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Impact of Travel Distance on Surgical Outcomes of Patients Surgically Treated for Non-Small Cell Lung Cancer: A Single-Center Study in Ehime, Japan

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Travel burden is a poor prognostic factor for many cancers worldwide because it hinders optimal diagnosis and treatment planning. Currently, the impact of travel burden on survival after surgery for non-small cell lung cancer (NSCLC) in Japan is largely unexplored. We examined the impact of travel distance on the postoperative outcomes of patients with NSCLC in Ehime Prefecture, Japan. The data of 1212 patients who underwent surgical resection for NSCLC were retrospectively reviewed. Patients were divided into quartiles based on the travel distance from their home to the hospital (≤13 km, 13-40 km, 40-57 km, and >57 km) in Ehime Prefecture. We found no significant differences among the quartiles in baseline clinicopathological characteristics, including sex, smoking status, histology, surgical procedure, clinical stage, and pathological stage. Overall survival (OS) and relapse-free survival (RFS) also were not significantly different among the travel distance quartiles. We conclude that travel distance did not impact OS or RFS among patients with NSCLC who underwent surgical resection at our institution.

Key words: non-small cell lung cancer, travel distance, travel burden, lung surgery, surgical outcome

In addition to tumor characteristics, sociodemographic factors such as race, ethnicity, sex, socioeconomic status, education level, and insurance type have important albeit passive roles in the management of patients with cancer [1]. Geographic factors, such as long travel distances and remote residential areas, may influence diagnosis, treatment, and outcomes for patients with cancer as they limit access to care. Long travel distances to specialized hospitals may contribute to physical and psychological distress and impede early diagnosis, timely interventions, and optimal follow-up care after cancer management [2,3]. Stoyanov *et al.* [4] reported a significant association between poorer survival and increased travel burden in patients with lung cancer. Travel expenses are non-medical costs sometimes referred to as "financial toxicity", which can be a matter of concern for patients with cancer and their families [5]. A study based on the data from the Surveillance, Epidemiology, and End Results Medicare-linked database concluded that travel distance needs to be acknowledged as a potential barrier to high-quality care for major cancer surgeries [6]. However, a recent review in the United States did not find a consistent relationship between travel distance and whether a patient received surgery [7]. Patients with early-stage non-small cell lung cancer (NSCLC) traveling long distances to high-volume hospitals

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reportedly have improved short- and long-term survival [8]. A positive association between the number of surgeries performed at high-volume hospitals and excellent outcomes has been reported for major cancer surgeries [9]. When considering the relationship between long travel distances and high-volume hospitals providing high-quality care, the survival impact of travel burden remains a controversial issue in countries implementing a policy of centralization for cancer care [10, 11].

As health service regions in Japan are smaller in scale than those in the United States and Europe, travel burden (measured as distance or time from a patient's residence to the hospital) may be overlooked in routine clinical practice. There has been insufficient analysis of the impact of travel burden on survival after cancer treatment in Japan [12]. Takenaka *et al.* [13] reported that the distance between the home and the hospital did not influence the long-term outcomes of patients with NSCLC who underwent surgical resection. That study was conducted in Fukuoka city, which has a population of 1.6 million (https://www.city.fukuoka.lg.jp accessed Nov, 2022) and is one of the major metropolitan areas in Japan. In comparison, the entirety of Ehime Prefecture, has a population of 1.3 million (https://www.pref.ehime.jp accessed Nov, 2022), with geographical and social environments that differ from those of Fukuoka Prefecture. The approximate extent of Ehime Prefecture is 150 km (from both east to west and north to south), and it includes high mountains and many islands. This prefecture has been historically divided into three regions: central (*Chuyo*), eastern (*Toyo*), and southern (*Nanyo*) areas. The NHO Shikoku Cancer Center is located in Matsuyama city (central area), which is the capital and largest town in Ehime Prefecture. In addition, lung surgeries are performed at a small number of specialist hospitals located in this central area by general thoracic surgeons certified by the Japanese Association for Chest Surgery (JACS) (https://www.jacsurg.gr.jp). Thus, patients living in the eastern and southern areas have to travel farther than those living in the central area. In this single-center study, we examined the impact of travel distance on the postoperative outcomes of patients with NSCLC who underwent surgical resection in Ehime Prefecture.

Materials and Methods

From January 2013 to March 2021, 1270 patients with NSCLC and no treatment history underwent lung resection with curative intent at our institution. After excluding patients living outside Ehime Prefecture (n = 50) and isolated islanders (n = 8), a total of 1212 patient records were available for retrospective analysis (Fig. 1). During the study period, we performed an average of 176 pulmonary resections for primary lung cancer per year at our institution. All surgeries were

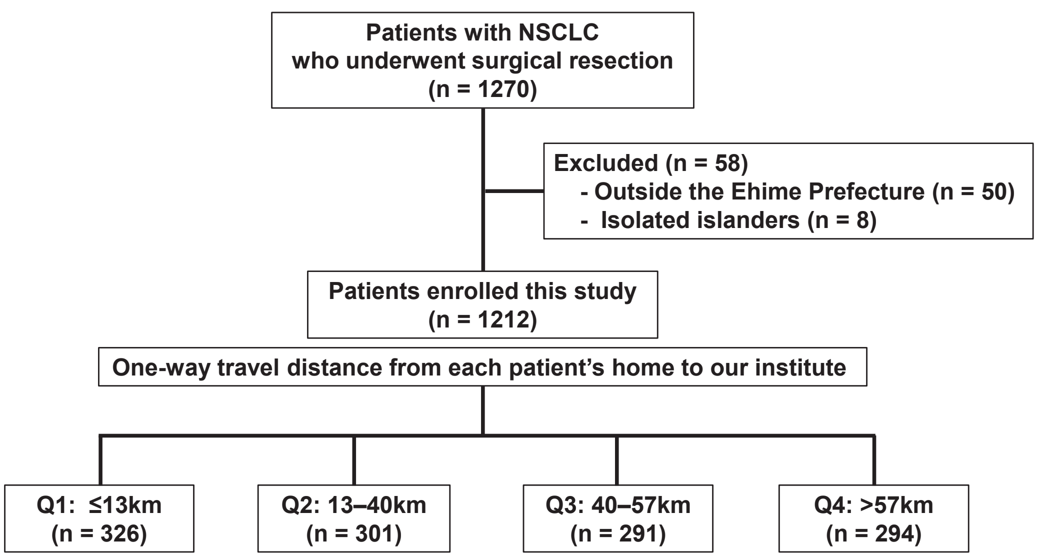

Fig. 1 Flowchart of patient selection. Travel distance was stratified into quartiles (Q1–Q4). NSCLC, non-small cell lung cancer.

performed by four (M.Y., H.S., H.S. and T.U.) thoracic surgeons certified by the JACS. The time of the data cutoff was October 1, 2022.

Clinicopathological characteristics including age, sex, smoking status, histology, surgical procedure, clinical/pathological stage, and survival data were reviewed from medical records. After surgery, patients were assessed at our institution at 3- to 6-month intervals for at least 5 years. However, some patients were followed by their local primary care clinicians or were lost to follow up. Patients were categorized into four groups according to the one-way travel distance from their residence to our institute (Fig. 1). The travel distance was stratified into quartiles with approximately equal numbers of patients in each quartile [14]. The first to third quartile values were 13 km, 40 km, and 57 km, respectively; thus, a travel distance of up to 13 km was the first quartile (Q1), and a travel distance of over 57 km was the fourth quartile (Q4). Travel distance and travel time were calculated by determining the shortest driving distance and time from the patient's residence (based on the postcode) to our institute using Google Maps (Google Inc., Mountain View, CA, USA; retrieved from http://www.google.co.jp/maps). This reflected the actual travel distance and time better than the straight-line distance would have [4, 15].

Continuous variables are presented as medians and interquartile ranges (IQRs), and categorical variables as numbers and percentages. Groups were compared using Fisher's exact test for categorical variables and the Kruskal–Wallis test for continuous variables. The Kaplan–Meier survival curve was used to analyze overall survival (OS) and relapse-free survival (RFS). The log-rank test was performed to compare the differences in OS and RFS among the groups. Univariable and multivariable Cox proportional hazards regression models were used to estimate hazard ratios (HRs) for OS and RFS. All p-values were two-sided, and p-values < 0.05 were considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria; version 2.13.0) [16].

This study was approved by the Institutional Review Board of the NHO Shikoku Cancer Center (2021-47). The need for written informed consent was waived because of the retrospective study design.

Results

The median age of the 1212 patients was 69 years (IQR, 63-74 years), and 615 (51%) patients were male. The median follow-up period for all populations was 49 months (IQR, 26-71 months), and that for patients alive at the time of analysis was 52 months (IQR, 29-72 months). Overall, the median travel distance was 40 km (IQR, 13-57 km) and estimated travel time was 44 min (IQR, 26-60 min). Among 1212 patients, 1039 (86%) were diagnosed with NSCLC of adenocarcinoma histology and 1029 (85%) with clinical stage 0 or I cancer. Lobectomy was performed in 836 (69%) patients, and pathological stage 0 or I was diagnosed in 963 (79%) patients.

Patient characteristics according to travel distance are summarized in Table 1. There were no differences in the median age or median length of follow-up among the groups. There were also no significant differences among the groups in the clinicopathological characteristics, including sex, smoking status, histology, surgical procedure, clinical stage, and pathological stage.

The long-term survival curves are shown in Fig. 2. The 5-year OS (95% confidence interval) rates were 91.3% (86.7-94.3), 86.1% (80.5-90.1), 87.5% (82.3-91.3), and 85.8% (80.2-89.8) in the Q1-Q4 groups, respectively. The 5-year RFS (95% confidence interval) rates were 84.6% (79.5-88.6), 78.5% (72.6-83.3), 80.0% (74.1-84.7), and 79.1% (73.2-83.9) in the Q1-Q4 groups, respectively. Although the survival curve in the Q1 group tended to be more favorable than that in other groups, there were no significant differences in OS (overall log-rank test: $p = 0.14$) (Fig. 2A) or RFS (overall log-rank test: $p = 0.25$) (Fig. 2B) based on travel distance.

A multivariable Cox proportional hazards regression model was used to evaluate the impact of travel distance as well as age, sex, smoking status, histology, and pathological stage, which have been shown to be clinical factors relevant to NSCLC prognosis. Older age, non-adenocarcinoma histology, and advanced pathological stage were independent poor prognostic factors for OS and RFS (Table 2). Patients with greater travel distances (Q2, Q3, and Q4 groups) had unfavorable HRs for OS and RFS, but these results were not statistically significant.

Table 1 Patients characteristics by travel distance

		Q1: <13 km n = 326	Q2: 13-40 km n = 301	Q3: 40-57 km n = 291	Q4: >57 km n = 294	*P*-value
Age (years)	Median [IQR]	68 [61-74]	68 [64-74]	69 [64-74]	69 [63-74]	0.182
Follow -up period (months)	Median [IQR]	49 [29-72]	49 [25-71]	49 [26-72]	48 [24-66]	0.328
Sex, n (%)	Male	153 (47)	153 (51)	152 (52)	157 (53)	0.394
	Female	173 (53)	148 (49)	139 (48)	137 (47)	
Smoking status, n (%)	Never	153 (47)	132 (44)	131 (45)	129 (44)	0.849
	Ever	173 (53)	169 (56)	160 (55)	165 (56)	
Histology, n (%)	Adenocarcinoma	279 (86)	255 (85)	248 (85)	257 (87)	0.710
	Squamous cell	38 (12)	32 (11)	35 (12)	30 (10)	
	Others	9 (3)	14 (5)	8 (3)	7 (2)	
Surgical procedure, n (%)	Lobectomy	215 (66)	207 (69)	201 (69)	213 (72)	0.338
	Segmentectomy	54 (17)	39 (13)	47 (16)	45 (15)	
	Wedge	57 (17)	55 (18)	43 (15)	36 (12)	
c-stage, n (%)	0	14 (4)	13 (4)	9 (3)	11 (4)	0.643
	I	271 (83)	245 (81)	232 (79)	234 (80)	
	II	30 (9)	26 (9)	38 (13)	33 (11)	
	III-IV	11 (3)	17 (6)	12 (4)	16 (5)	
p-stage, n (%)	0	33 (10)	25 (8)	21 (7)	17 (6)	0.498
	I	234 (72)	219 (73)	204 (70)	210 (71)	
	II	32 (10)	27 (9)	30 (10)	29 (10)	
	III-IV	27 (8)	30 (10)	36 (12)	38 (13)	

IQR, interquartile range.

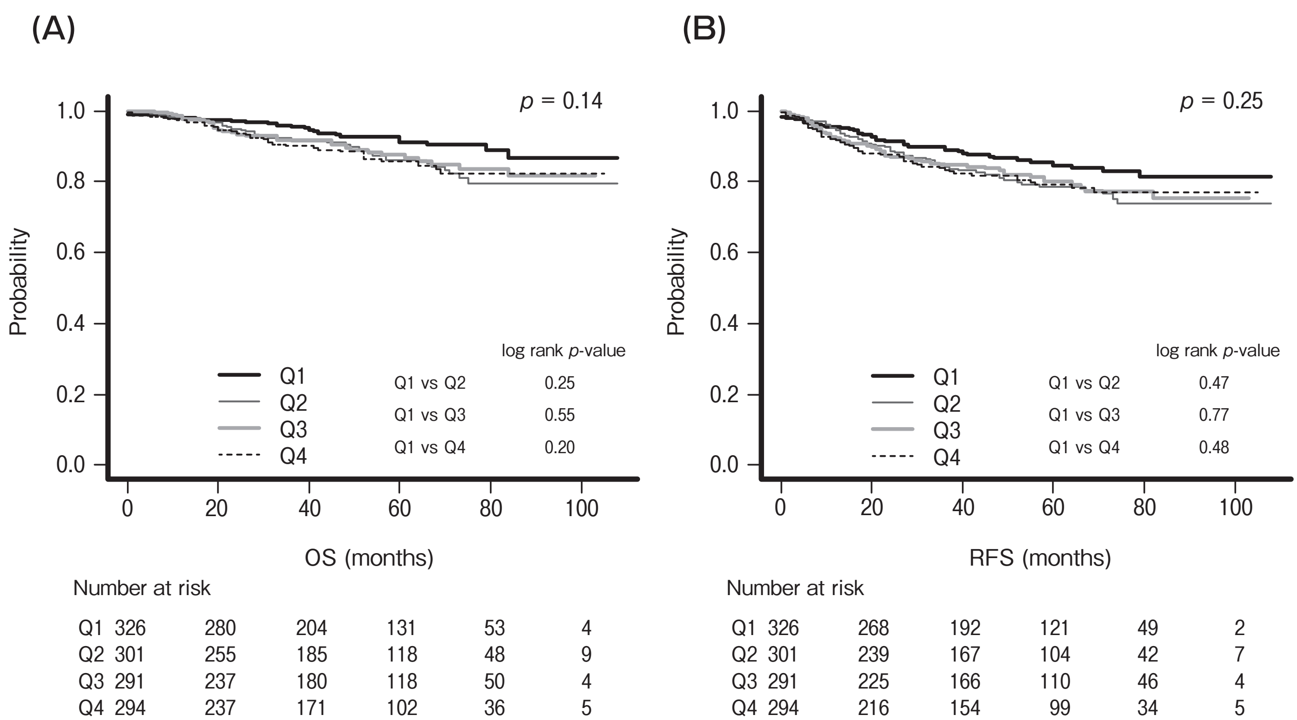

Fig. 2 Kaplan-Meier curves for OS (**A**) and RFS (**B**) according to travel distance.
OS, overall survival; RFS, relapse-free survival.

Table 2 Association of clinicopathological factors with OS and RFS in a multivariate Cox proportional hazards model

Variable		Multivariate for OS			Multivariate for RFS		
		HR	95% CI	*P*-value	HR	95% CI	*P*-value
Age (years)	<75	Ref			Ref		
	≧75	1.69	1.16–2.46	0.006*	1.38	1.02–1.88	0.039*
Sex	Male	Ref			Ref		
	Female	1.05	0.62–1.78	0.851	1.12	0.75–1.68	0.583
Smoking status	Never	Ref			Ref		
	Ever	1.54	0.86–2.74	0.146	1.39	0.90–2.13	0.135
Histology	Adenocarcinoma	Ref			Ref		
	Squamous cell	1.76	1.13–2.76	0.013*	1.18	0.80–1.72	0.400
	Others	2.33	1.24–4.38	0.009*	2.31	1.39–3.85	0.001*
p-stage	0–I	Ref			Ref		
	II	4.34	2.64–7.13	<0.001*	4.78	3.22–7.12	<0.001*
	III–IV	10.79	7.15–16.30	<0.001*	14.10	10.17–19.54	<0.001*
Travel distance	Q1: ≦13 km	Ref			Ref		
	Q2: 13–40 km	1.61	0.96–2.71	0.072	1.34	0.90–1.99	0.155
	Q3: 40–57 km	1.34	0.79–2.29	0.278	1.17	0.78–1.75	0.456
	Q4: >57 km	1.47	0.87–2.49	0.149	1.19	0.80–1.79	0.394

OS, overall survival; RFS, relapse-free survival; HR, hazard ratio; CI, confidence interval; Ref, reference.
*statistically significant *p*-values.

Discussion

In this single-center study, we evaluated the impact of travel distance on the survival of patients with NSCLC who underwent surgery in Ehime Prefecture. Our findings revealed no significant differences in OS or RFS based on travel distance. Therefore, patients from Ehime Prefecture who can access our institution can expect comparable surgical outcomes, regardless of the distance from residences to the hospital. However, since information on willingness to select facilities for treatment was not available, a possible selection bias cannot be excluded.

The Japanese health care system has two major policies: universal health insurance and free access to care [17]. However, a limited number of studies have evaluated the effect of travel distance or time to facilities, especially for patients with cancer. Tanaka *et al.* [12] reported that most patients with cancer (78% of 50,845 patients with seven types of cancers) in Japan resided within a 45-min driving distance from the nearest hospital. Variations in travel time across prefectures were also observed, and the proportion of patients with travel times exceeding 45 min was 31% in Ehime Prefecture. Further, the accessibility of treatment for liver and lung cancers was inferior to those for stomach and colorectal cancers; this was most likely due to the limited specialized medical resources. In our study, the median travel distance and travel time were 40 km and 44 min, respectively, and 47% (568 of 1212 patients) of the patients had travel times exceeding 45 min. As mentioned above, specialized hospitals for the treatment of lung cancer are generally located in the central area of Ehime Prefecture; therefore, patients residing in the eastern and southern areas traveled farther than those residing in the central area. Owing to the disproportionate distribution of thoracic surgeons and pulmonologists, the number of highly specialized centers in Ehime Prefecture is limited. These centers are concentrated in the central area, which has a large population. Lung surgery for NSCLC patients has become regionalized, which has increased the travel distance for patients in the outlying areas of Ehime Prefecture.

No association was observed between the cancer stage at the time of diagnosis and travel distance in our study. The proportions of clinical and pathological stages were comparable regardless of the travel distance. This indicates that the referral system for primary care clinicians functions well and causes few diagnostic and treatment delays. Bostock *et al.* [18] reported that patients who travel further have progressively poorer adherence to the recommended surveillance course over time. This is concerning, as inappropriate follow-up care reduces the chances of detecting recurrence or second primary lung cancer. In our study, the follow-up period after surgery did not vary by travel distance. We collaborate with primary care clinicians who are in remote locations using the postoperative clinical pathway to monitor disease recurrence and progression. However, we did not perform comprehensive evaluation of the data from patients with adjuvant chemotherapy or those with recurrence who needed chemotherapy or radiotherapy. The possibility that travel distance influenced postoperative treatment cannot be ruled out.

In addition to travel distance, residential area (*i.e.*, rural-urban areas, regional deprivation, residential segregation) may be associated with cancer survival [19]. Notably, Tamura *et al*. [20] reported that living environment and lifestyle, including the dietary habits of each region (central, eastern, and southern), influence the mortality of non-cancerous diseases in Ehime Prefecture. However, to date, the effect of regional health-related lifestyle factors on cancer mortality has not been explored. Future studies should investigate the characteristics and mortality rates of patients with lung cancer in each region.

Older age, non-adenocarcinoma histology, and advanced pathological stage were independent poor prognostic factors for OS and RFS in this study. Patients with long travel distances showed unfavorable HRs; however, the travel distance was not associated with OS or RFS in our multivariate analysis. Previous research on surgically resected lung cancer cases from Japan also concluded that travel distance did not influence long-term outcomes, although half of the patients lived within a radius of 10 km from the hospital [13]. In Japan, the travel distance seems to be tolerable in terms of survival, at least for patients who undergo surgical resection for lung cancer. However, the results may vary from prefecture to prefecture. To confirm this, it is important to analyze and compare the impact of travel distance on survival in other Japanese prefectures. Additional research may improve the quality and uniformity of access to care for lung cancer in the Japanese health care system.

Our study has some potential limitations. First, this study lacked statistical power because of its single-center retrospective design and small sample size in each quartile. Therefore, the results do not demonstrate meaningful differences in the impact of travel distance on survival. Further studies with large sample sizes and longitudinal follow-ups are warranted. Moreover, this study was limited to the surgical treatment of NSCLC patients and did not take into consideration the characteristics of patients with advanced cancer stages (clinical stage IIIB or IV). Therefore, the populations under consideration in this study may not be representative of all cancer stages in patients with lung cancer. Future studies examining treatment options other than surgery, such as chemotherapy and radiotherapy, are necessary to clarify travel burden as a barrier to care in a real-world setting among all patients with lung cancer. Second, the modes of travel were not accounted for in this study. We assumed that patients traveled by car, similar to the study populations in the majority of previous works on this subject [4]. Further, we explicitly excluded patients living on isolated islands arriving by ship. We may have underestimated the actual travel distance or time, considering the lack of public transportation in some areas, in which case patients without private vehicles may have taken more time to travel than that inferred from online maps. Lastly, this study focused on Ehime Prefecture, which is at an intermediate level in terms of population size and surface area among 47 prefectures; therefore, the distance cutoffs may not apply to all other prefectures or countries.

In summary, the results of this study indicate that surgical outcomes are not seriously affected by travel distance. Patients with NSCLC who underwent surgical resection at our institution in Ehime Prefecture had equivalent survival, regardless of travel distance. However, a long travel distance to the hospital is perceived as inconvenient and a hardship for some patients, especially for older patients and those with limited access to transportation. A better understanding of the impact of travel burden on surgical outcomes in such patients is crucial. Further studies should evaluate the impact of travel burden on treatment compliance, satisfaction, financial aspects, and quality of life among patients with lung cancer, as well as their families.

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References

1. Singh S and Sridhar P: A narrative review of sociodemographic risk and disparities in screening, diagnosis, treatment, and outcomes of the most common extrathoracic malignancies in the United States. J Thorac Dis (2021) 13: 3827–3843.
2. Ambroggi M, Biasini C, Del Giovane C, Fornari F and Cavanna L: Distance as barrier to cancer diagnosis and treatment: review of the literature. Oncologist (2015) 20: 1378–1385.
3. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J and Little J: Rural and urban differences in stage at diagnosis of colorectal and lung cancers. Br J Cancer (2001) 84: 910–914.
4. Stoyanov DS, Conev NV, Donev IS, Tonev ID, Panayotova TV and Dimitrova-Gospodinova EG: Impact of travel burden on clinical outcomes in lung cancer. Support Care Cancer (2022) 30: 5381–5387.
5. Lee A, Shah K and Chino F: Assessment of parking fees at National Cancer Institute-designated cancer treatment centers. JAMA Oncol (2020) 6: 1295–1297.
6. Stitzenberg KB, Chang Y, Smith AB and Nielsen ME: Exploring the burden of inpatient readmissions after major cancer surgery. J Clin Oncol (2015) 33: 455–464.
7. Herb J, Shell M, Carlson R and Stitzenberg K: Is long travel distance a barrier to surgical cancer care in the United States? A systematic review. Am J Surg (2021) 222: 305–310.
8. Muslim Z, Baig MZ, Weber JF, Connery CP and Bhora FY: Traveling to a high-volume center confers improved survival in stage I non-small cell lung cancer. Ann Thorac Surg (2022) 113: 466–472.
9. Begg CB, Cramer LD, Hoskins WJ and Brennan MF: Impact of hospital volume on operative mortality for major cancer surgery. JAMA (1998) 280: 1747–1751.
10. Kelly C, Hulme C, Farragher T and Clarke G: Are differences in travel time or distance to healthcare for adults in global north countries associated with an impact on health outcomes? A systematic review. BMJ Open (2016) 6: e013059.
11. Versteeg SE, Ho VKY, Siesling S and Varkevisser M: Centralization of cancer surgery and the impact on patients' travel burden. Health Policy (2018) 122: 1028–1034.
12. Tanaka H, Ishikawa KB and Katanoda K: Geographic access to cancer treatment in Japan: results from a combined dataset of the patient survey and the survey of medical institutions in 2011. J Epidemiol (2018) 28: 470–475.
13. Takenaka T, Inamasu E, Yoshida T, Toyokawa G, Nosaki K, Hirai F, Yamaguchi M, Seto T, Takenoyama M and Ichinose Y: Influence of the distance between home and the hospital on patients with surgically resected non-small-cell lung cancer. Eur J Cardiothoracic Surg (2016) 49: 842–846.
14. Knisery A, Huang Y, Melamed A, Tergas AI, St. Clair CM, Hou JY, Khoury-Collado F, Ananth CV, Neugut AI, Hershman DL and Wright JD: Travel distance, hospital volume and their association with ovarian cancer short- and long-term outcomes. Gynecol Oncol (2020) 158: 415–423.
15. Haddad AQ, Singla N, Gupta N, Raj GV, Sagalowsky AI, Margulis V and Lotan Y: Association of distance to treatment facility on quality and survival outcomes after radical cystectomy for bladder cancer. Urology (2015) 85: 876–882.
16. Kanda Y: Investigation of the freely-available easy-to-use software "EZR" (Easy R) for medical statistics. Bone Marrow Transplant (2013) 48: 452–458.
17. Kobayashi D, Otsubo T and Imanaka Y: The effect of centralization of health care services on travel time and its equality. Health Policy (2015) 119: 298–306.
18. Bostock IC, Hofstetter W, Mehran R, Rajaram R, Rice D, Sepesi B, Swisher S, Vaporciyan Am Waksh G and Antonoff MB: Barriers to surveillance imaging adherence in early-staged lung cancer. J Thorac Dis (2021) 13: 6848–6854.
19. Afshar N, English DR and Milne RL: Rural-urban residence and cancer survival in high-income countries: a systematic review. Cancer (2019) 125: 2172–2184.
20. Tamura Y, Saito I, Asada Y, Kishida T, Yamaizumi M, Yamauchi K and Kato T: Comparison of regional differences in health indicators and standard mortality ratio for stroke in subjects in Ehime Prefecture. J Rural Med (2013) 8: 198–204.