Published in final edited form as:
Ann Surg Oncol. 2010 January ; 17(1): 40–44. doi:10.1245/s10434-009-0705-0.

Practice Patterns and Outcomes for Anorectal Melanoma in the United States; Is more extensive surgical resection beneficial in all patients?

Douglas M. Iddings, DO[1], **Ani J. Fleisig, MD**[2,3], **Steven L. Chen, MD**[4], **Mark B. Faries, MD**[2,3], and **Donald L. Morton, MD**[2,3]

[1] Department of Surgical Oncology, Michigan State University, East Lansing, MI

[2] Department of Surgical Oncology in conjunction with the Roy E. Coats Research Laboratories of the John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA

[3] Department of Biostatistics Research in conjunction with the Roy E. Coats Research Laboratories of the John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA

[4] Department of Surgical Oncology, University of California, Davis, CA

Abstract

Introduction—Historically, the treatment of anorectal melanoma has been abdominoperineal resection (APR) but more recently local resection alone. Although treatment at melanoma centers has become less aggressive in the modern era, the adoption of this approach and related outcomes across the United States is unknown.

Methods—The Surveillance, Epidemiology and End Results (SEER) database was queried to identify patients treated for anorectal melanoma (1973-2003). Treatment patterns and survival were studied. Frequency of treatment was compared using the chi-square test; survival was calculated using the Kaplan-Meier method.

Results—The 183 patients identified from the SEER database had a median age of 68 years and a female-to-male ratio of 2.2:1. Of the 143 patients whose data were included, 51 underwent APR and 92 underwent trans-anal excision (TAE). Despite similar pathologic characteristics, median survival was similar in both groups: 16 months for APR and 18 months for TAE (p=ns). Five-year survival also was similar in both groups: 16.8% for APR and 19.3% for TAE (p = ns). The rate of APR was 27.0% between 1973 and 1996, as compared with 43.2% between 1997 and 2003 (p = ns).

Conclusion—This study, the largest series to analyze widespread practice patterns and outcomes for anorectal melanoma in the United States, did not reveal a survival difference comparing TAE to APR. Moreover, the study did not reveal a trend toward less aggressive surgical resection. Since the extent of surgical intervention did not correlate with survival or extent of primary tumor, APR should be reserved for selected patients in whom TAE is not technically feasible.

Keywords

Anorectal melanoma; Sentinel node biopsy; Trans-anal excision; Surveillance Epidemiology and End Results (SEER); APR

Correspondence to Douglas M Iddings D.O., AGOSA; Advanced General and Oncological Surgical Associates. 3500 Calkins Road; Suite A, Flint, MI 48532. Phone (810) 210-6397. Fax (810) 230-9607, diddings181@yahoo.com.

Presented in part at the American Society of Clinical Oncology 43rd Annual Meeting, June 1-5, 2007, Chicago, Illinois.

INTRODUCTION

Anorectal melanoma is a rare mucosal melanoma with a particularly aggressive biology compared with cutaneous melanoma of equal stage. Because of their location, anorectal melanomas often go unnoticed until symptoms occur; the majority of patients present with rectal bleeding and/or anal discomfort, clinically consistent with hemorrhoids. Less often patients present with palpable inguinal adenopathy, other regional adenopathy or synchronous distant metastasis. Despite the difficulty of early diagnosis, when the diagnosis is made most patients appear to have potentially curable local disease with or without regional lymphatic involvement. Historically, this disease has been treated with abdominoperineal resection (APR) and more recently with trans-anal excision (TAE) alone. Regardless of the extent of surgery, the local, regional and distant failures remain high; overall 5-year survival is 10% – 20% (1,2).

Several studies have investigated the extent of surgery needed to optimally treat this disease. Early reports were limited to small case series and few meaningful conclusions could be made; treatment with extensive surgical resection (i.e. APR) was common and reasonable considering there was no effective medical treatment (3,4). However, as early as 1982, a large case review series concluded that there was no difference in survival if patients were treated for curative intent with either TAE or APR (5). In their 1990 report of 26 patients, Ross et al found that patients treated with TAE did have a higher local recurrence rate but such recurrences often occurred concomitantly with distant metastasis (6). Since the median survival was independent of the extent of surgery, they recommended local excision. In 1995, a review of a single institution's 64-year experience with 74 cases concluded that more aggressive surgery (i.e., APR) resulted in better disease control (1). In that study, 9 of the 10 long-term survivors were treated with APR.

Since then multiple reports have advocated a more conservative treatment plan due to the consistently poor long-term outcome regardless of the extent of surgery (7–14). However, patients treated with a more conservative approach (i.e. TAE alone) often suffered nodal relapse prior to the development of distant disease, thus requiring delayed/salvage inguinal lymphadenectomy. Single-institution studies have neither been unable to identify a survival benefit in the patients treated with different surgical approaches nor within the group treated with nodal observation (some of whom developed palpable lymphatic disease). Therefore, even the prognostic value of nodal metastases has been questioned (13). Due to the lack of evidence supporting the efficacy of APR and the related morbidity of the procedure, investigators for > 15 years at tertiary cancer centers have been recommending a more conservative approach when technically feasible (i.e., TAE with nodal observation) (6,7,13,14). Based on the more conservative recommendations of TAE alone from multiple centers, a widespread shift toward less aggressive surgical intervention should have occurred over the past three decades. However, it is not clear to what extent these recommendations have affected practice patterns across the United States.

Our aim was to determine if practice patterns have changed over time and to determine if surgical treatment is consistent with current recommendations. We evaluated treatment patterns and outcomes recorded in the Surveillance, Epidemiology and End Results (SEER) database across three decades. Additionally, to determine the clinical impact of the sentinel lymph node biopsy (SLNB), we analyzed evidence from the SEER database supporting the prognostic significance of lymphatic metastases.

PATIENTS AND METHODS

SEER patients

To determine how often patients were treated in accordance with current recommendations, and to investigate disease stage and survival data, we queried the SEER database. The SEER database collects and publishes data on cancer incidence and survival from population-based U.S. cancer registries containing approximately 4.9 million patients. One hundred and eighty-six patients with anorectal melanoma were identified within this database (1973–2003) (SEER diagnostic codes from primary site: 21.0, 21.1, 21.12 and 21.8). Extent of surgical excision, stage, recurrence and survival were evaluated.

In patients who presented without distant metastasis, we evaluated the impact of the surgical treatment by APR versus TAE. This analysis excluded patients who were lost to follow-up or underwent an unknown surgical intervention.

In patients who presented with localized disease with or without concurrent regional nodal metastasis and/or distant metastasis, we evaluated the correlation between stage and survival, particularly with respect to surgical staging of the nodal basin. This analysis excluded patients without complete staging data.

Statistical Analysis

Data from the SEER database were analyzed using SPSS statistical software version 13.0. Differences in the type of surgery and between populations were analyzed. Fisher's exact tests were used when expected cell frequencies were below five. Age comparisons by gender were made using a standard t-test.

Median survival estimates in the samples were obtained using the nonparametric Kaplan-Meier method. Overall survival was estimated in SEER samples; the log-rank test was used to determine differences between surgery types and within each sample. Results yielding a *p*-value $\leq .05$ were considered statistically significant.

RESULTS

SEER patients

The 183 patients identified had a median age of 68 years and a female-to-male ratio of 2.2:1. Mean age was lower for males (63 versus 71 years; $p \leq 0.001$). When patients were grouped by 5-year age intervals, the mean age interval was 65–70 years. (The range of SEER 5-year age intervals was 30–35 years through ≥ 85 years.) Although males had a lower mean age interval than females (60–65 years versus 70–75 years; $p < 0.001$), corresponding rates of survival were not significantly different (59.3% versus 52.8% at 1 year, and 32.2% versus 22.8% at 2 years; p = ns).

Among the 143 patients who presented without distant metastasis, 51 (35.7%) underwent APR as an initial or salvage procedure (the SEER database records only the definitive procedure) and 92 underwent TAE with or without some degree of lymphadenectomy. Based on current recommendations a trend toward less aggressive surgical intervention would be anticipated; however, the rate of APR was 27% between 1973 and 1996, as compared with 43.2% between 1997 and 2003 (p = ns).

Limiting the extent of surgical resection (i.e. TAE) did not adversely affect outcome and although patients had similar pathologic characteristics, median overall survival after TAE versus APR was similar in both groups: 18 and 16 months, respectively. Five-year survival was also similar in both groups: 16.8% for APR versus 19.3% for TAE (p = ns) (Figure 1).

SEER patients: Prognostic impact of lymphatic metastasis

Of the 183 patients initially identified from the SEER database, 41 had incomplete staging data and were excluded from this portion of the analysis. Of the remaining 142 patients, 85 (60%) presented with localized disease, 19% presented with concurrent regional lymph node metastasis, and 21% presented with synchronous distant disease. Corresponding median survivals were 24 months, 17 months and 8 months, respectively ($p < 0.001$); 5-year survival rates were 26.7%, 9.8% and 0.0%, respectively ($p < 0.001$).

Most patients with localized disease had clinically normal regional lymph nodes and were managed by nodal observation; only 19 of the 85 patients underwent surgical staging of a nodal basin. In these 19 patients with pN0 disease, median survival was 20 months, similar to the 66 patients whose nodal basins were observed. This observation is not surprising because 16 of the 19 patients (84%) underwent assessment of mesorectal lymph nodes removed during APR; mesorectal nodes are unlikely to be involved with metastatic disease. In these patients the inguinal basin was not histologically sampled and our data reveal this location as a more likely site of metastasis from anorectal melanoma (15).

DISCUSSION

This study, the largest to analyze surgical treatment and outcomes for patients with anorectal melanoma in the United States, did not reveal a survival difference comparing TAE and APR. As recommendations regarding optimal surgical treatment for this disease have become more conservative over the past 30 years, we expected to find increased rates of conservative treatment, such as TAE, when compared with the less favorable APR. This study, however, did not reveal a trend toward less aggressive surgical resection. Our findings suggest that practice patterns across the country are inconsistent with current tertiary melanoma treatment center practices. Since the extent of surgical intervention does not correlate with survival, APR should be reserved for selected patients in whom TAE is not technically possible. Additionally, using this large database we show that nodal metastasis in anorectal melanoma has prognostic significance, suggesting that there is a role for selective lymphadenectomy (i.e., sentinel node biopsy; SLNB).

Recommendations provided by melanoma centers are not being applied effectively across the country. Over the past decade, national APR rates from the SEER database were significantly higher than those at our institution: 43.2% vs. 25.9%, even when including the salvage/delayed APR cases (15). These findings suggest some morbidity can be avoided in patients whose primary lesion could be removed with negative margins by TAE alone. Our experience suggests that even repeat attempts at TAE can be successful in obtaining negative margins while maintaining sphincter function. Moreover, this can still result in similar survival when compared with initially successful TAE.

In our analysis of the SEER database, TAE instead of APR did not adversely affect survival. Our analysis confirms that these patients can be managed with sphincter-preserving surgery and only selected patients with advanced disease may benefit from an APR. In our experience, patients at melanoma centers managed with TAE often have significantly better survival than patients managed with APR because only patients with significantly advanced disease undergo APR, thus reflecting a selection bias. SEER patients undergoing an APR did no worse than SEER patients undergoing TAE, indicating no significant selection bias.

The prognostic significance of nodal metastasis from anorectal melanoma has been particularly difficult to study, not only because of its relative rarity but also because most patients have not undergone histologic staging of the regional lymphatics most likely to be involved (13). Podnos and colleagues evaluated the SEER database from 1973–2001; they analyzed 126 patients with

anal melanoma and concluded that extent of disease correlated with overall survival (16). We analyzed a slightly different group of SEER patients in our study, which covered two additional years and included more patients with anorectal melanoma. Our analysis confirms that patients with localized disease have better survival than those with lymphatic metastasis and even better survival than those who present with distant disease: median survivals were 24 months for localized disease, 17 months for lymphatic metastasis and 8 months for distant disease ($p < 0.001$). Five-year survival rates were 26.7%, 9.8% and 0%, respectively ($p < 0.001$). These findings show that lymphatic metastasis is a biologically significant event.

As an alternative to APR or TAE alone with nodal observation and delayed/salvage lymphadenectomy, we have investigated TAE with lymphatic mapping and SLNB (15). We believe this approach can accurately identify patients with nodal disease and can allow early, beneficial completion lymphadenectomy.

The wide variation in post-operative management prohibited a meaningful analysis regarding the efficacy of adjuvant therapy in this patient population; the aim of our study was not to determine if adjuvant therapies were effective. Since the overall impact of chemotherapy or bio-chemotherapy for anorectal melanoma is unclear, we encourage patients to enroll in clinical trials to answer important questions regarding best adjuvant treatment options.

Obtaining negative margins while maintaining sphincter function should be the goal of resecting the primary anorectal melanoma; nodal metastasis is prognostic and provides useful data to the treating physicians. As lymphatic metastasis is prognostic then the concept of selective lymphadenectomy, i.e. SLNB, is reasonable and should be applied to the management of the regional nodal basin. This technique allows for the identification of the specific nodal basin(s) (usually inguinal) that receive(s) drainage from the primary tumor. Selective lymphadenectomy can avoid delayed lymphadenectomy in the patients without distant metastasis that present with clinically negative (cN0) inguinal nodes but who still harbor histologic metastasis within the nodal basin ($pN1_{(sn)}$). Further investigations are underway to determine the role of the SLNB in anorectal melanoma. In closing, anorectal melanoma continues to represent a significant challenge despite optimal surgical management and, thus, development of effective adjuvant therapy is critical to improve long-term survival.

Acknowledgments

Supported by grant CA29605 from the National Cancer Institute and by funding from the Amyx Foundation, Inc. (Boise, ID), the Wayne and Gladys Valley Foundation (Oakland, CA), Mr. and Mrs. Louis Johnson, (Stanfield, AZ), Berton M. Kirshner (Los Angeles, CA), Todd Kirshner (Los Angeles, CA), Heather and Jim Murren (Las Vegas, NV), Mrs. Marianne Reis (Lake Forest, CA), the Wallis Foundation (Los Angeles, CA), the Harold J. McAlister Charitable Foundation (Los Angeles, CA), the Family of Robert Novick (Los Angeles, CA), the Weil Family Fund (Los Angeles, CA), and the Wrather Family Foundation (Los Alamos, CA).

References

1. Brady MS, Kavolius JP, Quan SH. Anorectal melanoma. A 64-year experience at Memorial Sloan-Kettering Cancer Center. Dis Colon Rectum 1995;38:146–51. [PubMed: 7851168]
2. Chang AE, Karnell LH, Menck HR. The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 1998;83:1664–78. [PubMed: 9781962]
3. Quan SH, Deddish MR. Noncutaneous melanoma. Malignant melanoma of the anorectum. CA Cancer J Clin 1966;16:111–4. [PubMed: 4957071]
4. Pack GT, Oropeza R. A comparative study of melanoma and epidermoid carcinoma of the anal canal: A review of 20 melanomas and 29 epidermoid carcinomas (1930 to 1965). Dis Colon Rectum 1967;10:161–76. [PubMed: 6026797]

5. Cooper PH, Mills SE, Allen MS Jr. Malignant melanoma of the anus: report of 12 patients and analysis of 255 additional cases. Dis Colon Rectum 1982;25:693–703. [PubMed: 7128372]
6. Ross M, Pezzi C, Pezzi T, Meurer D, Hickey R, Balch C. Patterns of failure in anorectal melanoma. A guide to surgical therapy. Arch Surg 1990;125:313–6. [PubMed: 2306178]
7. Ballo MT, Gershenwald JE, Zagars GK, Lee JE, Mansfield PF, Strom EA, Bedikian AY, Kim KB, Papadopoulos NE, Prieto VG, Ross MI. Sphincter-sparing local excision and adjuvant radiation for anal-rectal melanoma. J Clin Oncol 2002;20:4555–8. [PubMed: 12454112]
8. Weyandt GH, Eggert AO, Houf M, Raulf F, Brocker EB, Becker JC. Anorectal melanoma: surgical management guidelines according to tumour thickness. Br J Cancer 2003;89:2019–22. [PubMed: 14647131]
9. Bullard KM, Tuttle TM, Rothenberger DA, Madoff RD, Baxter NN, Finne CO, Spencer MP. Surgical therapy for anorectal melanoma. J Am Coll Surg 2003;196:206–11. [PubMed: 12595048]
10. Yap LB, Neary P. A comparison of wide local excision with abdominoperineal resection in anorectal melanoma. Melanoma Res 2004;14:147–50. [PubMed: 15057046]
11. Pessaux P, Pocard M, Elias D, Duvillard P, Avril MF, Zimmerman P, Lasser P. Surgical management of primary anorectal melanoma. Br J Surg 2004;91:1183–7. [PubMed: 15449271]
12. Droesch JT, Flum DR, Mann GN. Wide local excision or abdominoperineal resection as the initial treatment for anorectal melanoma? Am J Surg 2005;189:446–9. [PubMed: 15820458]
13. Yeh JJ, Shia J, Hwu WJ, Busam KJ, Paty PB, Guillem JG, Coit DG, Wong WD, Weiser MR. The role of abdominoperineal resection as surgical therapy for anorectal melanoma. Ann Surg 2006;244:1012–7. [PubMed: 17122627]
14. Homsi J, Garrett C. Melanoma of the anal canal: a case series. Dis Colon Rectum 2007;50:1004–10. [PubMed: 17468984]
15. Iddings DM, Chen SL, Faries MB, Deacon L, Essner R, Morton DL. A new paradigm in the management of anorectal melanoma: trans-anal excision with sphincter preservation and sentinel node biopsy. J Clin Oncol 2007;25(18S) Abstract 8513.
16. Podnos YD, Tsai NC, Smith D, Ellenhorn JD. Factors affecting survival in patients with anal melanoma. Am Surg 2006;72:917–20. [PubMed: 17058735]

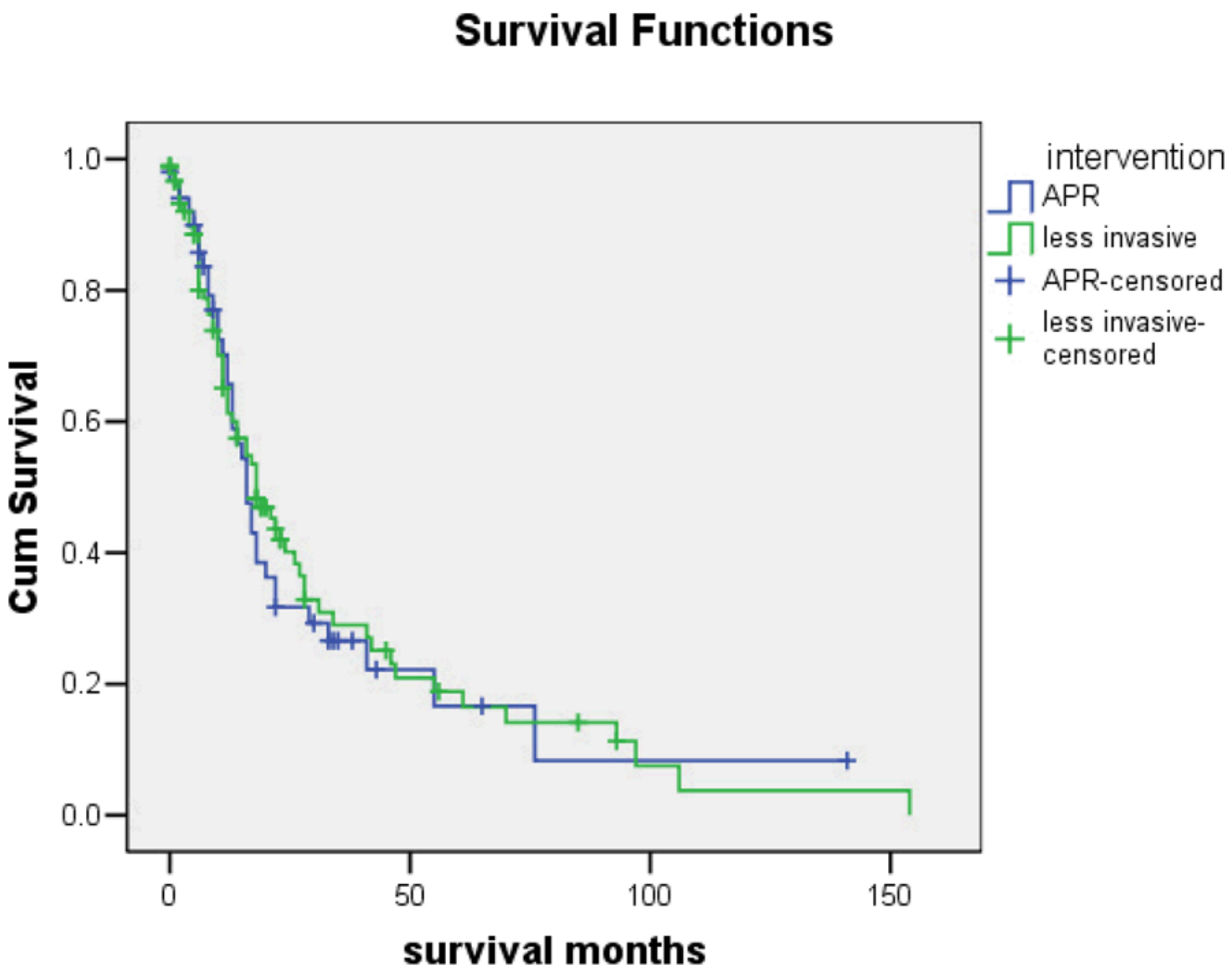

Figure 1.
Kaplan-Meier survival curves for SEER patients treated with APR versus TAE (*less invasive*); median survival was 16 months versus 18 months, respectively ($p = 0.775$).