Research Article,

Regional Variation in Lung Cancer Stage at an Irish Rapid Access Lung Clinic

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Abstract:

Introduction: Regional variation in cancer outcomes is undesirable. We aim to evaluate regional variation in lung cancer in Ireland focusing on stage at presentation.

Methods: A retrospective study was performed on patients who underwent surgical resection of primary lung cancer from June 2013 to March 2020. Patients included attended the St. Vincent's University Hospital rapid access lung clinic (RALC). Patients were divided into two groups depending on regional variability with Dublin and Wicklow assigned as Group 1 and the remainder assigned to Group 2. Pathological tumour size and lymph node status were compared between the two groups.

Results: Complete data was available on 152 patients. Group 1 (n=97) had significantly lower median tumour size (24.74 mm) compared to Group 2 (31.72 mm) (P = 0.026). Patients in group 1 had significantly lower stage (stage II 13.4%, stage III 9.3%) compared to Group 2 (stage II 29%, stage III 16.3%) (P = 0.013). Group 1 showed a lower incidence of squamous cell carcinoma (21.6%) compared to Group 2 (30.9%).

Conclusion: Regional variation in cancer presentation is evident in this study. Larger tumors and more advance stage are associated with a more rural location. This is seen in a clinic service with equal access of both populations to diagnostic modalities and treatment, suggesting differences at presentation rather than evaluation.

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Introduction:

Lung cancer in Ireland is the most common cause of cancer death with most patients are diagnosed at an advanced stage. 1, 2

Literature shows that people who live far from treatment centers may have a lower rate of surgical interventions. This impacts on outcomes despite controlling for economic reasons including the area-level deprivation or patient financial status. 3, 4.

In Ireland, the Rapid Access Lung Clinic (RALC) provides equal access to diagnostic and treatment procedures. The St. Vincent's University Hospital RALC serves a high density urban population as well as lower density and more rural population. Once attending RALC, patients have a common audited pathway with equal access to the same radiology, pathology, decision making at multidisciplinary team (MDT) and treatment.

The aim of the study is to assess if regional variation in lung cancer presentation persist in the setting the common diagnostic and treatment services.

Methods:

This is a retrospective study analyzing prospectively reported data. Approval was granted by intuitional audit committee. Patients were included who had a diagnosis of non-small cell lung cancer (NSCLC) and came through a single RALC. All patients included underwent surgical resection with curative intent from June 2013 to March 2020. Pathological data was explored for tumour size, tumour type, nodal status and stage. Complete data was available on 152 patients.

The RALC was established by the national cancer control program in 2012. An electronic GP referral system was set up giving equal access independent of geography. Following triage, suitable patients are offered an appointment. Appointments entail: review with respiratory consultant, medical history, physical examination, any further diagnostic appointments will be scheduled e.g. bronchoscopy, bloods, CT guided biopsy, etc. A follow report is sent to the referring doctor. The NCCP monitors performance with key performance indicators. This study evaluates the St. Vincent's University Hospital RALC which serves a high-density urban population in Co. Dublin and Wicklow as well as lower density and more rural population in counties Kilkenny, Carlow and Wexford.

Patients were divided into two groups based on distance from the treatment center in Dublin. Group 1 including the closest patients from Dublin and Wicklow (n=97). Group 2 included patients who were referred from away from lower density regions (n=55).

We excluded patients with unresectable cancer, who received induction chemotherapy or patient with clinical stage III and IV.

Statistical analysis was performed on nonparametric data with a Chi square test or Fisher exact depending on the assumption required for each test. Differences in continuous variables were tested with a Student t test. A significance criterion of P value ≤ 0.05 was used in the analysis. All analyses were performed using SPSS.

Results:

The study included 152 patients from initial 625 patients. In group 1 (n=97) 36 patients (37.1%) were male, and the mean age is 66.8 years old. In group 2 (n=55) 23 patients (41.8%) were male and the mean age is 66 years old. (Table.1). in group 1, 72.1% of patients were current or former smokers. The figure for group 2 was 69.1%. [Table.1]

Table 1: Patients characteristics

Name	value	Dublin group (n=97)	Non Dublin group (n=55)	P value
Age		66.8	66	0.632
Sex	M	36 (37.1%)	25 (41.8%)	0.313
	F	61 (62.9%)	30 (58.2%)	
Type of lung cancer	Adenocarcinoma	63 (65%)	29 (52.7%)	0.238
	SCC	21 (21.6%)	17(30.9%)	
	Carcinoid	9 (9.3%)	9 (16.3%)	
	Small cell	2 (2.05%)		
	Large cell	2 (2.05%)		
Smoking	Yes	70 (72.1%)	38 (69.1%)	0.688
	No	27 (27.9%)	17 (30.9%)	

Regarding the tumor histology, adenocarcinoma was more common in the group 1 comparing to group 2 (65% vs 52.7%). Squamous cell carcinoma was more common in the group 2 comparing to group 2 (21.6% vs 30.9%) (p = 0.238). [Table.2]

Table 2: Results

	value	Dublin group (n=97)	Non Dublin group (n=55)	P value
Lung cancer stage	I	75(77.3%)	30 (54.5%)	0.013
	II	13(13.4%)	16 (29%)	
	III	9 (9.3%)	9 (16.3%)	
Tumor size		24.74mm (16.53 SD)	31.72mm (21.27 SD)	0.026
N stage	N0	84 (86.6%)	42 (76.4%)	0.249
	N1	9 (9.2%)	8 (14.5%)	
	N2	4(4.2%)	5 (9.1%)	

Group 1 patients (n = 97) had a statistically significant lower mean tumour size (24.74mm) compared to the group 2 (31.72mm) (p = 0.026). Focusing on tumour subtype; the mean size of adenocarcinoma in group 1 is 24.3mm which is lower than group 2 which is 31.9mm. In patients with squamous cell carcinoma the mean size in group 1 was smaller than in group 2 (27.6mm vs 37.5mm). The proportion of N1 lymph nodes positive for carcinoma in group 1 was 9.2%. This is compared to 14.5% for group 2 but did not reach statistical significance. The proportion of N2 lymph nodes positive for carcinoma in group 1 was 4.2%. This is compared to 9.1% for group 2 but did not reach statistical significance (p value =0.249).

Putting the T data and nodal status together to define the pathological stage; Group 1 had a statistically significant lower stage (stage II 13.4%, stage III 9.3%) comparing to group 2 (stage II 29%, stage III 16.3%)(P value = 0.013). [Tab.2]

Discussion:

In this patient population, patients with primary lung cancer living in lower density parts of Ireland present with more advanced disease. Advanced stage is associated with higher lung cancer mortality and early detection of lung cancer changes treatment modality and survival outcomes. Understanding the factors which influence the stage at presentation assist in optimizing outcomes.

This study is notable in that the RALC delivers equal access to diagnostics, decision making and treatment once referred to the clinic. The availability of diagnostics and treatment is unlikely to be the deciding factor in the stage of patient disease in this population. The distinctive histological subtype, with more squamous cell carcinoma in the less dense population areas, suggests that at least some elements of the more advanced disease presentation relate to local factors.

This study does not assess what those local factors could be. Such local factors are likely to be multivariate in nature and include patient factors such as genetic pre-disposition, risk behavior exposures such as smoking or occupation or geographic exposures such as radon gas levels. Those in less densely populated areas were also noted to have larger tumour size and greater nodal involvement. This could relate to the same local factors as may have impacted on tumour biology, but could also reflect local behavioural differences. Behavioural patterns that increase the frequency of interactions with general practitioners, hospitals and emergency departments can lead to earlier opportunistic discovery of lung malignancy. 5

Increased attendance at healthcare facilities may reflect in a lower threshold at which a population seeks out medical assistance. Local medical infrastructure that rests before the referral to a RALC may also be distinctive with different access to GP services and greater distances to hospital emergency rooms or clinics. This may influence the initiation of the referral to the RALC.

In the most recent update of the National Cancer Registry in Ireland report, lung cancer in urban

and rural areas the incidence of lung cancer is higher in the urban areas with more patients presenting presented with early-stage (I, II) disease. 1, 2, 6, 7

A longitudinal study assessed the relationship between relative survival and patients' area of residence in the Irish population found a significantly larger proportion of urban patients (23%) as compared with rural patients (21%) received surgery (p<0.001). Similarly to our findings, they found that early-stage cancers (I, II) presented more frequently in urban patients with stage III disease present in rural patients comparing to urban patients (20% vs 18%). They found that there is a need for targeted policies addressing access to treatment centers for rural patients with non-small cell lung cancer. 6

Conversely, a 5 year study in an English population showed little difference between both the incidence and survival of lung cancer in urban and rural areas. 8

Graham et. al, studied retrospectively the correlation between smoking rates, lung cancer incidence, and mortality and the rural-urban area. They found that patients from rural areas who were diagnosed with stage I lung cancer underwent fewer surgeries (69% vs75%, p < 0.001) and had significantly reduced median survival (40 vs 52 months) when compared to the patients from urban areas, which may reflect inequality in access to surgical care. 9

A common assumption is that access to diagnostics; multi-disciplinary care and treatment are the determining factors. The explanation commonly used is that rural patients do not have equal access to equal standard services. However, our study is designed to exclude such bias with equal access to diagnostic, assessment and care in a rapid access lung clinic. This is one of 8 such clinics in the country. All of these clinics have reportable key performance indicators that monitor their performance, and this study would say that the differences in lung cancer stage at diagnosis pre-date the point of referral starting the diagnostic sequence.

A clearer understanding of this high density and low density population difference is part of selecting targeted measures to improve lung cancer outcomes in Ireland. Alternatively, it may be used to direct public policy when designing any early phase of a lung cancer screening system to lower density population areas first. This may not be the obvious first choice, as many would start with a higher population area to screen more people. However, the reward in improved lung cancer outcomes may be greatest if this was focused on lower density populations first. In communicating public health measures to the national population, this study may also suggest that difference approaches are needed tailored to local differences.

The limitation of our study is the small number of patients included. However, the key strength is that once in the RALC, the patients are managed in a standardized fashion independent of geography. This study may assist in focusing further work evaluating the factors that link patients to the referral doctors outside the major urban areas in Ireland.

Conclusion:

Higher stage in lung malignancy is associated with worse 5-year survival. Removal of regional variation in cancer outcomes is a national health goal. Our study shows that there is significant regional variation in lung cancer disease stage in our population and that patient status at the time of presentation is an important factor, rather than patient access to diagnostics, multi-disciplinary assessment and treatment. This may help focus efforts at the earlier phase in patient self presentation and opportunistic interactions with their local health services. Improving local and community interactions may diminish these population density differences in treatment and survival of lung cancer.

Conflict of interest's declaration: The authors declare that there is no conflict of interest.

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