



## **Impact of vulvar reconstruction on the accuracy of a nomogram for predicting local recurrence after surgery for vulvar cancer**

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# **1 Impact of vulvar reconstruction on the accuracy of a nomogram for predicting local 2 recurrence after surgery for vulvar cancer**

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31 Highlights

32 The prognosis of vulvar cancer reconstructions has been poorly studied

33 Nomograms are useful tools for diagnosis, management and follow-up of patients

34 Vulvar reconstruction is oncologically safe and has a better prognosis in aggressive cancers.

35 Vulvar reconstruction increases safe margins

36

## ABSTRACT

**Summary Background Data :** Vulvar carcinoma is a rare disease accounting for 3 %–5% of all gynaecological cancers. Although surgery is the standard treatment at an early stage, the outcomes are highly correlated with clear resection margins. Therefore, surgical defects can be important and require reconstruction. The aim of this study was to evaluate vulvar reconstructions using a previously validated nomogram predicting the risk of local recurrence at 2 years.

**Methods :** Patients who underwent surgery for vulvar cancer between 1998 and 2017 were extracted from eight FRANCOGYN centres. We estimated the probability of local recurrence at 2 years using a previously validated nomogram and compared it with actual relapse in patients with or without vulvar reconstruction. Patients were clustered into tertiles according to their nomogram score: low-, intermediate-, and high-risk for local relapse probability.

**Results:** We reviewed 254 patients, of whom 49 underwent immediate vulvar reconstruction. The predicted and actual probability of two-year local relapse were 20.1% and 15.7%, respectively, with a concordance index of 0.75. In the low- and intermediate-risk groups, the difference between predicted and observed recurrence was less than 10% in patients with or without vulvar reconstruction. For the high-risk group, the difference reached 25% and observed recurrence probability was lower in patients who underwent vulvar plasty compared with those who did not (20.0% vs. 36.2%, respectively). Local recurrence-free survival rates following vulvar reconstruction were comparable at two years (82.1 % vs. 84.8 %, respectively,  $p=0.26$ ).

**Conclusion :** Vulvar reconstruction after surgical resection for vulvar cancer is safe. Vulvar reconstruction should be considered in aggressive cases to decrease local recurrence.

Key-words : vulvar cancer, oncologic surgery, vulvar reconstruction

## INTRODUCTION

Vulvar carcinoma is a rare disease, accounting for 3 %–5% of all gynaecological cancers. The most common histological type is squamous cell carcinoma [1]. Surgery is the standard treatment for patients who present at an early stage, and often involves a combination of radical vulvectomy with sentinel lymph node or inguinal lymph node dissection [2,3].

Oncologic surgery follows strict technical standards. One of the major technical points is the obtention of free margins [4]. The latest European Society of Gynaecological Oncology recommendations require clinical margins larger than 1 cm. Reduction in margins is accepted when the resection approaches the anus, clitoris, or urethra, but should remain larger than 3 mm [5]. The surgical procedure can lead to significant defects, depending on the local extension of the tumour. Vulvar reconstruction techniques are frequently considered to achieve complete tumoral resection.

These reconstructions include advancement flaps and transpositional flaps [6]. The main flaps used are Dufourmentel flap, V-Y, rhomboid, anterolateral thigh (ATL), gluteal thigh flap, lotus, deep inferior epigastric artery perforator (DIEP), vertical rectus abdominis myocutaneous (VRAM) or Taylor flaps [7–9]. Selection of the reconstruction type depends on several factors. An increase in lesion size is correlated with the use of advancement gluteal flaps or DIEP flaps [10]. Depending on the tumour location, a V-Y technique may be chosen in the case of a lateral lesion, or an ATL technique in the case of a vertical tumour extending from the pubis to the posterior part of the labia majora. ATL is chosen if there is a need for inguinofemoral lymphadenectomy with butterfly resection [7].

A meta-analysis evaluating the complications of perineal reconstructions in the lower rectum or anal cancer reported better healing after using a flap procedure than when primary closure was performed [11]. Few studies have evaluated the prognosis of vulvar reconstruction in vulvar cancer. To date, no study has compared two large populations of patients with or without vulvar reconstruction. Tock et al. reported no difference in recurrence between different types of reconstruction, without a control group (patients without reconstruction). Sixty-one

patients who underwent vulvar reconstruction with 16 V-Y flap were enrolled. This reconstruction technique appears to have the least incidence of complications, as well as a lower average length of hospitalization and reoperation rate [8]. Giannini et al. compared 23 and 41 patients who underwent V-Y gluteal flaps and direct closure, respectively. Both studies reported a significant association between plastic reconstruction and adequate surgical margins [12].

Shortly before the change in the FIGO classification of vulvar cancer in 2009 [13], Rouzier et al. developed a two nomograms for predicting relapse-free survival [14]. Nomograms are statistical tools that enable users to calculate the overall probability of a specific outcome, that is, recurrence from a disease, for an individual patient [15]. Kim et al. validated in 2008 with 90 Korean patients, the first nomogram developed by Rouzier predicting recurrence-free survival [16]. The second nomogram for predicting local recurrence after vulvectomy included three variables : margin status, depth of invasion and lymphovascular involvement [17].

The aim of the present study was to to evaluate the impact of vulvar reconstruction on local recurrence using a previously validated nomogram.

## 99    **METHODS**

### 100    *Patient cohort*

101            Data of vulvar cancers from the FRANCOGYN group were included in this study. FRANCOGYN is a  
 102    French research group comprising several reference gynaecological and oncological surgery units in France. This  
 103    database includes eight French cancer centres. Vulvar cancers diagnosed between 1998 and 2017 were extracted  
 104    from the FRANCOGYN database using epidermoid cancer for the histologic subtype. Patients with available data  
 105    for components of the Rouzier nomogram (i.e. margin status, depth of invasion, and lymphovascular involvement)  
 106    were included. All cases were classified according to the 2009 revised FIGO staging system. Early stages were  
 107    defined as stages I and II, and advanced stages were defined as stages III and IV [18]. Patients who had received  
 108    neoadjuvant treatment were excluded. The study protocol was approved by the Institutional Review Board of  
 109    the College National des Gynécologues et Obstétriciens Français (CEROG 2021-GYN-0509).

110            Vulvar reconstruction comprised any reconstruction performed using a free flap or advancement flap. These  
 111    included the Dufourmentel, V-Y, rhomboid, ATL, gluteal thigh, lotus, DIEP, or Taylor flaps. All reconstructions  
 112    were performed immediately after vulvectomies.

### 113    *Model building*

114            The Rouzier nomogram was developed using multivariate logistic regression analysis [15]. The final  
 115    regression model was based on the clinical and statistical significance of the predictors, including margin status,  
 116    depth of invasion, and lymphovascular involvement. When the normal tissue margins on the definitive surgical  
 117    specimen were less than 3 mm, the margins were considered positive. The depth of invasion was recorded in  
 118    millimetres. For each patient, points were assigned to each of these three variables, and the total score was  
 119    calculated from the nomogram. The total points corresponded to the predicted two-year locale relapse-free  
 120    probability. To assess the accuracy of the nomogram, we assigned points to the predicted two-year cancer local  
 121    relapse-free probability according to the Rouzier nomogram for each patient.

Patients were then clustered into tertiles according to their nomogram score: low-, intermediate-, and high-risk groups for local relapse.

#### *Calibration*

The two-year local relapse-free probability in each tertile group was calculated using the Kaplan–Meier method and then compared with the predicted probability derived from the Rouzier nomogram. For each tertile group, we calculated the difference between the predicted and the observed two-year survival probabilities for recurrence. The mean error between the predicted and the observed two-year survival probabilities without local relapse was the sum of the differences for each tertile group. The calibration plot describes how far predictions are from actual outcomes and how the nomogram fits the data for tertiles.

#### *Discrimination*

Discrimination of the nomogram was quantified using the concordance index (CI). The CI is a modification of the area under the receiver operating characteristic curve (AUC), and is adapted to fit censored data. Its interpretation is similar to AUC. To test the performance of the nomogram, we calculated the CI in patients from our cohort and in those who did or did not undergo vulvar reconstruction. A CI of 1.0 indicates perfect concordance, while a score of 0.5 indicates no relationship.

#### *Other statistical tests*

Categorical and numerical variables were analysed using the Chi-square t-test and the Student's t-test respectively. Differences were considered significant at a level of  $p < 0.05$ . The two-year survival without local relapse probability following vulvar reconstruction was calculated using the Kaplan–Meier analysis and compared with the Cox model.



145           Data were analysed with the R package version 2.10.1 using the Design, Hmisc, Rms, Markdown and  
146   Verification libraries (<http://lib.stat.cmu.edu/R/CRAN/>).

## RESULTS

During the study period, 253 patients who fulfilled the inclusion criteria were enrolled to evaluate the Rouzier nomogram. Among them, 49 patients underwent concomitant vulvar reconstruction. In the vulvar reconstruction group, five had a Dufourmentel flap, 28 had a V-Y flap, one had a rhomboid flap, three had a gluteal thigh flap and four had a lotus flap. None of the patients underwent a VRAM reconstruction. In eight patients, the type of reconstruction was not specified. A flowchart of this process is shown in Figure 1.

Patient characteristics are listed in Table 1. Patients who underwent vulvar reconstruction had larger tumour (35.5 mm vs 26.7 mm,  $p = 0.04$ ), deeper tumoral depth (9.3 mm vs 5.5 mm,  $p = 0.02$ ) and presented at more advanced FIGO stages ( $p = 0.001$ ). On the basis of other variables, the two populations were not statistically different.

### *Discrimination*

The CI of the Rouzier nomogram for the entire population was 0.75 ( $\pm 0.07$ ). The CIs in patients with or without vulvar reconstruction were 0.66 ( $\pm 0.10$ ) and 0.77 ( $\pm 0.10$ ), respectively.

### *Calibration*

Among the entire population, the predicted and the actual probabilities of two-year local relapse were 20.1% and 15.7%, respectively (Table 2). The performance of the nomogram appears to be accurate, accounting for 4.4 % of the actual outcomes. The predicted and the actual probabilities depending on whether a vulvar reconstruction was performed or not are shown in Table 3 and Figure 2.

We then divided the population into three groups (low, intermediate, and high recurrence risk). In the low- and intermediate-risk groups, there was no statistical difference in tumour size, depth invasion and FIGO stage between patients who underwent reconstruction and those who did not. In the high-risk group, patients who underwent reconstruction had larger tumours (49.6 mm vs 31.7 mm,  $p=0.0038$ ) and a more advanced FIGO stages ( $p=0.03$ ). Depth invasion was not different ( $p=0.07$ ).

Regardless of reconstruction, the difference between predicted and observed recurrence probabilities was higher for patients belonging to the high-risk group (11.3%), and similar in the low- and intermediate-risk groups (Table 2). Among the patients who did not undergo vulvar reconstruction, the difference between the predicted and observed recurrence probabilities was less than 10% in the three risk groups (Table 3). Among the patients who underwent vulvar reconstruction, the difference between the predicted and observed relapse probabilities was higher for patients belonging to the high-risk group, which were 44.0% and 20.0% (24.6%), respectively. For the low-and intermediate-risk groups, the difference was less than 10% (Table 3).

Local recurrence-free survival following vulvar reconstruction was comparable over 2 years (Figure 3).

## DISCUSSION

The present study aimed to assess the impact of reconstruction on recurrence probability after surgery for vulvar cancer using Rouzier et al. nomogram. The prediction of local recurrence for vulvectomies without reconstruction was good for all risk groups, except for patients who underwent vulvar reconstruction. The calibration was accurate only for low- and intermediate- risk groups. For patients belonging to the high-risk group for local recurrence and who had reconstruction, the nomogram overestimated the risk of recurrence. This suggests that vulvar reconstruction reduces the risk of local recurrence in this population.

The Rouzier nomogram was initially developed as a tool for therapeutic decision- making. In this study, we provide the first external and independent validation of this nomogram regarding local recurrence probability, which is mandatory before it can be used in clinical practice. According to the FIGO classification, stage groupings are based on primary tumour spread, nodal extension, and metastasis to distant organs. However, other prognostic factors, such as those used in the nomogram (free resection margins, depth of invasion, and lymphovascular involvement), have also been demonstrated to have an effect on survival [4] and combining them into a simple mathematical model provides a more accurate prediction for the individual patients. In this study, the nomogram was used as a statistical tool to analyse the effect of reconstruction on the recurrence probability. Since conducting a randomized study evaluating the impact of reconstruction is unrealistic and unethical, comparing the expected and observed probabilities allowed us to study this effect. However, since the components of the nomogram are not available preoperatively, recurrence rate assessment is only possible after surgery, and the decision to perform reconstruction cannot be based on the Rouzier nomogram.

The Rouzier nomogram could also be used to evaluate the impact of adjuvant treatment, such as radiotherapy, on recurrence probability. In order to perform a one-time resection (i.e. to avoid a second surgery) and to avoid adjuvant radiotherapy, a large vulvectomy might be needed, and reconstruction should be considered. In the present study, patients with larger tumours and deeper invasion underwent reconstruction more frequently. Large tumours result in considerable defects to be reconstructed, requiring the use of reconstruction techniques.

In this study, we did not consider the type of reconstruction performed. Decisional algorithms allow surgeons to select the type of reconstruction according to tumour size, anatomical location, and the quality of the flap [19]. Our group was not homogeneous in terms of the type of reconstruction performed, with the majority receiving V-Y-type advancement flaps. This distribution does not allow for a reliable comparison between the different types of reconstruction. In the Rouzier study, the performance of a plasty was not mentioned. This makes the application of the nomogram on the realisation of reconstruction innovative.

Our study confirms that reconstruction after vulvar surgery is safe, as the observed recurrence probability is lower than the predicted recurrence probability in high-risk patients. Many studies have shown the impact of tumour-free margins on recurrence and survival in vulvar cancer, although the precise distance is still debated [4]. Joint management by gynaecological and plastic surgeons can improve the outcome of vulvar reconstructions, including larger margins and vulvectomies in larger tumours [20].

To our knowledge, the cohort of vulvar cancers described in the present study is the largest cohort comparing patients who underwent vulvar reconstruction with controls, in the literature. However, this study has several limitations. The follow-up period was set at 2 years because more than half of the local recurrences occur within 2 years of surgical resection [21]. The two-year local recurrence-free survival did not differ between patients with or without vulvar reconstruction.

Single-step vulvar reconstructions after vulvectomy was safe [9]. We found no difference in local recurrence-free survival between the reconstruction and control groups. We believe that vulvar reconstructions should be widely used. For this, the training and cooperation of surgeons is essential. Preoperative planning must be multidisciplinary, with a team-based approach between gynaecologic and plastic surgeons is necessary depending on the technical resources of centers treating vulvar cancers.

## 226 CONCLUSION

227           The nomogram predicting the risk of local recurrence at 2 years is accurate. Our study of vulvar  
228 reconstructions shows that vulvar reconstructions are safe for low- and intermediate-risk tumours. Vulvar  
229 reconstruction for large and advanced tumours reduce the risk of local recurrence.

230

231 **Table 1** : Baseline characteristics of the population.

Variable		Vulvar reconstruction		p-value
		Not performed (n=204)	Performed (n=49)	
Age	Median (mean)	72.5 (68.8)	71.0 (66.9)	0.46
	Range	60.0 - 81.0	55.0 - 80.0	
Tumour size (mm)	Median (mean)	25.0 (26.7)	32.0 (35.5)	0.04
	Range	14.5 - 35.0	13.5 - 55.0	
Nomogram score	Median (mean)	50.0 (55.3)	58.0 (68.0)	0.10
	Range	30.5 - 73.0	27.0 - 93.0	
Lymphadenectomy	n (%)	91 (44.6%)	23 (46.9%)	0.89
Nodal metastasis	n (%)	35 (17.2%)	12 (24.5%)	0.22
Margin	< 3 mm	111 (54.4%)	22 (44.9%)	0.30
	> 3mm	93 (45.6%)	27 (55.1%)	
Depth invasion (mm)	Median (mean)	4.0 (5.5)	6.0 (9.3)	0.02
	Range	1.0 - 8.0	1.5 - 12.0	
Lymphovascular space invasion	n (%)	37 (18.1%)	11 (22.4%)	0.48
Predicted local relapse probability (%)	Median (mean)	12.6 (18.8)	15.5 (25.4)	0.08
	Range	7.1 - 22.1	6.2 - 34.0	
Follow-up (month)	Median (mean)	21.6 (30.9)	23.7 (32.5)	0.69
	Range	7.2 - 44.4	9.5 - 50.1	

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Table 2: Local relapse probability: predicted and observed

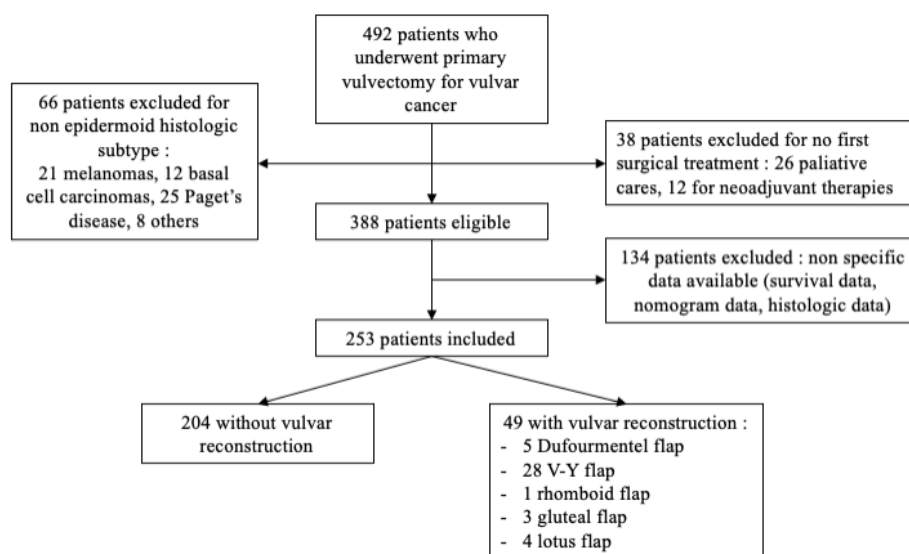
	Nomogram score	n	Predicted Local relapse probability	Observed Local relapse probability	Diff
Low risk	0 - 46	95	5.4 %	6.7 %	- 1.3
Middle risk	47 - 65	77	14.3 %	8.5%	5.8
High risk	66 - 247	82	42.5 %	31.2 %	11.3
Whole	0 - 247	254	20.1 %	15.7 %	4.4

Table 3: Local relapse probability: predicted and observed in patients with and without vulvar reconstruction

	Nomogram score	n	No vulvar reconstruction			Vulvar reconstruction			
			Predicted local relapse probability	Observed local relapse	Diff	n	Predicted local relapse probability	Observed local relapse	Diff
Low risk	0 : 46	79	5.5 %	5.2 %	0.3	16	5.1 %	14.3 %	- 9.2
Middle risk	47 : 65	66	14.4 %	7.3 %	7.1	10	13.6 %	16.7 %	- 3.1
High risk	66 : 247	59	41.6 %	36.4 %	5.2	23	44.6 %	20.0 %	24.6
Whole	0 :247	204	18.8 %	15.2 %	3.6	49	25.4 %	17.9%	7.5



243 **Figure 1:** Flowchart

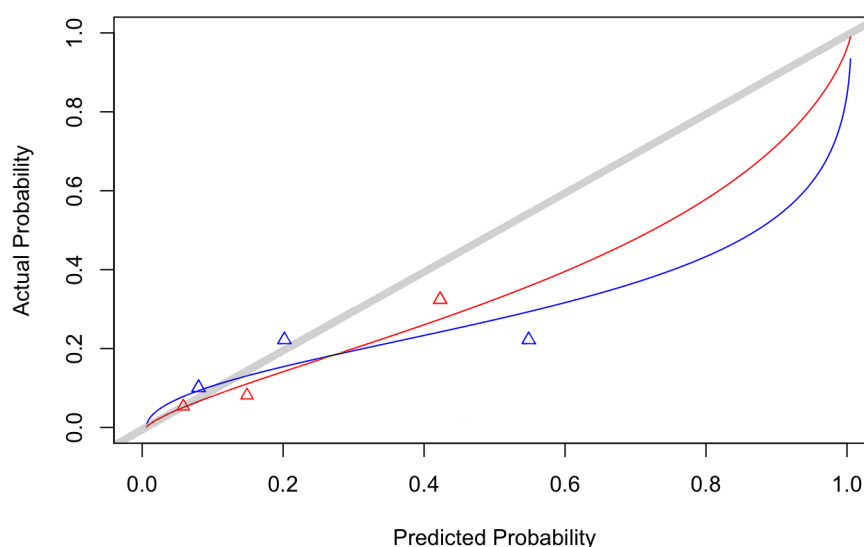


244

245 **Figure 2:** Correlation between predicted and estimated two-year overall survival according to the Rouzier in the

246 population with vulvar reconstruction (blue) and without vulvar reconstruction (red) with logistic calibration

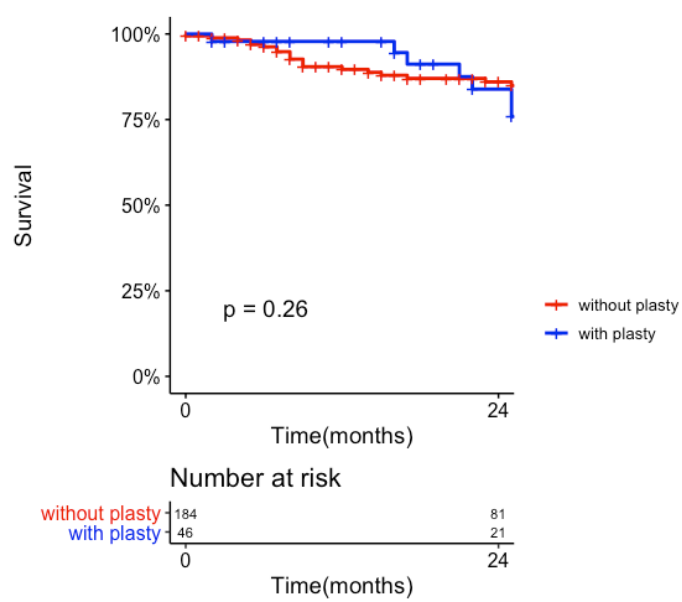
247 curves. *Colors should be used for this graphic*



248

249 **Figure 3:** Survival without local relapse (in red : patients without vulvar reconstruction, in blue : patients with

250 vulvar reconstruction)



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252

## 253 BIBLIOGRAPHY

- 254 [1] Alkatout I, Schubert M, Garbrecht N, Weigel MT, Jonat W, Mundhenke C, et al. Vulvar cancer:  
255 epidemiology, clinical presentation, and management options. *International Journal of Women's Health*  
256 2015;7:305–13. <https://doi.org/10.2147/IJWH.S68979>.
- 257 [2] Oonk MHM, Planchamp F, Baldwin P, Bidzinski M, Brännström M, Landoni F, et al. European Society  
258 of Gynaecological Oncology Guidelines for the Management of Patients With Vulvar Cancer. *Int J Gynecol*  
259 *Cancer* 2017;27:832–7. <https://doi.org/10.1097/IGC.0000000000000975>.
- 260 [3] Querleu D, Rychlik A, Guyon F, Floquet A, Planchamp F. [Management of the nodal disease in vulvar  
261 cancers. The ESGO guidelines]. *Bull Cancer* 2020;107:715–20. <https://doi.org/10.1016/j.bulcan.2019.06.010>.
- 262 [4] Raimond E, Delorme C, Ouldamer L, Carcopino X, Bendifallah S, Touboul C, et al. Surgical treatment  
263 of vulvar cancer: Impact of tumor-free margin distance on recurrence and survival. A multicentre cohort analysis  
264 from the francogyn study group. *European Journal of Surgical Oncology* 2019;45:2109–14.  
265 <https://doi.org/10.1016/j.ejso.2019.07.005>.
- 266 [5] Oonk MHM, Planchamp F, Baldwin P, Bidzinski M, Brännström M, Landoni F, et al. European Society  
267 of Gynaecological Oncology Guidelines for the Management of Patients With Vulvar Cancer. *Int J Gynecol*  
268 *Cancer* 2017;27:832–7. <https://doi.org/10.1097/IGC.0000000000000975>.
- 269 [6] Di Donato V, Bracchi C, Cigna E, Domenici L, Musella A, Giannini A, et al. Vulvo-vaginal  
270 reconstruction after radical excision for treatment of vulvar cancer: Evaluation of feasibility and morbidity of  
271 different surgical techniques. *Surgical Oncology* 2017;26:511–21. <https://doi.org/10.1016/j.suronc.2017.10.002>.
- 272 [7] Gentileschi S, Servillo M, Garganese G, Fragomeni S, De Bonis F, Scambia G, et al. Surgical therapy  
273 of vulvar cancer: how to choose the correct reconstruction? *J Gynecol Oncol* 2016;27:e60.  
274 <https://doi.org/10.3802/jgo.2016.27.e60>.
- 275 [8] Tock S, Wallet J, Belhadia M, Hudry D, Ghesquière L, Narducci F, et al. Outcomes of the use of  
276 different vulvar flaps for reconstruction during surgery for vulvar cancer. *European Journal of Surgical*  
277 *Oncology* 2019;45:1625–31. <https://doi.org/10.1016/j.ejso.2019.04.012>.
- 278 [9] Weikel W, Hofmann M, Steiner E, Knapstein PG, Koelbl H. Reconstructive surgery following resection  
279 of primary vulvar cancers. *Gynecologic Oncology* 2005;99:92–100.  
280 <https://doi.org/10.1016/j.ygyno.2005.05.031>.
- 281 [10] John HE, Jessop ZM, Di Candia M, Simcock J, Durrani AJ, Malata CM. An algorithmic approach to  
282 perineal reconstruction after cancer resection--experience from two international centers. *Ann Plast Surg*  
283 2013;71:96–102. <https://doi.org/10.1097/SAP.0b013e3182414485>.
- 284 [11] Devulapalli C, Wei AJ, DiBiagio J, Baez M, Baltodano P, Seal S, et al. Primary versus Flap Closure of  
285 Perineal Defects following Oncologic Resection: A Systematic Review and Meta-Analysis. *Plastic and*  
286 *Reconstructive Surgery* 2016;137:1602–13. <https://doi.org/10.1097/PRS.00000000000002107>.
- 287 [12] Giannini A, Di Donato V, D'Oria O, Schiavi MC, May J, Benedetti Panici P, et al. The V-Y gluteal fold  
288 advancement flap: Outcomes following radical surgery for vulvar malignancies. *Int J Gynaecol Obstet*  
289 2021;152:421–4. <https://doi.org/10.1002/ijgo.13430>.
- 290 [13] Hacker NF. Revised FIGO staging for carcinoma of the vulva. *Int J Gynaecol Obstet* 2009;105:105–6.  
291 <https://doi.org/10.1016/j.ijgo.2009.02.011>.
- 292 [14] Rouzier R, Preti M, Haddad B, Martin M, Micheletti L, Paniel B-J. Development and Validation of a  
293 Nomogram for Predicting Outcome of Patients With Vulvar Cancer 2006;107:6.
- 294 [15] Nomograms in oncology: more than meets the eye - The Lancet Oncology n.d.  
295 [https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(14\)71116-7/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(14)71116-7/fulltext) (accessed February 15,  
296 2021).
- 297 [16] Kim M-K, Kim JW, Lee J-M, Lee N-W, Cha M-S, Kim B-G, et al. Validation of a nomogram for  
298 predicting outcome of vulvar cancer patients, primarily treated by surgery, in Korean population: multicenter  
299 retrospective study through Korean Gynecologic Oncology Group (KGOG-1010). *J Gynecol Oncol*  
300 2008;19:191–4. <https://doi.org/10.3802/jgo.2008.19.3.191>.
- 301 [17] Pirot F, Chaltiel D, Ouldamer L, Touboul C, Raimond E, Carcopino X, et al. Patterns of first recurrence  
302 and outcomes in surgically treated women with vulvar cancer: results from FRANCOGYN study group. *J*  
303 *Gynecol Obstet Hum Reprod* 2020;49:101775. <https://doi.org/10.1016/j.jogoh.2020.101775>.
- 304 [18] FIGO staging for carcinoma of the vulva, cervix, and corpus uteri. *International Journal of Gynecology*  
305 *& Obstetrics* 2014;125:97–8. <https://doi.org/10.1016/j.ijgo.2014.02.003>.
- 306 [19] Salgarello M, Farallo E, Barone-Adesi L, Cervelli D, Scambia G, Salerno G, et al. Flap algorithm in  
307 vulvar reconstruction after radical, extensive vulvectomy. *Ann Plast Surg* 2005;54:184–90.  
308 <https://doi.org/10.1097/01.sap.0000141381.77762.07>.
- 309 [20] Aviki EM, Esselen KM, Barcia SM, Nucci MR, Horowitz NS, Feltmate CM, et al. Does plastic surgical  
310 consultation improve the outcome of patients undergoing radical vulvectomy for squamous cell carcinoma of the  
311 vulva? *Gynecol Oncol* 2015;137:60–5. <https://doi.org/10.1016/j.ygyno.2015.02.001>.

312 [21] Grootenhuis NC te, Zee AGJ van der, Doorn HC van, Velden J van der, Vergote I, Zanagnolo V, et al.  
313 Sentinel nodes in vulvar cancer: Long-term follow-up of the GRoningen INternational Study on Sentinel nodes  
314 in Vulvar cancer (GROINSS-V) I. Gynecologic Oncology 2016;140:8–14.  
315 <https://doi.org/10.1016/j.ygyno.2015.09.077>.  
316

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