RESEARCH ARTICLE

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Risk Factors Contributing to Disparities in Medical Treatment and Lower Survival Rates among Patients with Non-Small Cell Lung Cancer Induced by Residential Areas

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Abstract

Objective: Because of a lack of medical resources for cancer treatment, particularly in rural areas, there are disparities in receiving medical treatment between urban and rural area. This study examined the association between residential area or areal deprivation index (ADI) and lack of surgical treatment or chemotherapy in patients with non-small cell lung cancer (NSCLC) in rural area, Japan. **Methods:** We analyzed the Aomori population-based cancer registry data from 926 cancer patients with NSCLC diagnosed between January and December 2014. Multivariable logistic regression and Cox proportional hazards models were used to examine association of patients' residential area/ADI with either surgery/chemotherapy or survival time, respectively. The residential area was divided into six medical areas based on the location of specialist hospitals. The medical areas were defined by Aomori Prefecture. **Results:** The residential area (medical area) was strongly associated with access to cancer treatment for patients with NSCLC and ultimately contributed to lower survival rates. There was no significant influence in the distance from home to hospital and areal deprivation. **Conclusion:** We identified the risk factors related to a lack of medical treatment and shorter survival in rural area, Japan.

Keywords: disparity- areal deprivation index- treatment- surgery- chemotherapy- population-based cancer registry

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Introduction

Due to the lack of medical resources for cancer treatment particularly in rural areas, there are disparities in accessing medical treatment between urban and rural areas. Most patients with cancer require intensive treatment provided by specialist physicians or specialized medical resources. In many settings, a significant number of medical resources are concentrated in urban areas, leaving patients with cancer in rural areas burdened with long-distance travels for diagnosis and treatment. This disparity between urban and rural areas has resulted in lower patient survival rates in rural areas [1, 2]. Additionally, long-distance travel poses difficulties for certain patients, such as the elderly or those with comorbidities. Therefore, several factors may be related to travel distance to the hospital for patients with cancer receiving treatment [3-5].

There are disparities in cancer mortality rates among the 47 prefectures in Japan, and Aomori Prefecture, one of the depopulated areas in Japan, has had the highest cancer mortality rate since 2004 [6]. Aomori Prefecture is divided into six medical areas, and cancer-specialist hospitals are located in all areas except Area 4 (Figure 1). However, the distribution of specialist physicians and specialized medical resources is significantly biased, with a lack of lung cancer specialist physicians in Areas 4, 5, and 6 cancer specialist hospitals [7]. Many patients with cancer in Aomori are required to travel long distances to receive cancer treatment, especially surgery.

Non-small cell lung cancer (NSCLC) accounts for over 80% to 90% of all lung cancer cases. The treatment of NSCLC is stage-specific, and patients with stage I or II NSCLC should undergo complete surgical resection. Patients with NSCLC presenting with metastatic disease require systemic chemotherapy [8]. Therefore, examining whether standard NSCLC treatment is being administered is useful for estimating the disparity in medical resources between areas. This study aimed to clarify the risk factors contributing to the disparities in medical treatment among patients with NSCLC in Aomori.

Materials and Methods

Subjects

We analyzed data from 926 patients with NSCLC (using International Classification of Disease for Oncology, 3rd revision: ICD-O-3: C33-C34) diagnosed

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with their first primary cancer between January 1, 2014, and December 31, 2014, and were registered in the Aomori population-based cancer registry. The proportion of death certificate-only (DCO) and microscopically verified cases was 2.1% and 80.6%, respectively. We extracted the clinical and demographic information of the patients, including sex, age at diagnosis, date of diagnosis, address, hospital of the first visit, histological type, treatment decision (surgery and/or chemotherapy), date of death, and date of last contact. Patients aged over 100 years, those with in situ or small cell carcinoma (ICD-O-3: M8041/3), and those with DCO were excluded from the study.

Data availability

The data analyzed in this study are available in the Aomori Cancer Registry. Restrictions apply to the availability of the data, and in this study, the data were obtained under a license. Data are available from the authors upon reasonable request with permission from the Aomori Prefectural Government.

Areal deprivation index

Areal deprivation index (ADI) was calculated using Nakaya et al.'s formula using data collected during small subregional censuses as follows:

$ADI_i=k(2.99\times\text{proportion of old couple households}_i+7.57\times\text{proportion of old single households}_i+17.4\times\text{proportion of single-mother households}_i+2.22\times\text{proportion of rented houses and apartments}_i+4.03\times\text{proportion of sales and service workers}_i+6.05\times\text{proportion of agricultural workers}_i+5.38\times\text{proportion of blue-collar workers}_i+18.3\times\text{unemployment rate})$;

where i is the area index and k refers to a positive constant [9, 10]. The value k was determined to be 0.01575, based on the 2000 population census and estimated national poor household rate. The national poor household rate was defined by using the low income and subjective low social class identification, derived from representative nationwide social survey data (the Japanese General Society Survey data) [11].

We calculated the ADI of each small subregion in Aomori Prefecture in 2010 using a small subregional census (National Census, 2010). Then, by using the quintiles of ADI, the areas were categorized into area deprivation groups. Q1 indicates the least deprived group, while Q5 indicates the most deprived group. By including the patients' corresponding addresses in the area deprivation groups, we divided the patients into five deprivation groups.

Statistical analysis

The patients were classified into six groups according to their residential areas and five groups according to the area deprivation groups (Figure 1). Patients' characteristics were grouped as follows: age group (0-69, 70-79, and ≥ 80 years); distance from home to hospital at the first visit (0-19, 20-39, and over 40 km); type of hospital (specialist hospital or non-specialist hospital); histological type (squamous cell carcinoma [SCC], adenocarcinoma [ADC], and others); stage at diagnosis (localized, regional, distant, and unknown) [9]; surgery (surgery or not surgery); and chemotherapy (chemotherapy or no chemotherapy).

Multivariable logistic regression models were used to evaluate whether the risk of not undergoing surgery or chemotherapy was influenced by the patients' residential area. The relationship between residential area and survival time was evaluated using the Cox proportional hazards model. Multivariable logistic regression and Cox proportional hazards models were adjusted for sex, age, distance from home to the hospital at the first visit, type of hospital, histological type, stage at diagnosis, and residential area. All analyses were performed using Stata 15 software (Stata Corp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.).

Results

Patients' characteristics

Over half of patients living in areas 4, 5, and 6 traveled over 20 km to visit a hospital (Table 1). The first hospitals visited by almost all patients living in Areas 3, 5, and 6 were specialist hospitals. Deprivation was unequal among areas. Areas 1, 3, and 6 were relatively less deprived,

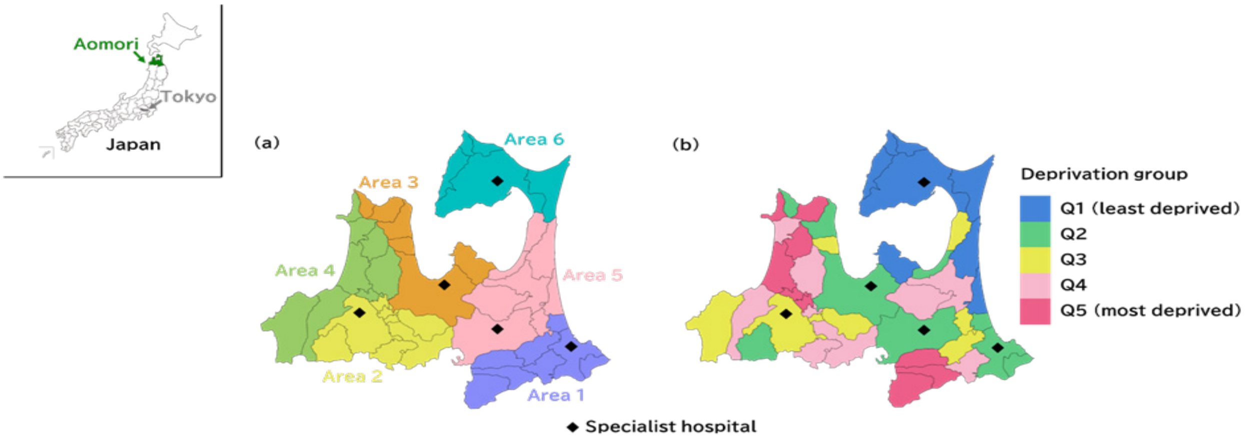

Figure 1. (a) Six medical areas in Aomori Prefecture, Japan. (b) Area deprivation group in Aomori Prefecture, Japan. Each diamond shape symbol represents a specialist hospital location. The area deprivation groups are divided into quintile based on the ADI. Q1 indicates the least deprived group, while Q5 indicates the most deprived group.

Table 1. Descriptive Characteristics by Medical Area in Aomori

		Residential area						p
		Area 1	Area 2	Area 3	Area 4	Area 5	Area 6	
Sex	Male	133 (66.2)	128 (66.0)	170 (64.9)	61 (66.3)	66 (62.9)	54 (72.0)	0.875
	Female	68 (33.8)	66 (34.0)	92 (35.1)	31 (33.7)	39 (37.1)	21 (28.0)	
Age	0-69 years	70 (34.8)	76 (39.2)	90 (34.4)	34 (37.0)	39 (37.1)	33 (44.0)	0.13
	70-79 years	78 (38.8)	74 (38.1)	96 (36.6)	30 (32.6)	51 (48.6)	23 (30.7)	
	80+ years	53 (26.4)	44 (22.7)	76 (29.0)	28 (30.4)	15 (14.3)	19 (25.3)	
Distance*	0-20 km	180 (89.6)	184 (94.8)	238 (90.8)	36 (39.1)	52 (49.5)	23 (30.7)	<0.001
	20-39 km	18 (9.0)	10 (5.2)	12 (4.6)	32 (34.8)	31 (29.5)	7 (9.3)	
	40+ km	3 (1.5)	0 (0.0)	12 (4.6)	24 (26.1)	22 (21.0)	45 (60.0)	
Deprivation group	Q1 (least deprived)	0 (0.0)	0 (0.0)	9 (3.4)	0 (0.0)	23 (21.9)	75 (100.0)	<0.001
	Q2	161 (80.1)	1 (0.5)	248 (94.7)	0 (0.0)	54 (51.4)	0 (0.0)	
	Q3	13 (6.5)	143 (73.7)	2 (0.8)	9 (9.8)	10 (9.5)	0 (0.0)	
	Q4	13 (6.5)	33 (17.0)	0 (0.0)	49 (53.3)	18 (17.1)	0 (0.0)	
	Q5 (most deprived)	14 (7.0)	17 (8.8)	3 (1.1)	34 (37.0)	0 (0.0)	0 (0.0)	
Type of hospital	Specialist hospital	117 (58.2)	73 (37.6)	215 (82.1)	37 (40.2)	84 (80.0)	72 (96.0)	<0.001
	Non-specialist hospital	84 (41.8)	121 (62.4)	47 (17.9)	55 (59.8)	21 (20.0)	3 (4.0)	
Histological type	SCC	52 (25.9)	41 (21.1)	67 (25.6)	18 (19.6)	32 (30.5)	15 (20.0)	0.623
	ADC	100 (49.8)	102 (52.6)	137 (52.3)	55 (59.8)	52 (49.5)	44 (58.7)	
	Others	49 (24.4)	51 (26.3)	58 (22.1)	19 (20.7)	21 (20)	16 (21.3)	
Stage at diagnosis	Localized	56 (27.9)	65 (33.5)	90 (34.4)	34 (37.0)	31 (29.5)	24 (32.0)	<0.001
	Regional	31 (15.4)	41 (21.1)	57 (21.8)	13 (14.1)	23 (21.9)	12 (16.0)	
	Distant	81 (40.3)	79 (40.7)	112 (42.7)	40 (43.5)	39 (37.1)	32 (42.7)	
	Unknown	33 (16.4)	9 (4.6)	3 (1.1)	5 (5.4)	12 (11.4)	7 (9.3)	
Surgery	Surgery	74 (36.8)	57 (29.4)	70 (26.7)	28 (30.4)	40 (38.1)	19 (25.3)	0.099
	No surgery	127 (63.2)	137 (70.6)	192 (73.3)	64 (69.6)	65 (61.9)	56 (74.7)	
Chemotherapy	Chemotherapy	110 (54.7)	74 (38.1)	93 (35.5)	36 (39.1)	50 (47.6)	38 (50.7)	<0.001
	No chemotherapy	91 (45.3)	120 (61.9)	169 (64.5)	56 (60.9)	55 (52.4)	37 (49.3)	

n (%); * Distance from home to hospital at the first visit; SCC, squamous cell carcinoma; ADC, adenocarcinoma

whereas Area 4 is the most deprived. The rates of surgical procedures ranged from 29.4% to 38.1%, while those of chemotherapy ranged from 35.5% to 54.7%. Other factors, such as sex, age, and histological type, did not differ among the different regional areas.

Risk factors of no medical treatment

The significant risk factors for not undergoing surgery were sex (male), age (≥ 70 years), histological type (SCC or other), stage at diagnosis (regional, distant, and unknown), and residential area (living in areas 2, 3, 4, 5, and 6) (Table 2a). The significant risk factors for not receiving chemotherapy were age (elderly), histological type (other), and residential area (living in areas 2, 3, 4, and 5). Adjusted odds ratios (OR) for patients who lived outside of regional area 1 were all above 2.00 compared to patients who lived in area 1. However, there was no significant association between area deprivation and not undergoing surgery or chemotherapy (Table 2b).

Risk factors of short survival

The significant risk factors for shorter survival were sex (male), age (≥ 70 years), type of hospital (non-specialist hospital), histological type (others), stage at diagnosis (regional, distant, and unknown), and residential area (living in Area 5) (Table 3a). The hazard ratio for patients who lived in Area 5 was 1.62 compared with patients who lived in Area 1. No significant association was observed between area deprivation and short survival (Table 3b).

Discussion

The residential area in Aomori influenced whether the patients underwent surgery or received chemotherapy for NSCLC. The survival times of patients who visited non-specialist hospitals first and those who lived in residential Area 5 were shorter than those of the other patients. However, there was no significant influence of distance from home to the hospital on area deprivation.

Several studies have also examined the influence of residential area on cancer treatment, with many focusing on residential socioeconomic status [12] For example, in southeastern Scotland, the association between economic deprivation and access to colorectal cancer treatment was not remarkable [12]. In Canada, residence in a high socioeconomic deprivation neighborhood is strongly associated with access to treatment for head and neck cancer [13].

Although our study did not consider residential

Table 2a. Multivariable Logistic Regression of Association between not Undergoing Surgery or Receiving Chemotherapy and Residential Area

		No surgery			No chemotherapy		
		OR**	p	95% CI	OR**	p	95% CI
Sex	Male	Reference			Reference		
	Female	0.52	0.005	(0.33, 0.82)	0.97	0.857	(0.67, 1.39)
Age	0-69 years	Reference			Reference		
	70-79 years	1.62	0.035	(1.03, 2.54)	2.12	<0.001	(1.48, 3.04)
	80+ years	12.7	<0.001	(6.58, 24.5)	8.39	<0.001	(5.21, 13.5)
Distance*	0-19 km	Reference			Reference		
	20-39 km	0.67	0.271	(0.33, 1.36)	1.02	0.929	(0.60, 1.75)
	40+ km	0.74	0.462	(0.33, 1.66)	1.17	0.625	(0.63, 2.19)
Type of hospital	Specialist hospital	Reference			Reference		
	Non-specialist hospital	1.44	0.169	(0.86, 2.43)	1.35	0.145	(0.90, 2.03)
Histological type	SCC	Reference			Reference		
	ADC	0.35	<0.001	(0.21, 0.58)	0.49	0.001	(0.32, 0.73)
	Others	2.73	0.009	(1.29, 5.81)	3.75	<0.001	(2.26, 6.22)
Stage at diagnosis	Localized	Reference			Reference		
	Regional	3.72	<0.001	(2.26, 6.13)	0.1	<0.001	(0.06, 0.17)
	Distant	57.2	<0.001	(31.6, 103.5)	0.1	<0.001	(0.06, 0.15)
	Unknown	227.8	<0.001	(26.9, 1927.3)	0.2	<0.001	(0.09, 0.43)
Residential area	Area 1	Reference			Reference		
	Area 2	3.81	<0.001	(1.94, 7.49)	2.65	<0.001	(1.58, 4.43)
	Area 3	4.98	<0.001	(2.63, 9.40)	3.36	<0.001	(2.08, 5.44)
	Area 4	3.49	0.007	(1.41, 8.63)	2.38	0.013	(1.20, 4.71)
	Area 5	2.3	0.048	(1.01, 5.27)	1.96	0.029	(1.07, 3.59)
	Area 6	6.74	<0.001	(2.34, 19.4)	1.51	0.208	(0.69, 3.29)

* Distance from home to hospital at the first visit; * *Adjusted for sex, age, histological type, distance, type of hospital, residential area. OR, Adjusted odds ratio; CI, confidence interval; SCC, squamous cell carcinoma; ADC, adenocarcinoma

Table 2b. Multivariable Logistic Regression of Association between not Undergoing Surgery or Receiving Chemotherapy and Deprivation Group

		No surgery			No chemotherapy		
		OR**	p	95% CI	OR**	p	95% CI
Sex	Male	Reference			Reference		
	Female	0.5	0.002	(0.32, 0.78)	0.99	0.907	(0.68, 1.40)
Age	0-69 years	Reference			Reference		
	70-79 years	1.63	0.031	(1.05, 2.52)	2.02	<0.001	(1.42, 2.88)
	80+ years	12.5	<0.001	(6.59, 23.8)	7.74	<0.001	(4.85, 12.3)
Distance*	0-19 km	Reference			Reference		
	20-39 km	0.53	0.061	(0.27, 1.03)	0.81	0.439	(0.47, 1.38)
	40+ km	0.77	0.464	(0.38, 1.56)	0.9	0.731	(0.50, 1.62)
Type of hospital	Specialist hospital	Reference			Reference		
	Non-specialist hospital	1.17	0.526	(0.72, 1.91)	1.2	0.364	(0.81, 1.77)
Histological type	SCC	Reference			Reference		
	ADC	0.38	<0.001	(0.23, 0.62)	0.48	<0.001	(0.32, 0.72)
	Others	2.86	0.005	(1.37, 5.97)	3.65	<0.001	(2.22, 6.01)
Stage at diagnosis	Localized	Reference			Reference		
	Regional	3.49	<0.001	(2.16, 5.65)	0.11	<0.001	(0.07, 0.18)
	Distant	46.5	<0.001	(26.6, 81.3)	0.1	<0.001	(0.07, 0.15)
	Unknown	99.9	<0.001	(12.6, 791.0)	0.14	<0.001	(0.07, 0.30)
Deprivation group	Q1 (least deprived)	Reference			Reference		
	Q2	0.59	0.174	(0.27, 1.27)	0.88	0.681	(0.48, 1.61)
	Q3	0.8	0.593	(0.35, 1.83)	1.01	0.973	(0.51, 1.99)
	Q4	0.77	0.569	(0.32, 1.88)	1.33	0.43	(0.66, 2.70)
	Q5 (most deprived)	0.98	0.964	(0.36, 2.62)	1.58	0.272	(0.70, 3.55)

*, Distance from home to hospital at the first visit; ** Adjusted for sex, age, histological type, distance, type of hospital, deprivation area; OR, adjusted odds ratio; CI, confidence interval; SCC, squamous cell carcinoma; ADC, adenocarcinoma

Table 3a. Multivariable Cox Proportional Hazard Models of Association between Survival Time and Residential Area

		HR**	p	95% CI
Sex	Male	Reference		
	Female	0.6	<0.001	(0.46, 0.77)
Age	0-69 years	Reference		
	70-79 years	1.5	0.003	(1.15, 1.97)
	80+ years	1.94	<0.001	(1.47, 2.56)
Distance*	0-19 km	Reference		
	20-39 km	0.79	0.209	(0.54, 1.14)
	40+ km	0.71	0.111	(0.46, 1.08)
Type of hospital	Specialist hospital	Reference		
	Non-specialist hospital	1.37	0.014	(1.06, 1.76)
Histological type	SCC	Reference		
	ADC	0.85	0.219	(0.66, 1.10)
	Others	1.53	0.003	(1.16, 2.02)
Stage at diagnosis	Localized	Reference		
	Regional	2.9	<0.001	(1.93, 4.35)
	Distant	5.83	<0.001	(4.10, 8.29)
	Unknown	5.07	<0.001	(3.08, 8.33)
Residential area	Area 1	Reference		
	Area 2	1.21	0.256	(0.87, 1.69)
	Area 3	1.18	0.308	(0.86, 1.64)
	Area 4	1.43	0.118	(0.91, 2.23)
	Area 5	1.62	0.021	(1.08, 2.44)
	Area 6	1.62	0.076	(0.95, 2.76)

*, Distance from home to hospital at the first visit; **, Adjusted for sex, age, histological type, distance, type of hospital, residential area; HR, adjusted hazard ratio; CI, confidence interval; SCC, squamous cell carcinoma; ADC, adenocarcinoma

Table 3b. Multivariable Cox Proportional Hazard Models of Association between Survival Time and Residential Area

		HR**	p	95% CI
Sex	Male	Reference		
	Female	0.59	<0.001	(0.46, 0.76)
Age	0-69 years	Reference		
	70-79 years	1.58	0.001	(1.21, 2.07)
	80+ years	2.03	<0.001	(1.54, 2.68)
Distance*	0-19 km	Reference		
	20-39 km	0.85	0.395	(0.58, 1.24)
	40+ km	0.75	0.176	(0.49, 1.14)
Type of hospital	Specialist hospital	Reference		
	Non-specialist hospital	1.25	0.081	(0.97, 1.61)
Histological type	SCC	Reference		
	ADC	0.84	0.195	(0.65, 1.10)
	Others	1.55	0.002	(1.18, 2.04)
Stage at diagnosis	Localized	Reference		
	Regional	2.99	<0.001	(1.99, 4.49)
	Distant	5.83	<0.001	(4.10, 8.30)
	Unknown	5.51	<0.001	(3.39, 8.98)
Deprivation group	Q1 (least derived)	Reference		
	Q2	0.69	0.056	(0.47, 1.01)
	Q3	0.68	0.089	(0.43, 1.06)
	Q4	1.02	0.948	(0.64, 1.60)
	Q5 (most deprived)	0.58	0.051	(0.34, 1.00)

*, Distance from home to hospital at the first visit; **, Adjusted for sex, age, histological type, distance, type of hospital, residential area; HR, adjusted hazard ratio; CI, confidence interval; SCC, squamous cell carcinoma; ADC, adenocarcinoma

socioeconomic status, the low survival rate in Area 5 may have been influenced by economic deprivation. In Aomori Prefecture, the smoking rate was higher than the Japanese average, and the obesity rate (body mass index ≥ 25 kg/m2) was higher than the national average [14]. Patients who smoked had a higher background mortality and greater variations in comorbidity than non-smokers. Therefore, the patients living in Area 5 may have had a higher prevalence of comorbid conditions. Further research is needed to clarify the association of cancer survival rates with socioeconomic status and comorbidities.

Although the doctors preference is to refer patients with cancer to another hospital when more intensive and specialized therapy are required; however, medical resources, such as specialist physicians may have been lacking in Area 5. This could be due to ineffective functioning of the hospital network. In contrast, there were no specialist physicians in Areas 4 and 6 and there was no difference between their one-year survival rates. This is because the hospital network works well in Areas 4 and 6, ensuring that patients receive appropriate treatment. A previous study that examined hospital and physician volume or specialization on outcomes in patients with cancer reported a volume-outcome relationship in the treatment of patients with lung cancer [15]. Therefore, making changes in the hospital network to improve the access to appropriate treatment by patients with cancer in Area 5, might extend their survival rates.

The following limitations of the study should be noted. First, ADI may be inappropriate for estimating deprivation in rural areas. Because of the larger number of agricultural, forestry, and fishery workers compared with the national average in the entire area of Aomori, it might be difficult to observe a significant difference in small subregions. Second, we did not available the cancer registry data in Aomori after 2014, and we did not examine the long-term survival rates. This is because we were unable to utilize the cancer registry data in Aomori after 2014 owing to database migration. However, a difference was apparent in the one-year survival rates, which clearly reflect disparity in the medical treatments provided.

In conclusion, We identified risk factors related to the lack of medical treatment and shorter survival in Aomori, Japan. Residential area is strongly associated with undergoing cancer treatment for NSCLC and ultimately contributes to lower survival rates.

Author Contribution Statement

Rina Tanaka: Conceptualization, Methodology, Formal analysis, Writing-original draft, Writing-review & editing. Masashi Matsuzaka: Writing-original draft, Writing-review & editing. Yoshihiro Sasaki: Writing-review & editing.

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Ethical considerations

This study was approved by the ethics committee of Hirosaki university graduate school of medicine.

Data availability

The data analyzed in this study are available in the Aomori Cancer Registry. Restrictions apply to the availability of the data, and in this study, the data were obtained under a license. Data are available from the authors upon reasonable request with permission from the Aomori Prefectural Government.

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