


Surgery vs non-surgery in cutaneous melanoma based on SEER database

A cross-sectional study

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Abstract

This study was to assess the survival outcome of cutaneous melanoma (CM) patients with surgery vs non-surgery through inverse probability of treatment weighting (IPTW) using the propensity score. Patients diagnosed as CM were selected from the Surveillance, Epidemiology, and End Results Program (SEER) database. The survival outcome was estimated and compared by IPTW using the propensity score. Totally 2203 CM patients were identified, in which 1921 cases received surgical treatment (surgery group), while 282 cases didn't (non-surgery group). The median survival time of surgery and non-surgery groups was respectively 150 months and 15 months (unmatched cohort), 70 months and 40 months (matched cohort) and 130 months vs. 75 months (IPTW-weighted cohort). Compared with the non-surgery group, the surgery group had a lower risk of death in unmatched [hazard ratio (HR): 0.647, 95% confidence interval (CI): 0.509–0.821, $P < .001$] and matched (HR: 0.636, 95%CI: 0.459–0.882, $P < .01$) cohorts. In multivariate Cox model of IPTW-weighted cohort, the risk of death in the surgery group decreased notably than the non-surgery group (HR: 0.423, 95%CI: 0.383–0.468, $P < .001$). In conclusion, CM patients receiving surgical treatment are associated with a better survival outcome compared with those without surgical treatment through IPTW using the propensity score.

Abbreviations: AJCC = American Joint Committee on Cancer, CI = confidence interval, CM = cutaneous melanoma, HR = hazard ratio, IPTW = inverse probability of treatment weighting, OS = overall survival, SEER = Surveillance, Epidemiology, and End Results Program, SMD = standardized mean difference, SWOG = Southwest Oncology Group, UV = ultraviolet.

Keywords: cutaneous melanoma, inverse probability of treatment weighting, propensity score, surgery, survival outcome

1. Introduction

Cutaneous melanoma (CM) derived from epidermal melanocytes is potentially the most fatal type of skin cancer and can result in 90% of skin cancer mortality.^[1] In 2012, 232, 000 new cases of CM and 55, 000 deaths were estimated worldwide, and the regions affected were largely those with white populations, such

as Northern America, Australia and New Zealand.^[2] In recent years, the incidence of CM has been increasing steadily despite use of various prevention measures. In 2019, there was an estimated 96, 480 new cases of CM and 7230 deaths in the United States.^[3] However, it remains unclear about the etiology of CM. There was an evidence suggesting that excessive ultraviolet (UV) irradiation could burn the skin and induce tumor-initiating DNA mutations in melanocytes, which is thought to be an important etiological factor in the development of malignant melanoma.^[4,5]

Surgical excision continues to be the first-line treatment of primary lesions and congenital diseases.^[6] The importance of surgical excision in each staging of malignant melanoma has been highlighted by the American Joint Committee on Cancer (AJCC).^[7] For the patients with early melanoma, wide extended resection should be performed as quickly as possible after biopsy, while for patients with stage I-II melanoma of positive sentinel node biopsy and those with stage III melanoma, regional lymph node dissection should be added to excise the involved lymph nodes as completely as possible.^[8,9] In addition, the surgery is reserved for palliation of stage IV melanoma or in the setting of a mixed response or stable disease with one or two progressive lesions.^[10] In a Southwest Oncology Group (SWOG) trial, it was found that complete surgical resection could prolong the overall survival (OS) of appropriately selected patients with stage IV melanoma.^[11] However, in the last decade, the studies have suggested that immunotherapy and targeted therapy can dramatically improve the survival of patients with metastatic melanoma.^[12,13] Therefore, the role of surgery remains to be determined in the modern era.

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In this study, we collected the clinical data of 2203 CM patients from the Surveillance, Epidemiology, and End Results Program (SEER) database between 2004 and 2015, and compared the survival outcome of patients treated by surgery and those without surgery through inverse probability of treatment weighting (IPTW) using the propensity score, with the aim of providing some evidences for CM treatment.

2. Materials and methods

2.1. Study population

The initial cohort was obtained from the SEER database (2004–2015, <https://seer.cancer.gov/data/access.html>), which approximately covered 27.8% of the U.S. population. The patients aged 18 years above at diagnosis and diagnosed as CM were identified, and those without the following information were excluded, such as treatment modality, gender, age, year of diagnosis, tumor histology, primary site, grade, AJCC stage, summary stage, tumor extension, the number of in situ/malignant tumors and so on. A total of 2203 patients were finally enrolled in the study.

The data used in this study were obtained from SEER database, an openly available dataset, and all private information has been carried out the desensitization, thereby the approval from the Institutional Review Board of Shenzhen People's Hospital was not required. The SEER database agreement was signed and provided a license for accessing the SEER information (ID 21583-Nov2019).

2.2. IPTW using the propensity score

The propensity score refers to a subject's possibility of treatment selection which is rely on the observed baseline covariates. Logistic regression model established from the factors that potentially influence the determination of treatment modalities (surgery vs non-surgery) was used to estimate the propensity score. With the estimated propensity score, a one-to-one matched cohort was built by the nearest-neighbor method.^[14] In this study, the covariates controlled by the propensity score included gender, age, year of diagnosis, tumor histology, primary site, grade, AJCC stage, summary stage, AJCC T stage, AJCC N stage, AJCC M stage, tumor extension and the number of in situ/malignant tumors.

The subjects weighted by inverse probability of treatment can establish a synthetic sample in which the treatment modality is independent of measured baseline covariates. IPTW using the propensity score permits one to acquire impartial estimates of average treatment effects.^[15] IPTW was calculated based on the formula: $1/(\text{propensity score})$ for the surgery group and $1/(1-\text{propensity score})$ for the non-surgery group.^[14] And meanwhile, the weights were standardized to 1.^[16] The propensity score was estimated using the factors including the gender, age, year of diagnosis, tumor histology, primary site, grade, AJCC stage, summary stage, AJCC T stage, AJCC N stage, AJCC M stage, tumor extension and the number of in situ/malignant tumors. The study population was weighted to ensure that survival analysis could be conducted directly after the generation of weights.

In terms of baseline characteristics between surgery and non-surgery groups, a balance examination should be performed after matching or weighting. A balance examination method was to calculate the standardized mean difference (SMD) of variables.^[15] The balance was acceptable if the SMD was less than

0.1.^[17] Therefore, SMDs were calculated through the incidence of variables between surgery and non-surgery groups after the baseline characteristics in this study were confirmed as dichotomous variables.

2.3. Statistical analysis

R software (version 3.6.1, The R Foundation for Statistical Computing, Vienna, Austria) was used to analyze the data. The factors that led to the selection of each treatment modality were identified using Chi-square (χ^2) test, and were incorporated into the model generating the propensity score as the covariates. Cox regression model that adjusted all the variables was established in the unmatched, matched, and IPTW-weighted cohorts to compare the survival difference between surgery and non-surgery groups. $P < .05$ was thought to be statistically significant.

3. Results

3.1. Baseline characteristics of included CM patients

In this study, 2203 CM patients were totally identified from the SEER database between 2004 and 2015, in which 1921 cases (87.2%) received any kind of surgical excision (surgery group), while 282 cases (12.8%) accepted other therapies except the surgery (non-surgery group). The baseline characteristics of patients in surgery and non-surgery groups were compared in Table 1. It was found that there were all significant differences between two groups in gender, tumor histology, primary site, grade, AJCC stage, summary stage, AJCC T stage, AJCC N stage, AJCC M stage, tumor extension and the number of in situ/malignant tumors (all $P < .05$).

3.2. Baseline balance of two groups in unmatched, matched, and IPTW-weighted cohorts

As shown in Table 2 and Figure 1, the baseline balance of surgery and non-surgery groups was worse in the unmatched cohort, while this balance improved in IPTW-weighted cohort, and the SMDs of other variables were almost less than 0.2 except the tumor extension.

3.3. Cox regression analysis of the factors influencing prognosis

Before unmatching, the survival time of patients in surgery and non-surgery groups was compared based on different stages (Fig. 2). It was observed that the survival time of surgery group was longer than that of non-surgery group in stage T1/T2 ($P < .001$) and stage T3/T4 ($P = .030$), but not stage T0 ($P = .061$). The median survival time of surgery and non-surgery groups was respectively 150 months and 15 months (unmatched cohort), 70 months and 40 months (matched cohort) and 130 months vs 75 months (IPTW-weighted cohort).

As listed in Table 3, univariate Cox regression model of unmatched cohort revealed that the risk of death in the surgery group was significantly lower than that in the non-surgery group [hazard ratio (HR): 0.223, 95% confidence interval (CI): 0.190–0.262, $P < .001$]. After adjustment of other covariates, the risk of death in the surgery group was still lower compared with the non-surgery group (HR: 0.647, 95% CI: 0.509–0.821, $P < .001$), but the HR increased to some extent. This risk of death was similar to

Table 1.
Baseline characteristics of patients with cutaneous melanoma in surgery and non-surgery groups [n(%)].

Variables	Non-surgery group (n=282)	Surgery group (n=1921)	P
Gender			.037
Male	188 (66.7)	1152 (60.0)	
Female	94 (33.3)	769 (40.0)	
Age, years			.077
20–49	43 (15.2)	398 (20.7)	
50–69	117 (41.5)	783 (40.8)	
≥70	122 (43.3)	740 (38.5)	
Year of diagnosis			.221
2004–2006	73 (25.9)	452 (23.5)	
2007–2009	71 (25.2)	417 (21.7)	
2010–2012	76 (27.0)	531 (27.6)	
2013–2015	62 (22.0)	521 (27.1)	
Tumor histology			<.001
Superficial spreading	20 (7.1)	458 (23.8)	
Nodular melanoma	6 (2.1)	151 (7.9)	
Lentigo maligna melanoma	2 (0.7)	123 (6.4)	
Other or unspecified	254 (90.1)	1189 (61.9)	
Primary site			<.001
Scalp and neck	10 (3.5)	189 (9.8)	
Trunk	38 (13.5)	615 (32.0)	
Upper limbs and shoulder	25 (8.9)	496 (25.8)	
Lower limbs and hip	20 (7.1)	329 (17.1)	
Skin, not otherwise specified	189 (67.0)	292 (15.2)	
Grade			<.001
I	17 (6.0)	232 (12.1)	
II	18 (6.4)	544 (28.3)	
III	189 (67.0)	848 (44.1)	
IV	58 (20.6)	297 (15.5)	
AJCC stage, 6th			<.001
I	33 (11.7)	1164 (60.6)	
II	11 (3.9)	292 (15.2)	
III	21 (7.4)	168 (8.7)	
IV	157 (55.7)	75 (3.9)	
Unstaged	60 (21.3)	222 (11.6)	
Summary stage			<.001
Localized	52 (18.4)	1519 (79.1)	
Regional	29 (10.3)	251 (13.1)	
Distant	160 (56.7)	86 (4.5)	
Unknown/unstaged	41 (14.5)	65 (3.4)	
AJCC T stage, 6th			<.001
T0	104 (36.9)	11 (0.6)	
T1	39 (13.8)	1117 (58.1)	
T2	7 (2.5)	240 (12.5)	
T3	7 (2.5)	240 (12.5)	
T4	11 (3.90)	195 (10.2)	
TX	114 (40.4)	173 (9.0)	
AJCC N stage, 6th			<.001
N0	95 (33.7)	1598 (83.2)	
N1	51 (18.1)	113 (5.9)	
N1+	13 (4.6)	100 (5.2)	
NX	123 (43.6)	110 (5.7)	
AJCC M stage, 6th			<.001
M0	84 (29.8)	1753 (91.3)	
M1	157 (55.7)	75 (3.9)	
MX	41 (14.5)	93 (4.8)	
Tumor extension			<.001
≥3 cm	39 (13.8)	1460 (76.0)	
<3 cm	146 (51.8)	375 (19.5)	
NA	97 (34.4)	86 (4.5)	
Number of in situ/malignant tumors			.027
≤3	198 (70.2)	1215 (63.2)	
>3	84 (29.8)	706 (36.8)	

Grade represents differentiated degrees. AJCC=American Joint Committee on Cancer. NA=missing value.

Table 2.
The baseline balance of surgery and non-surgery groups in unmatched, matched, and IPTW-weighted cohorts.

Variables	Unmatched cohort Non-surgery vs surgery (282 vs 1921)	Matched cohort Non-surgery vs surgery (134 vs 134)	IPTW-weighted cohort Non-surgery vs surgery (2559 vs 2194)
Gender			
Male	0.139	0.128	0.153
Female	0.139	0.128	0.153
Age, years			
20–49	0.143	0.159	0.185
50–69	0.015	0.382	0.077
≥70	0.096	0.464	0.083
Year of diagnosis			
2004–2006	0.055	0.248	0.006
2007–2009	0.082	0.035	0.151
2010–2012	0.016	0.035	0.039
2013–2015	0.119	0.268	0.172
Tumor histology			
Superficial spreading	0.476	0.110	0.267
Nodular melanoma	0.265	0.153	0.121
Lentigo maligna melanoma	0.311	0.140	0.089
Other or unspecified	0.698	0.054	0.148
Primary site			
Scalp and neck	0.254	0.083	0.127
Trunk	0.453	0.086	0.190
Upper limbs and shoulder	0.459	0.020	0.102
Lower limbs and hip	0.311	0.168	0.156
Skin, not otherwise specified	1.237	0.122	0.200
Grade			
I	0.212	0.025	0.024
II	0.605	0.065	0.043
III	0.473	0.121	0.059
IV	0.133	0.117	0.048
AJCC Stage, 6th			
I	1.181	0.244	0.058
II	0.392	0.271	0.004
III	0.048	0.001	0.118
IV	1.371	0.067	0.049
Unstaged	0.264	0.048	0.048
Summary stage			
Localized	1.524	0.061	0.158
Regional	0.087	<0.001	0.148
Distant	1.375	0.066	0.061
Unknown/unstaged	0.398	0.158	0.024
AJCC T stage, 6th			
T0	1.050	0.059	0.061
T1	1.040	0.171	0.091
T2	0.387	0.145	0.043
T3	0.303	0.032	0.141
T4	0.246	0.168	0.025
TX	0.781	0.075	0.055
AJCC N stage, 6th			
N0	1.160	0.256	0.021
N1	0.382	0.044	0.060
N1+	0.028	0.218	0.291
NX	0.977	0.412	0.264
AJCC M stage, 6th			
M0	1.615	0.120	0.119
M1	1.371	0.067	0.049
MX	0.332	0.247	0.214
Tumor extension			
≥3 cm	1.600	0.345	0.279
<3 cm	0.714	<0.001	0.244
NA	0.815	0.363	0.086
Number of in situ/malignant tumors			
≤2	0.148	0.923	0.029
>2	0.148	0.923	0.029

Grade represents differentiated degrees. AJCC=American Joint Committee on Cancer. NA=missing value.

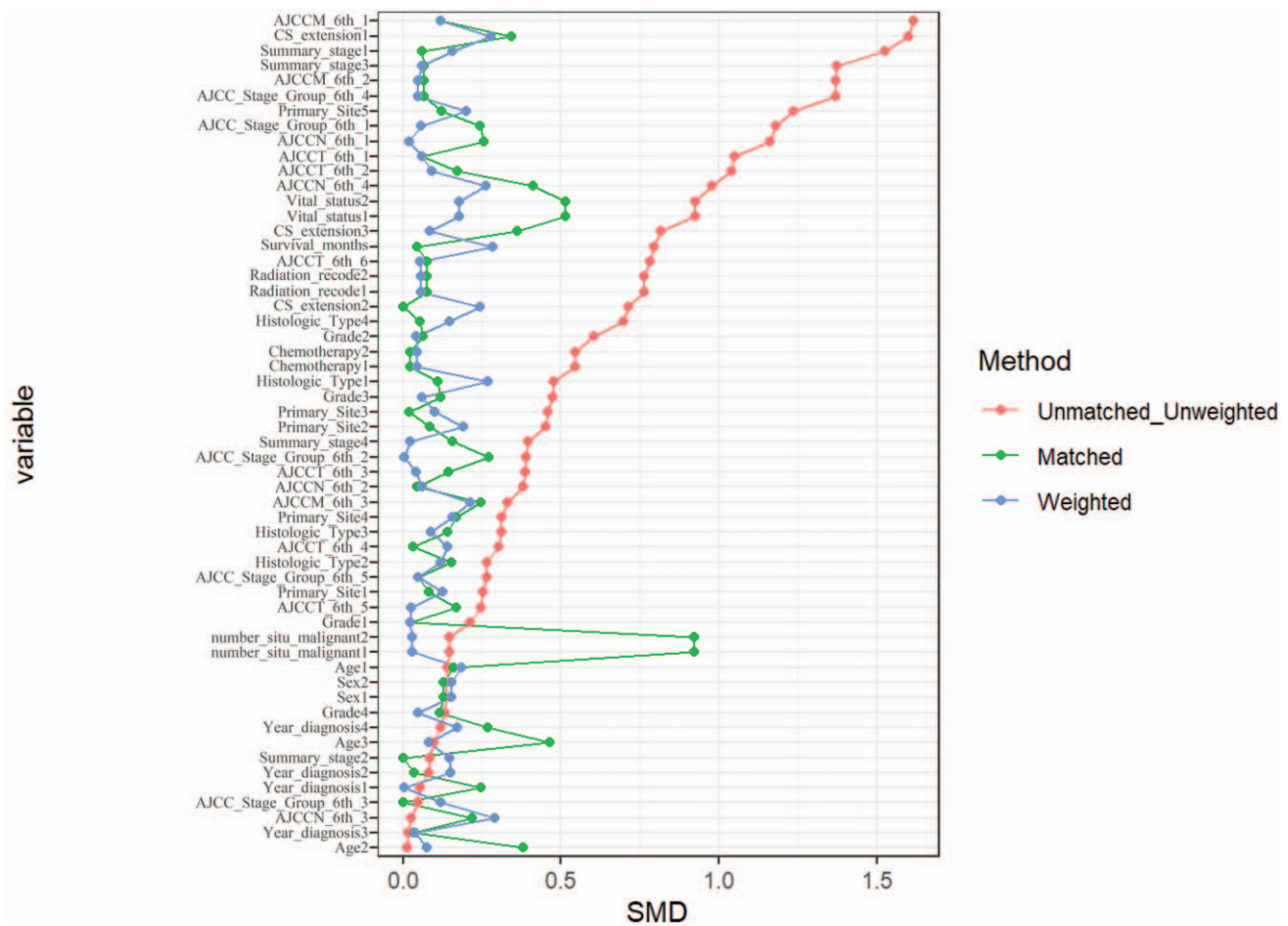


Figure 1. The baseline balance of surgery and non-surgery groups in unmatched, matched, and IPTW-weighted cohorts.

that of matched cohort (HR: 0.636, 95%CI: 0.459–0.882, $P < .01$). In multivariate Cox model of IPTW-weighted cohort, however, the risk of death in the surgery group was found to decrease notably compared with the non-surgery group (HR: 0.423, 95%CI: 0.383–0.468, $P < .001$).

4. Discussion

In this study, a total of 2203 CM patients were identified from the SEER database between 2004 and 2015. To prevent the selection bias from determining the treatment modality (surgery vs. non-surgery), two major approaches frequently used in large observational studies were applied, including the propensity score and IPTW. After adjustment of various confounding factors that affected the prognosis of CM patients through IPTW using the propensity score, our results demonstrated that the patients receiving surgical treatment had a lower risk of death compared with those without surgical treatment, which suggested that for CM patients, surgical resection might provide a survival advantage over non-surgical resection.

CM pertains to a high-grade malignant tumor, with the early presentation of local skin lesions that sequentially invade the deep tissue until distant metastases emerge. Surgical resection is of great importance to CM treatment and prognosis. The Melanoma Staging and Classification revised by AJCC in 2010

emphasizes the importance of surgical resection in different stages of CM.^[18] For stage I and II melanoma, wide excision is usually performed based on the safety margin of surgery to achieve a better efficacy; for stage III melanoma of specific lymphatic metastases, surgical resection can create conditions for postoperative adjuvant therapy by further confirming the diagnosis and relieving the tumor load, consequently prolonging the survival time. Even when patients are subjected to stage IV metastatic melanoma (single metastasis or resectable metastases), the surgery can still be performed to excise the lesions. Some evidences indicated that the optimal initial option for properly selected patients with stage IV melanoma was complete metastasectomy when technically feasible, but not systemic chemotherapy or biologic therapy.^[19–21] Howard et al reported that over half of stage IV melanoma patients undergoing surgery showed improved survival than those treated with systemic medical therapy alone, regardless of metastatic number and sites.^[19] Compared with those without metastasectomy, both the median survival time and 5-year survival rates of stage IV melanoma patients undergoing metastasectomy significantly improved (12 months vs 5 months; 16% vs 7%).^[22] In this study, the results before unmatched showed that the survival time of surgery group was longer than that of non-surgery group either in stage T1/T2 or in stage T3/T4, suggesting a dominance of surgical treatment in the treatment of early and advanced CM.

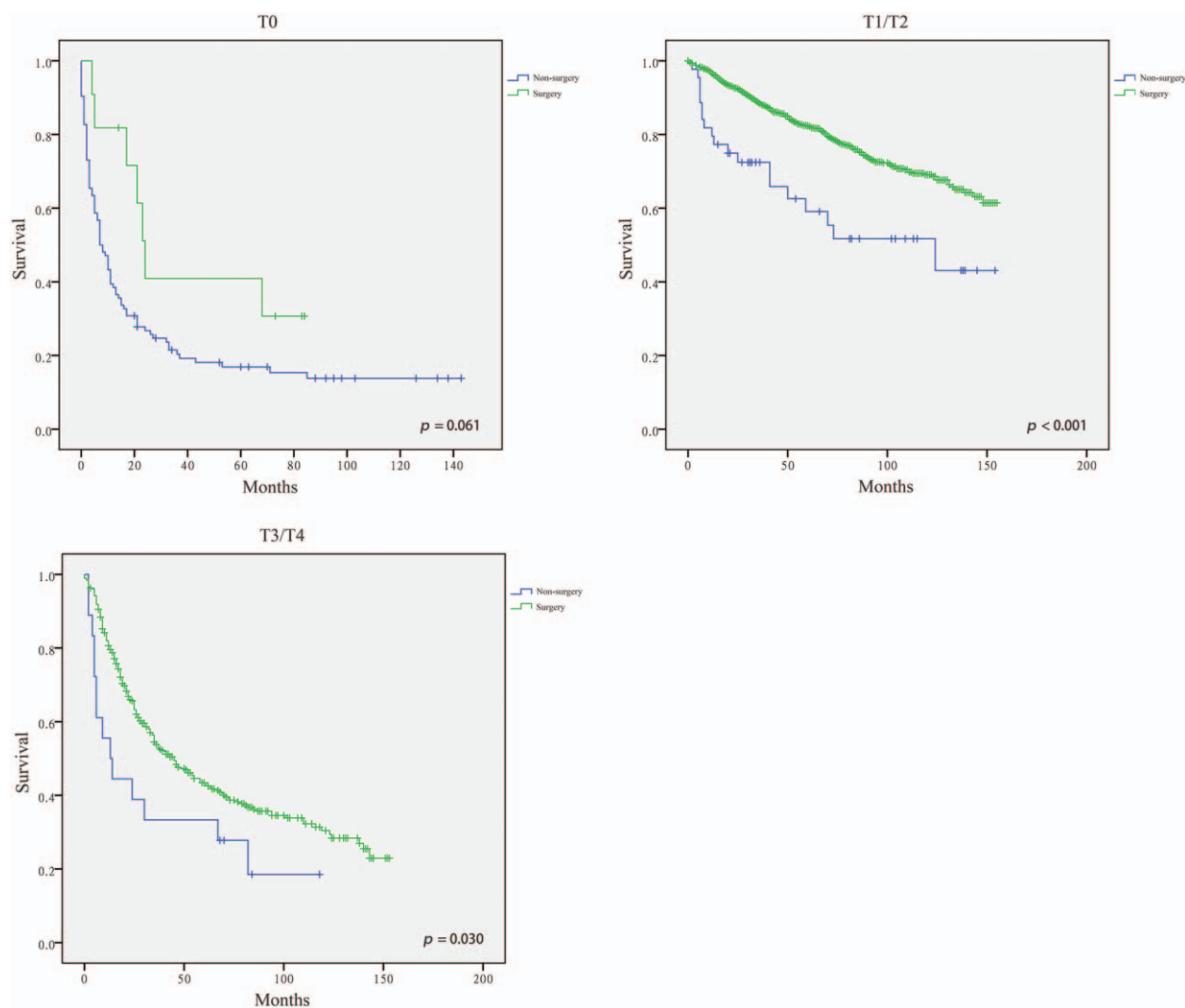


Figure 2. Comparison of the survival time between surgery and non-surgery groups based on different stages.

IPTW was used to calculate the propensity score to make the variables reach the post randomization. By comparison to survival curves, our results suggested that the median survival time of patients undergoing surgical resection was significantly longer than those without surgical resection whether in unmatched or matched, IPTW-weighted cohorts. It is thus speculated that surgical resection may be the most essential treatment modality for malignant melanoma.

There are several factors related to the survival outcome of CM patients except the treatment modality, such as age, gender, primary site, tumor stage and so on. Older age was associated with an unfavorable prognosis of CM patients.^[23,24] Men diagnosed with CM had a survival disadvantage compared with women, which might result from the difference in behavior and/or biologic trait.^[23–25] There was an evidence suggesting that the tumor site played a crucial role in prognosis of CM patients, and the tumors in the middle and lower back, supramammary and mammary areas were independently associated with a poor prognosis.^[26] Additionally, distant metastases and thickness of the primary CM were also found to be prominent negative predictors of the survival outcome.^[27] After adjustment of

multiple confounding factors through IPTW using the propensity score, such as gender, age, tumor histology, primary site and so on, our results showed that the patients undergoing surgical resection had a reduced risk of death compared with those without surgical resection, manifesting a superiority of surgical resection in survival outcome.

To our knowledge, this observational study was the first to confirm the survival difference of CM patients undergoing surgery and those not undergoing surgery based on the propensity score and IPTW. IPTW, an effective method of reducing confounding bias in observational data, plays a key role in managing confounding bias of variables among multiple groups.^[28,29] Although the survival outcome of surgery and non-surgery groups was analyzed in detail before and after weighting, there were still some limitations in this study. Firstly, some information about specific surgical options, chemotherapy regimens, recurrence and adverse reactions was not recorded explicitly in the SEER database. Secondly, statistical approaches used in our study only ruled out the factors available in the SEER database, neglecting the risk of unrecorded confounders. Hence, in the future, more large-scale, well-designed randomized

Table 3
Cox regression analysis of the prognosis factors in unmatched, matched and IPTW-weighted cohorts.

Variables	Unmatched cohort		Matched cohort	IPTW-weighted cohort
	Univariate, HR (95%)	Multivariate, HR (95%)	Multivariate, HR (95%)	Multivariate, HR (95%)
Gender				
Male	–	–	–	–
Female	0.733 (0.633, 0.850) ^{***}	0.940 (0.806, 1.097) ^{***}	0.998 (0.698, 1.427)	1.016 (0.911, 1.133)
Age, years				
20–49	–	–	–	–
50–69	1.667 (1.286, 2.160) ^{***}	1.622 (1.245, 2.113) ^{***}	1.251 (0.708, 2.209)	1.842 (1.538, 2.206) ^{***}
≥70	4.533 (3.557, 5.776) ^{***}	4.011 (3.110, 5.172) ^{***}	2.275 (1.310, 3.950) ^{**}	3.810 (3.1885, 4.554) ^{***}
Year of diagnosis				
2004–2006	–	–	–	–
2007–2009	0.877 (0.733, 1.048)	0.823 (0.686, 0.989) [*]	0.782 (0.495, 1.235)	0.807 (0.699, 0.930) ^{**}
2010–2012	0.710 (0.588, 0.857) ^{***}	0.684 (0.565, 0.830) ^{***}	0.864 (0.553, 1.349)	1.080 (0.947, 1.231)
2013–2015	0.565 (0.446, 0.716) ^{***}	0.630 (0.495, 0.802) ^{***}	0.825 (0.492, 1.381)	1.020 (0.882, 1.192)
Tumor histology				
Superficial spreading	–	–	–	–
Nodular melanoma	3.274 (2.443, 4.387) ^{***}	1.219 (0.885, 1.679)	2.493 (0.918, 6.771)	1.520 (1.196, 1.931) ^{***}
Lentigo maligna melanoma	1.792 (1.259, 2.551) ^{**}	1.248 (0.868, 1.795)	1.922 (0.342, 10.787)	4.087 (3.160, 5.286) ^{***}
Other or unspecified	2.307 (1.862, 2.858) ^{***}	0.942 (0.744, 1.195)	1.723 (0.784, 3.785)	1.788 (1.504, 2.126) ^{***}
Primary site				
Scalp and neck	–	–	–	–
Trunk	0.604 (0.470, 0.775) ^{***}	0.825 (0.639, 1.064)	1.125 (0.562, 2.253)	0.967 (0.805, 1.163) ^{***}
Upper limbs and shoulder	0.569 (0.438, 0.739) ^{***}	0.686 (0.525, 0.897) ^{**}	0.814 (0.388, 1.707)	0.620 (0.511, 0.752) ^{***}
Lower limbs and hip	0.498 (0.371, 0.670) ^{***}	0.729 (0.534, 0.994) [*]	0.907 (0.411, 2.002)	0.920 (0.746, 1.134)
Skin, not otherwise specified	1.525 (1.201, 1.937) ^{***}	0.949 (0.728, 1.236)	0.934 (0.475, 1.836)	0.625 (0.516, 0.756) ^{***}
Grade				
I	–	–	–	–
II	0.808 (0.587, 1.112)	0.889 (0.643, 1.229)	0.668 (0.261, 1.713)	0.749 (0.584, 0.961) [*]
III	2.212 (1.676, 2.919) ^{***}	1.202 (0.902, 1.602)	1.214 (0.626, 2.354)	2.139 (1.780, 2.571) ^{***}
IV	2.582 (1.909, 3.492) ^{***}	1.187 (0.868, 1.623)	1.147 (0.551, 2.389)	1.913 (1.559, 2.347) ^{***}
AJCC stage, 6th				
I	–	–	–	–
II	3.896 (3.176, 4.778) ^{***}	1.636 (1.161, 2.305) ^{**}	1.010 (0.356, 2.837)	0.749 (0.584, 0.961) ^{***}
III	4.449 (3.510, 5.639) ^{***}	2.510 (1.622, 3.884) ^{***}	1.559 (0.444, 5.483)	2.139 (1.780, 2.571) ^{***}
IV	17.081 (14.010, 20.825) ^{***}	3.804 (1.799, 8.046) ^{***}	1.878 (0.379, 9.280)	1.913 (1.559, 2.347) ^{***}
Unstaged	2.926 (2.341, 3.657)	1.606 (1.159, 2.226) ^{**}	1.109 (0.468, 2.629)	1.913 (1.559, 2.347)
Summary stage				
Localized	–	–	–	–
Regional	2.895 (2.403, 3.488) ^{***}	1.101 (0.806, 1.503)	0.655 (0.257, 1.665)	0.563 (0.440, 0.719) ^{***}
Distant	10.849 (9.134, 12.887) ^{***}	2.112 (1.048, 4.254) [*]	2.163 (0.515, 9.078)	1.022 (0.549, 1.900)
Unknown/unstaged	2.128 (1.553, 2.916) ^{***}	1.135 (0.777, 1.659)	1.104 (0.581, 2.095)	0.722 (0.566, 0.922) ^{**}
AJCC T stage, 6th				
T0	–	–	–	–
T1	0.093 (0.073, 0.119) ^{***}	0.702 (0.469, 1.051)	0.636 (0.255, 1.579)	0.373 (0.282, 0.493) ^{***}
T2	0.213 (0.159, 0.285) ^{***}	1.206 (0.813, 1.789)	1.312 (0.517, 3.327)	1.407 (1.089, 1.817) ^{***}
T3	0.328 (0.248, 0.435) ^{***}	1.029 (0.694, 1.527)	1.404 (0.532, 3.708)	1.959 (1.522, 2.523) ^{***}
T4	0.522 (0.400, 0.679) ^{***}	1.485 (1.023, 2.157) [*]	1.376 (0.609, 3.106)	2.003 (1.583, 2.535) ^{***}
TX	0.519 (0.404, 0.668) ^{***}	1.167 (0.883, 1.544)	1.166 (0.628, 2.164)	0.913 (0.743, 1.122)
Number of in situ/malignant tumors				
≤2	–	–	–	–
>2	1.225 (1.064, 1.409) ^{***}	1.072 (0.925, 1.242)	1.064 (0.750, 1.510)	1.105 (0.995, 1.226)
Surgical treatment				
No	–	–	–	–
Yes	0.223 (0.190, 0.262) ^{***}	0.647 (0.509, 0.821) ^{***}	0.636 (0.459, 0.882) ^{**}	0.423 (0.383, 0.468) ^{***}

Grade represents differentiated degrees. AJCC=American Joint Committee on Cancer. ^{**} and ^{***} represent $P < .01$ and $P < .001$, respectively.

controlled trials are required for implementation to further verify our results.

5. Conclusions

Based on IPTW using the propensity score, CM patients receiving surgical treatment are associated with a better

survival outcome compared with those without surgical treatment.

Author contributions

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