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Anal versus Rectal Melanoma: Does Site of Origin Predict Outcome?

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Abstract

Background—Anatomic site is a predictive factor in subtypes of cutaneous and mucosal melanoma.

Objective—The aim of this study was to examine the clinical relevance of location of origin of anorectal melanoma as a prognostic factor.

Design—Using a prospectively maintained database, clinical characteristics, management, and outcomes were compared according to site of origin.

Settings, Patients, Interventions—A retrospective review was conducted of patients diagnosed with anorectal melanoma from 1994–2010. Tumors were defined as *anal*, *anorectal* or *rectal* melanoma according to their anatomic relationship to the dentate line.

Main Outcome Measures—Clinicopathologic factors were compared by Chi-square test. Time-to-event analysis was performed by Kaplan Meier analysis.

Results—Of the 96 patients included (41 anal, 32 anorectal, 23 rectal), patients with rectal and anorectal mucosal melanoma had advanced primary tumors (median Breslow thickness 12mm and 8mm respectively, p =0.002), while anal lesions could be found at earlier depths (median thickness 6.5mm). Patients with anal tumors more commonly underwent transanal excision (p <0.02) and sentinel lymph node biopsy (p=0.004) versus anorectal and rectal tumors. Patterns of recurrence were also distinct; nearly two-thirds of anorectal and rectal tumors recurred systemically, while anal melanoma more often recurred within the lymph nodes first (63%; p <0.02). Recurrence occurred in 24 (59%) patients with anal tumors, 23 (72%) anorectal tumors, and 16 (70%) rectal tumors. Median OS was 22 months for anal melanoma, 28 months for anorectal melanoma and 27 months for rectal melanoma. Recurrence and survival were not statistically different between the groups.

Limitations—This study is limited by small sample size and its retrospective nature.

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Conclusions—This study represents the only series describing the outcomes of anorectal melanoma by anatomic location. Lesions at or proximal to the dentate line present with more advanced disease, possibly related to a delay in diagnosis. Lesions distal to the dentate line more commonly recur within lymph nodes, which may represent differences in nodal drainage. Irrespective of location, long-term prognosis remains poor for all cases of anorectal melanoma.

Keywords

Anorectal melanoma; Mucosal melanoma; Rectal melanoma

Introduction

Anorectal mucosal melanoma (ARMM), a subtype of mucosal melanoma, remains a lethal disease with a dismal prognosis. Five-year overall survival is estimated at 20–22% with a disease-free survival of 16–17%.[1–8] ARMM accounts for between 1–2% of lower gastrointestinal malignant tumors and 0.4–1.6% of all melanomas.[2–3,9] Although the reasons remain unclear, the incidence of ARMM is thought to be increasing.[1,4,10] After mucosal melanoma of the head and neck and female genital tract, melanoma of the anorectum is the third most common mucosal site of involvement.[1] Diagnosis is often delayed because these tumors are amelanotic in 20–25% of cases, and are often confused with benign diseases such as hemorroids.[3–4,6,11–12] Sixty-five percent of anorectal melanomas are located within the anal canal or anal verge; however, in 35% of cases, disease is also found in the distal rectum.[5,10] Yap and Neery categorized anorectal melanoma by location, defining *anal* as lesions situated below the dentate line, *rectal* as masses located above the dentate line, and *anorectal* if the tumor was located around the dentate line.[9]

In this disease, recurrence is most often distant and fatal. Perineural invasion in the primary tumor has been suggested to be a predictor of poor outcome.[7] Unlike in cutaneous melanoma, lymph node status has not been linked to recurrence or survival outcome in ARMM.[6–7] Despite use of multiple treatment modalities, including surgery, radiotherapy and systemic therapy, prognosis and overall survival remains bleak for ARMM. Commonly, the stage at diagnosis is advanced, with regional and systemic metastases rates as high as 20% and 40% respectively.[1–5,10,13] Neither abdominopelvic resection (APR) nor wide local excision (WLE) has clearly shown a survival benefit.[2,7,9,12–14] Although WLE may be associated with a higher rate of local recurrence, there is a higher morbidity associated with APR. Multiple investigators now advocate for the use of WLE, reserving APR only for tumors not amenable to local excision or for palliative treatment of large, obstructing lesions.[2,7,9,12,14] There may be some role for radiation as palliative therapy in locally advanced, recurrent, or metastatic disease, but this too has not impacted survival.

In both cutaneous and mucosal melanoma, site of origin predicts prognosis. In several studies to date, it has been shown that patients with scalp or neck melanoma have a lower 5-year survival than other anatomic sites.[15–16] Analysis of the SEER database demonstrated that cutaneous melanomas arising from the scalp and neck, even when adjusted for age, sex, thickness, and ulceration, had almost 2 times the rate of melanoma specific death (HR 1.84, 95% CI 1.62–2.10) than melanomas arising from the extremity.[16] In both mucosal melanoma of the head and neck and of the female genital tract, primary melanoma site also correlates with survival.[17–20] For example, vulvar mucosal melanomas have a superior 5-year overall survival (8–55%) compared to that of vaginal melanoma (5–25%).[17,19–20] Although rich lymphatic and vascular drainage, diagnostic difficulty, cosmetic concerns, and molecular differences have been hypothesized to play a role, the exact reason for these poorer survival outcomes by anatomic site still remains unclear.

No study to date has examined if survival differences exist in terms of clinical behavior in ARMM by site. This study investigates the clinical relevance of location of origin of ARMM as a prognostic factor.

Methods

Data were obtained from a prospectively maintained database at Memorial Sloan-Kettering Cancer Center (MSKCC). The institutional review board approved the utilization and analysis of these data. Patients with incomplete records (n=1), metastases at diagnosis (n=17), or who did not undergo primary tumor resection (n=6) were excluded. Tumors were defined as *anal* if they were distal to the dentate line and *rectal* if they were proximal to it. Lesions traversing or arising from the dentate line were called *anorectal*. All rectal lesions (n=32) were classified as proximal to, and not including, the dentate line. If location could not be definitively identified, pathologic results documenting type of mucosa – either columnar or squamous – were used to ascertain if the lesion was anorectal or anal in origin (Table 1). Additionally, lymph node basins were used to help determine anatomic site – patients with inguinal adenopathy were classified as anal while those with mesenteric lymphadenopathy were rectal or anorectal in origin. Of our entire series, 85% of ARMM (n=82) tumors were classified by the anatomic location criteria defined in Table 1. Fourteen patients (15%) were classified according to the secondary characteristics of histology (n=9) and lymph node drainage patterns (n=5) listed in Table 1. Half of these were anal (n=7) and half were anorectal (n=7).

Patients who underwent transanal excision or abdominoperineal resection but were referred to MSKCC for later management were included in this database. These patients underwent pathologic review at MSKCC. Margin status was documented in all but five patients (4 anal and 1 anorectal). Recurrences were identified from clinical follow-up visits and radiographic studies. They were categorized as local, nodal, or systemic. Local recurrences were defined as recurrences at the site of resection, nodal recurrences were defined as recurrences in the draining nodal basin from the primary lesion, and systemic recurrences included recurrences in all other locations. Overall survival was defined as the time from the date of pathologic diagnosis to the date of death or last follow-up; recurrence-free survival was defined as time from the date of diagnosis to the date of relapse.

Clinicopathologic factors were compared by χ^2-test. Survival distributions were estimated by Kaplan-Meier methodology and comparisons made by the log rank test. All analyses were performed by SPSS software (Version 19). A P value of <0.05 was considered statistically significant.

Results

The prospective melanoma database identified 120 patients diagnosed with anorectal melanoma from 1994 to 2010. After exclusion by the previously described criteria, 96 patients remained, of which 41 were anal, 32 were anorectal, and 23 were rectal.

Patient Demographics and Primary Tumor Characteristics

Clinical and pathologic data describing patients in the anal, anorectal, and rectal groups are listed in Table 2. There was no difference between these three groups in median age and gender; all three anatomic sites demonstrated a female predominance. All patients diagnosed with anal melanoma in this series were Caucasian, while anorectal and rectal melanoma were found in African American, Asian and Caucasian patients. Although no staging system has been shown to reliably divide cases of ARMM into low- or high-risk groups, there is a trend toward significance of anal lesions being discovered at an earlier stage using the 2010

American Joint Committee on Cancer Cutaneous Melanoma staging system[21] than anorectal or rectal lesions ($P = 0.056$). Approximately 37% of anal lesions were diagnosed as Stage IIB or less versus 22% of anorectal and 26% of rectal lesions. The majority of tumors of anal, anorectal and rectal origin were advanced in thickness at diagnosis. However, anal melanoma tumors presented at a lesser median depth when compared with anorectal and rectal melanomas ($P = 0.002$). A significant percentage (37%) of anal lesions were diagnosed ≤4.00 mm, 10% of which were ≤2.00 mm, while only 6% of anorectal lesions and 9% of rectal tumors were found with a thickness of ≤4.00 mm and none of these tumors had a depth of ≤2.00 mm. Multifocal disease was found in 14% of anal lesions, 22% of anorectal tumors, and 17% of rectal lesions; this difference was not significant. A high percentage of anal (68%), anorectal (62.5%), and rectal (48%) lesions were ulcerated or had an unknown ulceration status, but there were no significant differences between these groups. When documented, anal lesions had a higher prevalence of lymphovascular invasion (LVI) (22%) and perineural invasion (PNI) (15%) relative to anorectal (19% LVI, 6% PNI) or rectal (13% LVI, 4% PNI) tumors. However, there was no significant difference in LVI or PNI status between primary site. When documented on pathologic inspection, there was a mitotic index ≥1 identified in 39% of anal lesions compared with 19% of anorectal and 17% of rectal tumors. This difference was not statistically significant.

Surgical Management

All patients underwent surgery in our series. All patients but one (98%) with anal melanoma underwent transanal excision compared with 78% of anorectal tumors and 70% of rectal tumors ($P < 0.02$) (Table 3). The abdominoperineal resection rate for anorectal melanoma was 22% and for rectal melanoma was 26%. One patient with a high rectal melanoma 10 cm from the anal verge underwent a low anterior resection (LAR).

Margin positivity was similar between groups. Anal melanoma tumors had positive margins in 29% of patients, anorectal in 22% and rectal in 22%. Upon closer analysis of margin positivity, no patients had oral or proximal margins positive alone. For anal tumors with positive margins (n=12), 7 (58%) had deep or vertical margins positive, 2 (17%) had anal margins positive and 2 (17%) had all margins positive. Specific margins were not stated for one (8%) patient. For anorectal patients with positive margins (n=7), 1 (14%) was positive at the deep margins, 4 (57%) had all margins positive and 2 (29%) patients' margin status was unspecified. No patients had anal or distal margins positive. Lastly, of the rectal patients with positive margins (n=5), 2 patients (40%) had deep margins positive, one (20%) had anal margins positive and one (20%) had all margins positive. One patient's margin location (20%) was unspecified. Due to the small number of patients in each group, there was no statistical difference in margin location between anatomic site. Additionally, due to the small sample size, it is difficult to draw definitive conclusions from this data. Deep margins were most often positive in the anal and rectal groups, while all margins were most often positive in the anorectal groups. Many of the patients with positive margins underwent re-excision to gain local control of this disease. In agreement with previous studies, there was no difference in survival between patients who underwent curative WLE or curative APR, in which all known tumor was removed.[2,7,12–14] Where WLE is unable to remove all tumor, APR should be performed. In our patient population, when local control could not be achieved through WLE, APR was offered.

Likely due to the accessibility of anal lesions, sentinel lymph node biopsy (SLNB) was more commonly performed in patients with anal melanoma (27%) compared with anorectal tumors (6%) and rectal tumors (0%; $P = 0.004$). Of patients who underwent SLNB, 64% of SLNB in anal tumors and 100% of SLNB in anorectal tumors were positive for melanoma. Of the seven anal melanoma patients with a positive SLNB, three (43%) underwent a completion lymph node dissection (CLND), while all of the anorectal melanoma patients

underwent a CLND. Few patients underwent adjuvant radiation; there was no difference by anatomic site. Adjuvant treatment, including different chemotherapeutic regimens and types of immunotherapy, was administered to patients at similar rates by site of origin. Adjuvant therapy did not demonstrate any survival benefit for the entire series and when broken down by cohort.

Patterns of Recurrence and Survival

Median length of follow-up was 22 months for our patient series. Median follow-up for each cohort was 20 months for anal, and 24 months for anorectal and rectal tumors. Of the 12 patients lost to follow-up, 7 (17%) were anal, 4 (13%) were anorectal, and 1 (4%) was rectal in location. The distribution of recurrence by site is depicted in Table 4. Anal primary lesions metastasized to lymph nodes, either alone or in combination with systemic disease, initially ($P = 0.016$) and more often overall ($P<0.001$) compared to that of anorectal or rectal melanoma. Those anorectal and rectal tumors that recurred regionally frequently recurred in the inguinal lymph node basin. However, eventually the disease, regardless of site of origin, becomes systemic with 75% of anal lesions, 78% of anorectal lesions, and 63% of rectal tumors eventually recurring systemically. Recurrence free survival (RFS) was not significantly different by site of origin (Figure 1). The median time to recurrence was 23 months for anal, 28 months for anorectal and 27 months for rectal tumors. Median overall survival (OS) was not different by site; median OS for anal tumors was 22 months, 28 months for anorectal and 27 months for rectal tumors. Despite being diagnosed at an earlier depth, 5 year OS was shorter for anal tumors (11%) than anorectal (24%) and rectal tumors (18%), although this difference was not significant (Figure 2).

Discussion

To our knowledge, this is the first paper examining the role of anatomic site of ARMM on prognosis. Clinical differences between primary site of disease in this series do exist. In our study, anal melanoma was more common in the Caucasian population. While it is interesting to note that racial differences exist by anatomic site, due to the fact that patient numbers are small, it is difficult to draw many conclusions from this finding. It is known that although the absolute incidence of mucosal melanoma is greatest in Caucasians, the proportion of anorectal mucosal melanoma in African Americans, Hispanics, and Asians, similar to other types of mucosal melanoma, is greater than that observed in Caucasians.[1,17] Additionally, patterns of racial distribution may be reflective of an institutional referral bias. Differences in Breslow thickness can be seen between primary tumor sites and thinner lesions are observed in the anal melanoma group. Anal melanoma tumors are also diagnosed at earlier stages. This may be due to the fact that some anal lesions are identified by visual inspection of the anal verge, whereas anorectal and rectal tumors are often diagnosed only when patients are symptomatic from disease. Despite some anal tumors being thinner at the time of diagnosis, diagnosis at an earlier pathologic stage does not significantly alter survival outcomes when compared with anorectal or rectal primary sites.

Patterns of surgical management differ by primary location. While the majority of patients with anal melanoma underwent transanal excision, in part owing to the facts that no surgical operation has shown a survival benefit and transanal excision has a lower morbidity than APR, patients with anorectal or rectal melanoma were more likely to undergo APR. APR is often reserved for cases not amenable to local excision or for palliation. Due to the fact that ARMM can often be multifocal and amelanotic in up to 20–25% of cases, achieving curative resection by WLE can be challenging.[5] Additionally, the radial growth phase component of a melanoma may extend beyond the visible tumor. These factors likely also contributed to our margin positivity rate.

Sentinel lymph node biopsy was performed in more anal melanoma patients, perhaps due to its distal location and technical feasibility compared to more proximal tumors. Of note, sentinel lymph node biopsy had been performed on mucosal melanoma tumors as part of a prior institutional protocol. As lymph node status has not proven to be prognostic in anorectal melanoma, and given that no therapy has demonstrated an improvement in survival, there was no standardization of management based upon the results of these biopsies.

There was no improvement in survival for those patients who received adjuvant systemic or radiation therapy in our study. As no level 1 or 2 evidence exists to direct the physician in the management of ARMM in the adjuvant setting, the standard of care is observation. If a patient develops systemic metastases or the risk of systemic metastases is considered high, adjuvant therapy is administered or patients are enrolled in clinical trials at our institution in which they receive it.

Patterns of recurrence differed between these groups. Anal melanomas more frequently recurred in the lymph nodes initially, either alone or in combination with distant disease, compared to more proximal tumors. This recurrence pattern may be a reflection of initial surgical intervention; patients with anorectal or rectal melanoma undergoing APR have their draining lymph node basin removed in the mesorectum at initial operation, whereas those with anal lesions, who mostly underwent transanal excision, had their nodal basin left intact. This pattern may also reflect a difference in the ability to detect lymph node metastases by anatomic location. Inguinal adenopathy is more readily detected on physical examination, whereas mesorectal lymph node metastases require radiographic imaging for discovery. Therefore, inguinal adenopathy may be more easily recognized and diagnosed for anal lesions, while mesorectal lymphadenopathy may not be apparent until cross-sectional imaging is performed to assess for systemic disease.

Despite these differences in tumor thickness, surgical resection, and recurrence patterns, overall survival is not significantly different among ARMM of distinct primary sites. These findings reinforce the need for continued research in this disease. Because of the uniformly poor prognosis of ARMM, efforts centering on combining surgical excision with systemic therapy as first-line treatment are ongoing and effective systemic therapy is required for the successful treatment of this disease.

Recently, significant advances have been made in the field of both immunotherapy and targeted therapy in the treatment of cutaneous metastatic melanoma. Ipilimumab, a new human monoclonal antibody that targets cytotoxic T-lymphocyte antigen 4 (CTLA-4), was the first agent to show improvement in overall survival in patients with metastatic melanoma in a phase III, randomized, control trial.[22–23] Additionally, vemurafenib, an inhibitor of mutant BRAF, has demonstrated a significant impact on both progression-free and overall survival in a phase III trial in patients with melanoma containing the V600E BRAF mutation. Lastly, various inhibitors of KIT, such as imatinib mesylate, sunitinib, nilotinib and dasatinib, have also demonstrated activity in a subset of patients with metastatic melanoma harboring KIT alterations.[24] It is known that certain mucosal melanomas, including ARMM, contain these BRAF and KIT mutations at varying rates according to anatomic site.[25–26] Thus, it can be hypothesized that some ARMM may represent better targets for drugs such as ipilimumab which function through immune system modulation, while those which demonstrate a specific actionable mutation may respond more optimally to targeted inhibitors, such as imatinib and vemurafenib. Currently there is no data available on these new effective immune therapeutic agents and targeted drugs in the treatment of ARMM specifically. However, new trials utilizing these agents, including Ipilimumab, BRAF- and KIT-inhibitors, for the treatment of all mucosal melanomas, are underway.

There are a few limitations of our study. For the purpose of this study, we excluded patients with distant metastases who were not considered for curative resection. In doing so, our data represent outcomes for patients considered good surgical risk, most of whom were referred to our institution for surgical treatment and therefore contain a certain selection bias. Because anorectal melanoma is a rare disease, our total population is relatively small with our anatomic subsets including a limited number of patients, increasing the possibility of type II error. Also, given that some patients were lost to follow-up, there were limitations in our ability to accurately assess dates of recurrence and, therefore, recurrence free survival. Lastly, when defining primary anatomic location not all anal tumors could be definitively confirmed as mucosal melanomas. Two anal tumors may have been located on perianal skin. However, description of these lesions as documented by physical examination was consistent with anal verge melanoma. Therefore, we have chosen to include these 2 anal patients due to the likelihood that these tumors were mucosal melanomas.

This study represents the only series describing the outcomes of anorectal melanoma by anatomic location of the primary lesion. Lesions at or proximal to the dentate line present with more advanced disease, possibly related to a delay in diagnosis. Lesions distal to the dentate line more commonly recur within lymph nodes, which may represent differences in nodal drainage. Irrespective of location, long-term prognosis remains poor for all cases of anorectal mucosal melanoma; however, progress in the development of systemic therapy for this disease holds the promise for improved outcomes in the future.

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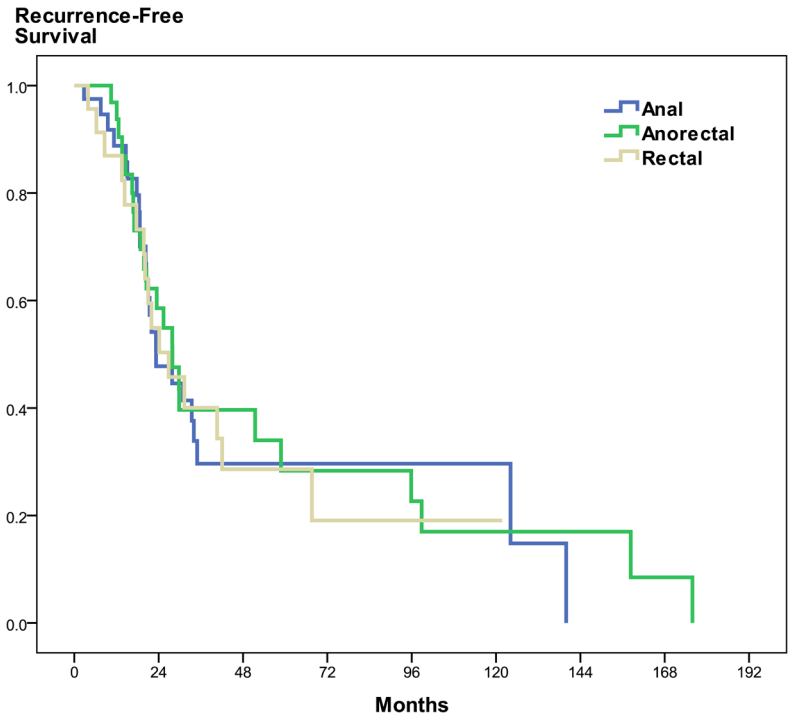

Figure 1.
Recurrence-free survival anal (n = 41) versus anorectal (n = 32) versus rectal (n = 23). Median recurrence-free survival was 23 months, 28 months, and 27 months respectively (P = 0.887).

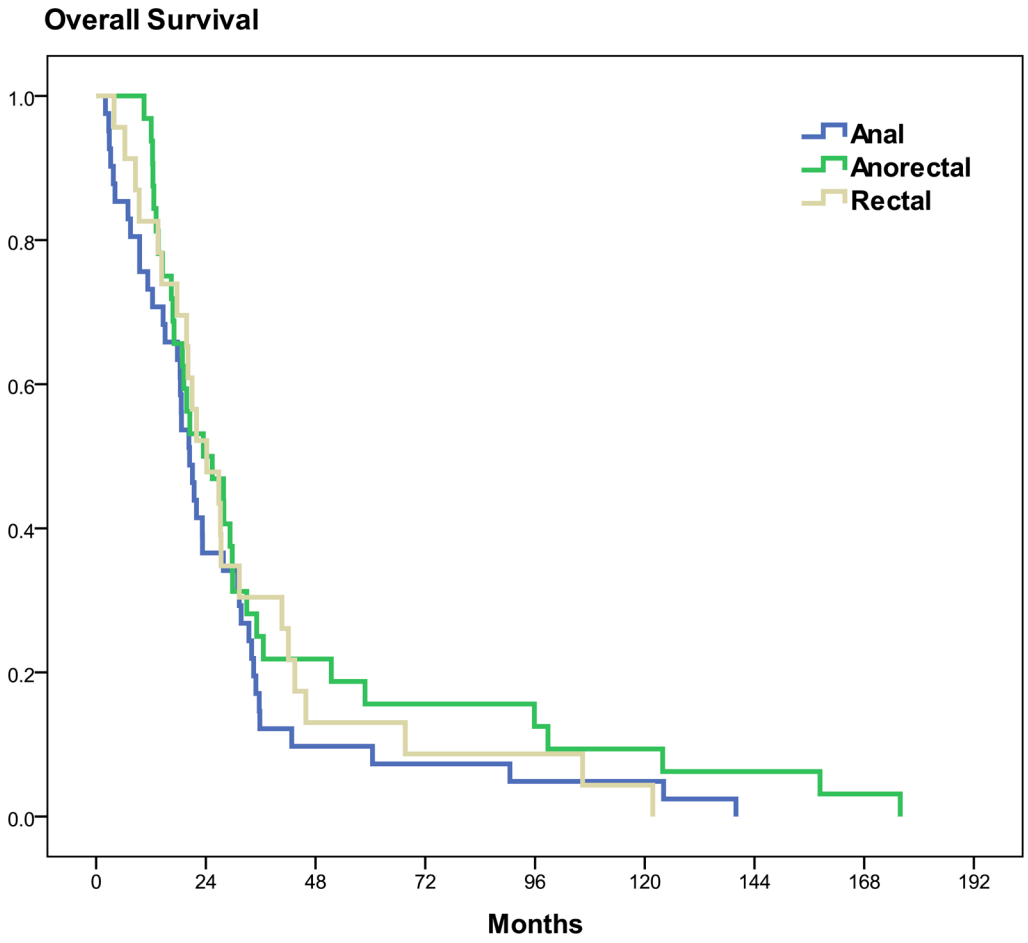

Figure 2.
Overall survival anal ($n = 41$) versus anorectal ($n = 32$) versus rectal ($n = 23$). Median overall survival was 22 months, 28 months, and 27 months respectively ($P = 0.696$).

Table 1

Determination of Anatomic Site of Origin

If Anatomic Location Documented:
• **Anal** was defined as **distal** to the dentate line • **Anorectal** was defined as **at** or **traversing** the dentate line • **Rectal** was defined as **proximal** to the dentate line
If Exact Anatomic Location Uncertain:
• Histology: – **Anal melanoma** was identified by **squamous mucosa** – **Anorectal** or **Rectal melanoma** was identified by **colonic mucosa** • Lymphatic Drainage: – **Anal melanoma** metastasized to **inguinal** lymph nodes – **Anorectal** or **Rectal melanoma** metastasized to **mesenteric** lymph nodes

TABLE 2

Patient Demographics and Primary Tumor Characteristics

Characteristic	Anal *n* = 41	Anorectal *n* = 32	Rectal *n* = 23	*P* value
Median Age (range)	61 (42–85)	65 (36–89)	67 (38–82)	NS
Sex, *n* (%)				
Male	16 (39%)	12 (37%)	5 (22%)	NS
Female	25 (61%)	20 (63%)	18 (78%)	
Race, *n* (%)				
Asian	0 (0%)	3 (9%)	5 (22%)	<0.03
African American	0 (0%)	1 (3%)	0 (0%)	
Caucasian	41 (100%)	28 (88%)	18 (78%)	
AJCC Stage at Diagnosis, *n* (%)				
Stage IA	2 (5%)	0 (0%)	0 (0%)	0.056
Stage IB	0 (0%)	0 (0%)	0 (0%)	
Stage IIA	5 (12%)	1 (3%)	2 (9%)	
Stage IIB	8 (20%)	6 (19%)	4 (17%)	
Stage IIC	12 (29%)	13 (41%)	6 (27%)	
Stage IIIA	1 (2%)	0 (0%)	3 (13%)	
Stage IIIB	8 (20%)	2 (6%)	1 (4%)	
Stage IIIC	5 (12%)	7 (22%)	3 (13%)	
Unreported	0 (0%)	3 (9%)	4 (17%)	
Breslow Thickness (mm), Median (range)	6.5 (0.4–17.0)	12.0 (2.1–55.0)	8.0 (3.0–18.0)	0.002
≤1.00, *n* (%)	2 (5%)	0 (0%)	0 (0%)	
1.01–2.00	2 (5%)	0 (0%)	0 (0%)	
2.01–4.00	11 (27%)	2 (6%)	2 (9%)	
>4.00	25 (61%)	25 (78%)	13 (56%)	
Unknown/Undocumented	1 (2%)	5 (16%)	8 (35%)	
Multifocality, *n* (%)				
No	31 (76%)	22 (69%)	14 (61%)	NS
Yes	6 (14%)	7 (22%)	4 (17%)	
Unknown/Undocumented	4 (10%)	3 (9%)	5 (22%)	
Ulceration, *n* (%)				
No	5 (12%)	0 (0%)	3 (13%)	NS
Yes	28 (68%)	20 (62.5%)	11 (48%)	
Unknown/Undocumented	8 (20%)	12 (37.5%)	9 (39%)	
Lymphovascular Invasion (LVI), *n* (%)				
No	7 (17%)	6 (19%)	4 (17%)	NS
Yes	9 (22%)	6 (19%)	3 (13%)	
Unknown/Undocumented	25 (61%)	20 (62%)	16 (70%)	
Perineural Invasion (PNI), *n* (%)				
No	10 (24%)	5 (16%)	7 (31%)	NS
Yes	6 (15%)	2 (6%)	1 (4%)	

Characteristic	Anal *n* = 41	Anorectal *n* = 32	Rectal *n* = 23	*P* value
Unknown/Undocumented	25 (61%)	25 (78%)	15 (65%)	
Mitoses, *n* (%)				
No	1 (2%)	0 (0%)	0 (0%)	NS
Yes	16 (39%)	6 (19%)	4 (17%)	
Unknown/Undocumented	24 (59%)	26 (81%)	19 (83%)	

* IQR = Interquartile Range

TABLE 3

Surgical Data by Site of Origin

Characteristic	Anal *n* = 41	Anorectal *n* = 32	Rectal *n* = 23	*P* value
Surgery, *n* (%)				
Transanal Excision	40 (98%)	25 (78%)	16 (70%)	<0.02
LAR	0 (0%)	0 (0%)	1 (4%)	
APR	1 (2%)	7 (22%)	6 (26%)	
Margins, *n* (%)				
Negative	25 (61%)	24 (75%)	18 (78%)	NS
Positive	12 (29%)	7 (22%)	5 (22%)	
Unknown/Undocumented	4 (10%)	1 (3%)	0 (0%)	
Sentinel Lymph Node Biopsy, *n* (%)				
No	30 (73%)	30 (94%)	23 (100%)	0.004
Yes	11 (27%)	2 (6%)	0 (0%)	
% Positive SLN Biopsy	7/11 (64%)	2/2 (100%)	N/A	
% Completion LND for Positive SLN	3/7 (43%)	2/2 (100%)	N/A	
Adjuvant Radiation, *n* (%)				
No	39 (95%)	30 (94%)	23 (100%)	NS
Yes	3 (5%)	2 (6%)	0 (0%)	
Adjuvant Treatment, *n* (%)				
No	32 (78%)	27 (84%)	18 (78%)	NS
Yes	9 (22%)	5 (16%)	5 (22%)	

TABLE 4

Patterns of Recurrence and Survival

Characteristic	Anal *n* = 41	Anorectal *n* = 32	Rectal *n* = 23	*P* value
Recurrence, *n* (%)	24 (59%)	23 (72%)	16 (70%)	NS
Site of First Recurrence, *n* (%)	(N=24)	(N=23)	(N=16)	
Local	5 (21%)	3 (13%)	5 (32%)	NS
Nodal	8 (33%)	2 (9%)	0 (0%)	
Systemic	4 (17%)	10 (43%)	8 (50%)	
Local and Nodal	3 (12.5%)	3 (13%)	1 (6%)	
Local and Systemic	0 (0%)	2 (9%)	0 (0%)	
Nodal and Systemic	3 (12.5%)	2 (9%)	1 (6%)	
Local, Nodal, and Systemic	1 (4%)	1 (4%)	1 (6%)	
Site of First Recurrence, *n* (%)				<0.02
First Local (Alone or LocalPlus Other Sites)	9 (38%)	9 (39%)	7 (44%)	
First Nodal (Alone or Nodal Plus Other Sites)	15 (63%)	8 (35%)	3 (19%)	
First Systemic (Alone or Systemic Plus Other Sites)	8 (33%)	15 (65%)	10 (63%)	
Site of Overall Recurrence, *n* (%)				
Local	11 (46%)	12 (52%)	7 (44%)	<0.001
Regional	19 (80%)	9 (39%)	3 (19%)	
Systemic	18 (75%)	18 (78%)	10 (63%)	
Recurrence Free Survival (months)				
Median (IQR)	23(19–124)	28 (17–96)	27 (18–68)	NS
Overall Survival (months)				
Median (IQR)	22 (18–36)	28 (16–59)	27 (20–43)	NS
5 year OS	11%	24%	18%	
Length of Follow-Up (months)				
Median (IQR)	20 (10–34)	24 (15–36)	24 (14–42)	NS

Interquartile Range (IQR)