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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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23

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25

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30

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

37 **ABSTRACT**

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

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

48 **Results:** We reviewed 254 patients, of whom 49 underwent immediate vulvar reconstruction. The predicted and
49 actual probability of two-year local relapse were 20.1% and 15.7%, respectively, with a concordance index of
50 0.75. In the low- and intermediate-risk groups, the difference between predicted and observed recurrence was less
51 than 10% in patients with or without vulvar reconstruction. For the high-risk group, the difference reached 25%
52 and observed recurrence probability was lower in patients who underwent vulvar plasty compared with those who
53 did not (20.0% vs. 36.2%, respectively). Local recurrence-free survival rates following vulvar reconstruction were
54 comparable at two years (82.1 % vs. 84.8 %, respectively, $p=0.26$).

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

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58

59

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

61

62 INTRODUCTION

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

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

73 These reconstructions include advancement flaps and transpositional flaps [6]. The main flaps used are
74 Dufourmental flap, V-Y, rhomboid, anterolateral thigh (ATL), gluteal thigh flap, lotus, deep inferior epigastric
75 artery perforator (DIEP), vertical rectus abdominis myocutaneous (VRAM) or Taylor flaps [7–9]. Selection of the
76 reconstruction type depends on several factors. An increase in lesion size is correlated with the use of advancement
77 gluteal flaps or DIEP flaps [10]. Depending on the tumour location, a V-Y technique may be chosen in the case of
78 a lateral lesion, or an ATL technique in the case of a vertical tumour extending from the pubis to the posterior part
79 of the labia majora. ATL is chosen if there is a need for inguinofemoral lymphadenectomy with butterfly resection
80 [7].

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

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

91 Shortly before the change in the FIGO classification of vulvar cancer in 2009 [13], Rouzier et al. developed
92 a two nomograms for predicting relapse-free survival [14]. Nomograms are statistical tools that enable users to
93 calculate the overall probability of a specific outcome, that is, recurrence from a disease, for an individual patient
94 [15]. Kim et al. validated in 2008 with 90 Korean patients, the first nomogram developed by Rouzier predicting
95 recurrence-free survival [16]. The second nomogram for predicting local recurrence after vulvectomy included
96 three variables : margin status, depth of invasion and lymphovascular involvement [17].

97 The aim of the present study was to to evaluate the impact of vulvar reconstruction on local recurrence
98 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.

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

124

125 *Calibration*

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

132

133 *Discrimination*

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

139

140 *Other statistical tests*

141 Categorical and numerical variables were analysed using the Chi-square t-test and the Student's t-test
142 respectively. Differences were considered significant at a level of $p < 0.05$. The two-year survival without local
143 relapse probability following vulvar reconstruction was calculated using the Kaplan–Meier analysis and compared
144 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/>).

147 RESULTS

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

153 Patient characteristics are listed in Table 1. Patients who underwent vulvar reconstruction had larger
154 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
155 more advanced FIGO stages ($p = 0.001$). On the basis of other variables, the two populations were not statistically
156 different.

157 *Discrimination*

158 The CI of the Rouzier nomogram for the entire population was 0.75 (+/- 0.07). The CIs in patients with
159 or without vulvar reconstruction were 0.66 (+/- 0.10) and 0.77 (+/- 0.10), respectively.

160 *Calibration*

161 Among the entire population, the predicted and the actual probabilities of two-year local relapse were
162 20.1% and 15.7%, respectively (Table 2). The performance of the nomogram appears to be accurate, accounting
163 for 4.4 % of the actual outcomes. The predicted and the actual probabilities depending on whether a vulvar
164 reconstruction was performed or not are shown in Table 3 and Figure 2.

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

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

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

178

179 DISCUSSION

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

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

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

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

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

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

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

224

225

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	

232

233

234 Table 2: Local relapse probability: predicted and observed

235

	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

236

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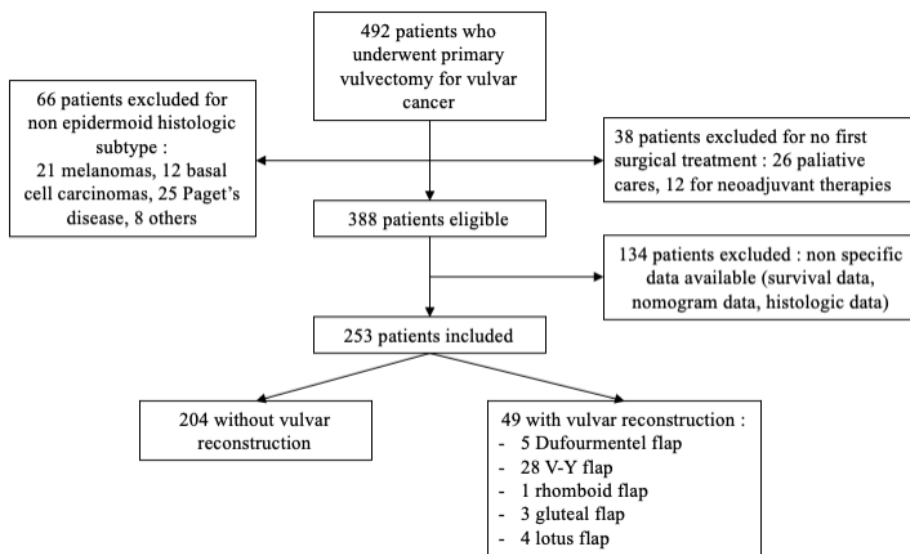
239 Table 3: Local relapse probability: predicted and observed in patients with and without vulvar reconstruction

240

	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

241

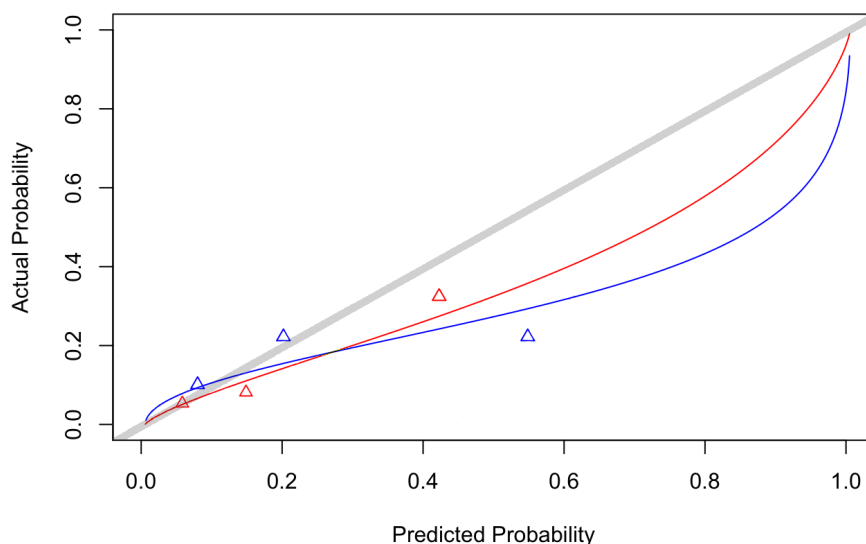
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243 Figure 1: Flowchart

244

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

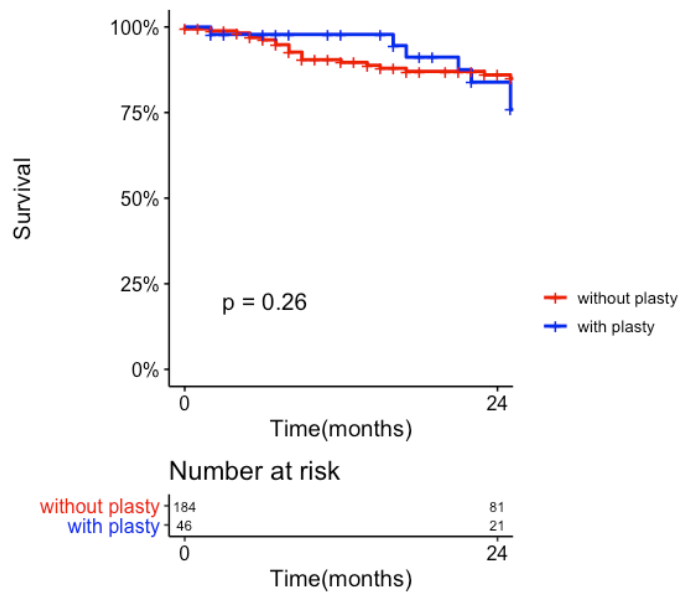
246 population with vulvar reconstruction (blue) and without vulvar reconstruction (red) with logistic calibration

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)



251

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.0000000000002107>.
- 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>.
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