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Incomplete uptake of EGFR mutation testing and its impact on estimation of mutation prevalence in patients with non-squamous NSCLC: A population-based study in New Zealand

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ABSTRACT

Background: Epidermal Growth Factor Receptor (EGFR) mutation testing is recommended for patients with non-squamous non-small cell lung cancer (NSCLC) but not all eligible patients get tested, which may bias the mutation prevalence estimated. This study aims to examine trends in the uptake of EGFR mutation testing in patients with non-squamous NSCLC in New Zealand; to develop a composite metric that quantifies the influences of demographic and clinico-pathological factors on the testing uptake; and to estimate the prevalence of EGFR mutation if all patients were tested.

Methods: This population-based study involved all patients who were diagnosed with non-squamous NSCLC in four health regions in New Zealand between January 2010 and December 2015. Eligible patients were identified from the New Zealand Cancer Registry and information on EGFR mutation testing was obtained through linkage to TestSafe, a clinical information sharing service, and laboratory records.

Results: Of 2701 eligible patients, 1059 (39.2%) were tested for EGFR mutation. The testing prevalence increased (3.7% in 2010 to 64.6% in 2014) and the influences of demographic and clinic-pathological factors decreased from 2010 to June 2014, and remained stable afterward. Of the tested patients, 229 (21.6%) were mutation positive with a decreasing trend observed from 2010 (43.8%) to June 2014 (16.8%). The best-fit log-linear model estimated the prevalence of EGFR mutation, if all patients were tested, as 15.5% (95% CI: 13.2%–18.0%).

Conclusion: The methods described here allowed a more accurate estimation of the prevalence of EGFR mutation.

1. Introduction

Epidermal Growth Factor Receptor (EGFR) mutations are present in subsets of patients with non-squamous non-small cell lung cancer (NSCLC), and associated with sensitivity to EGFR tyrosine kinase inhibitors (TKIs). Since 2013, standard oncology practice guidelines recommend EGFR mutation testing of non-squamous NSCLC to select advanced-stage patients for first-line treatment with EGFR-TKIs [1–3]. However, practical barriers such as accessibility, costs, insufficient quantity or quality of tissue specimen available for testing and variable testing referral practices may limit full uptake of testing by all eligible patients [4–6]. Incomplete testing uptake may have an impact on estimation of mutation prevalence.

Accurate estimation of the prevalence of EGFR mutation is necessary to inform policy and practice. Many studies have assessed the mutation prevalence in different settings and patient groups. A recent meta-analysis pooled the results of 456 studies published to June 2013, and reported that the prevalence of EGFR mutation was 32.3% (95% CI 30.9%–33.7%) with a higher prevalence observed in Asians, females, non-smokers and patients with adenocarcinoma [7]. Similar findings were observed in earlier meta-analyses [8–10]. However, testing was incomplete and selective in many studies, which may bias the estimates

Abbreviations: CI, confidence interval; EGFR, epidermal growth factor receptor; NHI, National Health Index; NSCLC, non-small cell lung cancer; NZCR, New Zealand Cancer Registry; NZDep, New Zealand Deprivation Index; TKI, tyrosine kinase inhibitor

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Table 1
Patient characteristics by EGFR mutation testing and mutation status.

	Total	Patients tested for EGFR mutation			EGFR mutation positive patients among those tested		
		Number	%	p-value	Number	%	p-value
Total	**2701**	**1059**	**39.2**		**229**	**21.6**	
Age							
< 60 years	514	255	49.6	< 0.0001	68	26.7	0.09
60-69 years	794	347	43.7		63	18.2	
70-79 years	807	343	42.5		72	21.0	
80+ years	586	114	19.5		26	22.8	
Gender							
Male	1323	474	35.8	0.0004	86	18.1	0.01
Female	1378	585	42.5		143	24.4	
Ethnicity							
New Zealand Maori	450	153	34.0	0.0002	21	13.7	< 0.0001
Pacific	273	107	39.2		28	26.2	
Asian	273	139	50.9		71	51.1	
European	1677	646	38.5		104	16.1	
Others/unknown	28	14	50.0		5	35.7	
Site of tumour							
Main bronchus incl. Carina, Hilus	137	52	38.0	< 0.0001	7	13.5	0.5
Upper lobe, bronchus or lung	1301	531	40.8		113	21.3	
Middle lobe, bronchus or lung	126	60	47.6		16	26.7	
Lower lobe, bronchus or lung	623	280	44.9		62	22.1	
Mixed or unspecified	514	136	26.5		31	22.8	
Extent of tumour							
Localised to organ of origin	209	98	46.9	< 0.0001	30	30.6	0.1
Invasion of adjacent tissue or organ	119	70	58.8		19	27.1	
Regional lymph nodes	296	162	54.7		33	20.4	
Distant	1404	514	36.6		104	20.2	
Unknown	673	215	31.9		43	20.0	
Histology							
Adenocarcinoma	1674	935	55.9	< 0.0001	215	23.0	0.02
Others specified	91	37	40.7		3	8.1	
Not otherwise specified	431	72	16.7		8	11.1	
No pathological diagnosis[a]	505	15	3.0		3	20.0	
Basis of diagnosis							
Cytology or haematology	941	392	41.7	< 0.0001	74	18.9	0.1
Histology of primary	1013	534	52.7		131	24.5	
Histology of metastasis	242	118	48.8		21	17.8	
Clinical investigation	505	15	3.0		3	20.0	
NZDep 2006							
1-2	424	184	43.4	0.01	45	24.5	0.3
3-4	421	176	41.8		44	25.0	
5-6	584	242	41.4		50	20.7	
7-8	552	209	37.9		36	17.2	
9-10	711	243	34.2		52	21.4	
Unknown	9	5	55.6		2	40.0	
Area of residence							
Main urban area	2241	871	38.9	0.4	194	22.3	0.2
Others	445	180	40.4		32	17.8	
Unknown	15	8	53.3		3	37.5	
DHB							
Auckland	635	219	34.5	0.002	50	22.8	0.9
Counties Manukau	851	324	38.1		73	22.5	
Waitemata	865	381	44.0		79	20.7	
Northland	350	135	38.6		27	20.0	
Period of diagnosis							
Jan-Dec2010	429	16	3.7	< 0.0001	7	43.8	0.09
Jan-Dec 2011	427	33	7.7		11	33.3	
Jan-Jul 2012	258	47	18.2		12	25.5	
Aug-Dec 2012	185	96	51.9		18	18.8	
Jan-Jun 2013	202	118	58.4		22	18.6	
Jul-Dec 2013	226	134	59.3		31	23.1	
Jan-Jun 2014	240	155	64.6		26	16.8	
Jul-Dec 2014	237	141	59.5		27	19.1	
Jan-Jun 2015	256	165	64.5		40	24.2	
Jul-Dec 2015	241	154	63.9		35	22.7	

[a] "No pathological diagnosis" includes those notified on the basis of a non-pathological diagnosis (i.e., only by clinical investigation).