 cycles of chemo with PF- completed on 12-03-11	3	20	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	No residual tumor	Free	Right inguinal 8/8 free, Left inguinal 7/7 free	0 out of 15	Negative	Negative	I	Nil	Nil	Nil	Nil	18	18	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	No residual tumor	Free	Right inguinal 5/5 free, Left inguinal 5/5 free	0 out of 10	Negative	Negative	I	Nil	Nil	Nil	Nil	17	17	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC Gr-II	Free	Right inguinal 2/11 +ve, Left inguinal 10/10 free	2 out of 21	Positive	Positive without ECS	III	50GY EBRT 25 #	Nil	Nil	Nil	15	15	Alive
Radical Vulvectomy	Bilateral inguinofemoral Block Dissection	Nil	Skin flap necrosis	SCC Gr-I	Free	Right inguinal 11/11 free, Left inguinal 6/6 free	0 out of 17	Negative	Negative	I	Nil	Nil	Nil	Nil	14	14	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Marginal skin flap necrosis,secondary suturing on 16-06-11	SCC-Gr-I	Free	Right inguinal 8/8 free, Left inguinal 9/9 free	0 out of 17	Negative	Negative	I	Nil	Nil	Nil	Nil	6	6	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC Gr-II	Free	Right inguinal 2/10 +, Left inguinal 5/14 +	7 out of 24	Positive	Positive without ECS	III	50GY EBRT 25 #	Nil	Nil	Nil	3	3	Alive
Radical Vulvectomy	Bilateral Inguinofemoral Block Dissection	Nil	Uneventful	SCC Gr-I	Free	Right inguinal 9/9 free, Left inguinal 8/8 free	0 out of 17	Negative	Negative	I	Nil`	Nil	Nil	Nil	2	2	Alive