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Predictors of Treatment Choice in High-Risk and Metastatic Melanoma: Evidence From Linked Electronic Medical Records and Administrative Claims Data

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Background

In the last 50 years (1950–2001), the incidence of malignant melanoma has increased 690%, and the mortality rate has increased by 165%. Although the overall survival rate for early stage tumors has improved over time because of early detection and improved surgical procedures, treatment for advanced and/or metastatic melanoma continues to be a considerable unmet medical need due to the unsatisfactory efficacy and significant toxicities of the currently available drugs. Although physician treatment guidelines and clinical research can provide information about how we expect advanced melanoma to be treated, real-world treatment patterns may vary greatly from treatment guidelines and controlled trials. It is therefore necessary to understand and document the treatment choices that are currently being made for the treatment of advanced/metastatic melanoma in real-world clinical settings and to assess the factors that influence the choice of treatment.

Objective

To evaluate predictors of four major therapeutic choices (surgery, radiation, chemotherapy, immunotherapy) in high-risk (stage IIB/C, III) and metastatic (stage IV) melanoma.

Methods

Study design

Retrospective longitudinal analysis of the Convergence CT (CCT) database consisting of linked electronic medical records (EMR) and administrative claims data.

Database description

- Longitudinal EMR data (July 2003 through November 2006) from large physician practices, clinics, ambulatory centers, and hospitals in the United States.
- Database includes (among other variables) the following
  - Patient demographics
  - Dates of diagnosis
  - Clinical data (e.g. pathology reports, laboratory tests and results)
  - Healthcare use (including prescription drug use) and associated charges.
- No death data.

Analysis definitions

- Patients with ≥1 diagnosis of malignant melanoma (ICD-9-CM 172.xx or 172.xx or V10.82) at stage IIB or higher included for analysis.
- Index date defined as date of first stage IIB or higher diagnosis.
- Staging captured via pathology reports.
- Where pathology reports were not available, stage IV patients were identified via diagnosis codes for secondary malignant neoplasm (ICD-9-CM 197.xx, 198.xx).
- Distinction between stage IIIA/B and IIIC not possible with this database.
- Patients of all ages included in the analysis; subgroup of patients <65 years analyzed separately.
- A Charlson Comorbidity Index (CCI) score that includes 17 categories of comorbidities, as defined by ICD-9 diagnosis codes, with associated weights corresponding to the severity of the comorbid condition of interest[1] calculated for each person.

Treatment definitions

- Melanoma treatments were defined based on evidence of relevant Health Care Financing Administration Common Procedure Coding System (HCPCS), ICD-9-CM procedure codes, ICD-9-CM diagnostic codes, and administrative revenue codes
  - Surgical procedures: excision of skin lesions/tumors and removal of lymph nodes
  - Radiation
  - Chemotherapies: dacarbazine, vincristine, paclitaxel, cisplatin, carboplatin, vinblastine, carmustine, temozolomide, and bleomycin
  - Immunotherapies: interleukin-2 and interferon.

Statistical analysis

- Multivariate logistic regression models estimated to evaluate and identify the key patient and disease characteristics that influence treatment choice.
- Logistic regressions estimated took the following general form:

$$\text{THERAPY}_i = \beta_0 + \beta_1\text{STAGE III} + \beta_2\text{STAGE IV} + \beta_3\text{X}_i + \varepsilon.$$

- Covariates included age, gender, race, CCI score, and disease stage at index date.
- βs converted into odds ratios for ease of interpretation.

Outcomes

The following outcomes were analyzed

- Baseline characteristics of patients diagnosed with stage IIB/C, III, or IV melanoma.
- Number and percentage of patients receiving surgery, radiation, chemotherapy, immunotherapy, and combinations of the four, at any point post-index date.
- Key predictors of treatment choice.

Results

Patient characteristics (Table 1)

- A total of 268 patients were identified for study inclusion.
- Approximately 62% were male and 72% were white.
- More than half were >65 years.
- Stage distribution
  - IIB/C: 18%
  - III: 21%
  - IV: 61%.
- Disproportion of stage IV due to record-based algorithm to identify additional stage IV patients where pathology data were not available; record-based algorithm could not be used to identify additional patients in stages IIB/C or III.
- Median follow-up time (by stage) defined as number of months between index date and last observed medical record
  - IIB/C: 14 months
  - III: 13 months
  - IV: 11 months.

Table 1. Characteristics of the study sample.

	All patients		Melanoma stage at index date					
			IIB/C		III		IV	
	n	%	n	%	n	%	n	%
Total sample	268	100	49	18.28	55	20.52	164	61.19
Gender								
Male	165	61.57	38	77.55	26	47.27	101	61.59
Female	94	35.07	10	20.41	27	49.09	57	34.76
Unknown	9	3.36	1	2.04	2	3.64	6	3.66
Age at index date								
<18	1	0.37	–	–	1	1.82	–	–
18–29	4	1.49	–	–	1	1.82	3	1.83
30–44	19	7.09	1	2.04	8	14.55	10	6.1
45–54	26	9.7	5	10.2	10	18.18	11	6.71
55–64	51	19.03	8	16.33	10	18.18	33	20.12
65–74	59	22.01	11	22.45	8	14.55	40	24.39
75–84	66	24.63	16	32.65	12	21.82	38	23.17
≥85	31	11.57	7	14.29	3	5.45	21	12.8
Unknown	11	4.1	1	2.04	2	3.64	8	4.88
Race/ethnicity								
White	192	71.64	30	61.22	42	76.36	120	73.17
Black	2	0.75	–	–	1	1.82	1	0.61
Other	1	0.37	–	–	1	1.82	–	–
Unknown	73	27.24	19	38.78	11	20	43	26.22
Patient identification method								
Pathology reports	168	62.69	49	100	55	100	64	39.02
Electronic medical records algorithm	100	37.31	–	–	–	–	100	60.98
Follow-up duration (months)*								
Mean (SD)	12.26 (10.89)		13.78 (9.85)		13.49 (10.38)		11.40 (11.31)	
Median	10		15		13		8	
Range (min, max)	(0, 51)		(1, 34)		(0, 51)		(0, 50)	
CCI score								
Mean (SD)	2.71 (3.83)		1.27 (2.34)		1.87 (3.19)		3.41 (4.21)	
Median	0		0		0		1	
Range (min, max)	0, 15		0, 11		0, 12		0, 15	

Max = maximum; min = minimum; SD = standard deviation
*Duration of follow-up defined as the number of continuous months between the patient's index date and their last observed electronic medical record

Treatment patterns (Figure 1)

- Surgery was highly prevalent, but less common in stage IV patients
  - Skin lesion/tumor excision was the most common surgical procedure across all stages
  - 29% of stage IV patients had a skin lesion/tumor excision (32% for patients <65 years).
- Chemotherapy was prevalent in 27% and 31% of stage III and IV patients, respectively. Chemotherapy use was higher for patients <65 years (31% and 42% for stage III and IV, respectively)
  - Dacarbazine and cisplatin was the most commonly used chemotherapy overall, but not used among stage IIB/C patients
  - Both dacarbazine and cisplatin seen in 5% of stage III patients and 10% of stage IV patients (6% and 12%, respectively, for patients <65 years).
- Immunotherapy was relatively uncommon, except in stage III patients
  - Interferon was the most common immunotherapy for stage IIB/C and III; interleukin was more common in stage IV.
  - Interferon was most prevalent in stage III patients
    - 15% of stage III patients in overall study sample used interferon
    - 25% of patients <65 years used interferon.

Conclusions

- Results suggest that beyond surgery as a first-line approach, relatively few patients received other types of treatments.
- Despite wide acceptance as a standard chemotherapy in melanoma, dacarbazine utilization in this population remains relatively low.
- Older patients were less likely to receive active treatment.
- White patients were more likely to receive active treatment.

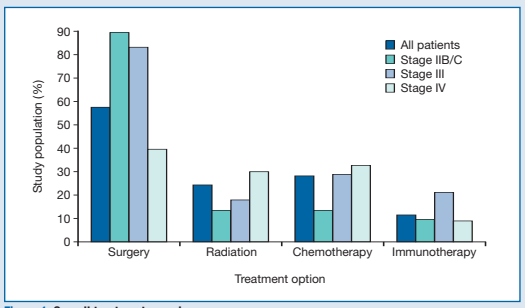

Figure 1. Overall treatment prevalence.

Predictors of treatment choice (Table 2)

- Increasing age was associated with significantly reduced likelihood of receiving active treatment following index date, especially systemic therapies
  - For patients <65 years, advanced age (45 and older) was associated with an increased likelihood of surgery, chemotherapy, and immunotherapy.
- Males were less likely to receive radiation than females.
- White patients were significantly more likely to receive surgery and less likely to receive no active therapy.
- Compared with stage IIB/C, patients in stage III were more likely to receive all forms of active treatment except surgery
  - For patients <65 years, stage III patients were more likely to receive radiation and immunotherapy, but not surgery and chemotherapy.
- Compared with stage IIB/C, patients in stage IV were more than seven times as likely to receive no active treatment following index date, and substantially less likely to receive surgery.

Table 2. Factors affecting choice of overall melanoma treatment at any point post-index date.

	Odds ratio (95% confidence interval)				
Covariate[†]	No treatment[‡]	Surgery	Radiation	Chemotherapy	Immunotherapy
Age 65+	2.190** (1.103, 4.347)	0.549** (0.301, 0.999)	0.566* (0.306, 1.047)	0.428*** (0.237, 0.772)	0.244*** (0.099, 0.602)
Gender male	1.312 (0.673, 2.558)	0.961 (0.526, 1.756)	0.651* (0.347, 1.220)	1.268 (0.681, 2.360)	1.502 (0.598, 3.771)
Race white	0.443** (0.220, 0.891)	2.371** (1.191, 4.720)	0.701 (0.354, 1.391)	0.909* (0.465, 1.775)	1.449 (0.521, 4.033)
CCI score	0.941 (0.886, 1.022)	0.922** (0.855, 0.994)	1.059 (0.984, 1.141)	1.084** (1.009, 1.165)	0.947 (0.834, 1.074)
Stage III at first high-risk diagnosis	2.096 (0.533, 8.241)	0.474 (0.150, 1.495)	1.096 (0.340, 3.533)	2.356 (0.785, 7.076)	2.211 (0.583, 8.383)
Stage IV at first high-risk diagnosis	7.307*** (2.384, 22.390)	0.083*** (0.032, 0.216)	2.377* (0.908, 6.220)	2.645** (1.009, 6.934)	0.921 (0.264, 3.212)

*P<0.10; **P<0.05; ***P<0.01
[†]Reference groups for all models are as follows: age under 65, female gender, non-white race, and stage IIB/C at first high-risk melanoma diagnosis
[‡]No treatment indicates no evidence of surgery, radiation, chemotherapy, or immunotherapy. Can also be referred to as 'best supportive care'

Limitations

- Our analysis of specific systemic agents used in high-risk and metastatic melanoma is limited by the varying detail with which systemic therapies are coded for purposes of insurance reimbursement.
- Due to the lack of a stage variable within the CCT database, a review of pathology reports was the only way to capture stages IIB/C and III. These stages may therefore be under-represented.
- Our algorithms rely primarily on administrative claims submitted solely for purposes of insurance reimbursement (and not for purposes of research) with no access to information collected from either the attending physician or the patient. The impact of misclassification bias stemming from analyses of claims data has been described in previous research.[2,3]
- This study included patients from large, often integrated, health care systems that may not be generalizeable to the overall US population.

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