

## INTISARI

**Latar Belakang:** Pengembangan terapi target untuk adenokarsinoma paru, tipe tersering dari keganasan yang paling mematikan, dilaporkan memberikan tingkat kesintasan yang lebih baik dibandingkan kemoterapi konvensional. Di antaranya, terapi TKI terbukti efektif pada adenokarsinoma paru yang bermutasi *EGFR*. Pemeriksaan mutasi *EGFR* sebelum pengobatan wajib dilakukan karena setiap ekson memberikan respon terapi yang berbeda. Di daerah dengan akses pemeriksaan genetik yang sulit, diperlukan strategi lain untuk memprediksi status mutasi *EGFR*. Beberapa karakteristik radiologis dilaporkan berkorelasi signifikan dengan keberadaan mutasi *EGFR*. Namun, belum ada penelitian yang menemukan korelasi antara lokasi tumor dan jenis mutasi *EGFR* pada pasien adenokarsinoma paru di Indonesia.

**Tujuan:** Studi ini bertujuan untuk mengidentifikasi frekuensi mutasi *EGFR* pada kasus adenokarsinoma paru lokal dan hubungannya dengan lokasi tumor.

**Metode:** Data klinis pasien adenokarsinoma paru ( $n = 272$ ) yang terdiagnosis melalui sitopatologi *CT-guided TTNA* dan efusi pleura pada tahun 2018-2022 diperoleh secara retrospektif dari Instalasi Patologi Anatomi, RSUP Dr. Sardjito, D.I. Yogyakarta. Hasil *qRT-PCR* terkait status mutasi *EGFR* diperoleh dari *database* di Departemen Patologi Anatomi, Fakultas Kedokteran, Kesehatan Masyarakat, dan Keperawatan, Universitas Gadjah Mada, D.I. Yogyakarta. Hubungan antara data-data tersebut dianalisa menggunakan uji statistik *Pearson Chi-Square* dan *Fisher's exact test* (perangkat lunak STATA, versi 14).

**Hasil:** Mutasi *EGFR* dideteksi pada 60.7% pasien, dengan mutasi paling banyak adalah pada ekson 19 (58,2%) dan ekson 21 L858R (21,2%). Status mutasi berhubungan signifikan dengan jenis kelamin ( $p = 0,022$ ) dan usia ( $p = 0,029$ ) pasien, tetapi tidak dengan lokasi tumor ( $p = 0,093$  untuk lateralitas paru dan  $p = 0,382$  untuk lobus paru). Frekuensi mutasi ekson 19 pada paru kiri lebih tinggi di lobus atas (65,3%), sedangkan pada paru kanan lebih tinggi di lobus bawah dan campuran (masing-masing 66,7%). Mutasi ekson 21 L858R ditemukan lebih sering muncul di paru kanan (25,3%) dan lobus tengah (39,1%). Setelah dilakukan stratifikasi, kasus adenokarsinoma paru dengan mutasi ekson 19 ditemukan memiliki frekuensi paling tinggi di hampir setiap lobus pada laki-laki berusia tua, walaupun hubungan ini tidak bermakna secara statistik.

**Kesimpulan:** Frekuensi setiap jenis mutasi *EGFR* tidak memiliki hubungan signifikan dengan lokasi adenokarsinoma pada studi ini, meskipun untuk mutasi ekson 19 dan ekson 21 L858R didapatkan kecenderungan ditemukan pada tumor di lobus paru tertentu.

**Kata Kunci:** Adenokarsinoma paru, mutasi *EGFR*, lokasi tumor, lobus paru, lateralitas paru.

## ABSTRACT

**Background:** The development of targeted therapies for lung adenocarcinoma, as the most common type of the deadliest malignancy, has been reported to give a more favorable overall survival than conventional chemotherapy. Among the available targeted therapies, TKI was shown to benefit well in lung adenocarcinoma with *EGFR* mutation. Unfortunately, *EGFR* mutation examination prior to TKI treatment are mandatory as different exons respond differently to these therapies. In areas that have low accessibility to genetic examinations, other strategies are needed to predict these distinct *EGFR* mutations. Several radiologic characteristics have been reported to significantly correlate with *EGFR* mutation positivity. However, there have not been any studies to find the correlation between tumor location and *EGFR* mutation types in lung adenocarcinoma patients in Indonesia.

**Objective:** This study aims to identify the frequency of *EGFR* mutation in local lung adenocarcinoma cases and its association with tumor location.

**Method:** Clinical data of lung adenocarcinoma patients ( $n = 272$ ) that were diagnosed via CT-guided TTNA and pleural effusion cytopathology in 2018-2022 were retrospectively taken from the Installation of Anatomical Pathology, Dr. Sardjito Hospital, D.I. Yogyakarta. The *qRT-PCR* result for *EGFR* mutation status was obtained from the database in the Department of Anatomical Pathology, Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University, D.I. Yogyakarta. The association between these data were analyzed by Pearson Chi-Square statistical test and Fisher's exact test (STATA software, version 14).

**Result:** *EGFR* mutation were detected in 60.7% patients, in which 58.2% were exon 19 mutation and 21.2% were exon 21 L858R mutation. Mutation status was found to be associated with the patient's gender ( $p = 0.022$ ) and age ( $p = 0.029$ ), but not with the tumor location ( $p = 0.093$  for lung laterality and  $p = 0.382$  for lung lobes). The frequency of exon 19 mutation in left lung was higher in the upper lobe (65.3%), while it was higher in the lower and multiple lobes (66.7% each) for the right lung. Exon 21 L858R mutation was found to occur more frequently in the right lung (25.3%) and in the middle lobe (39.1%). By further stratification, it was found that exon 19 mutation had the highest frequency in most of the lobes in older males with lung adenocarcinoma, although the association was not statistically significant.

**Conclusion:** The frequency of each type of *EGFR* mutation did not have a significant association with the location of adenocarcinoma in this study, although the exon 19 and exon 21 L858R mutations showed a tendency to be found in tumors of certain lung lobes.

**Keywords:** Lung adenocarcinoma, *EGFR* mutations, tumor location, lung lobes, lung laterality.