



ORIGINAL ARTICLE

## Is diabetes mellitus a negative prognostic factor for the treatment of advanced non-small-cell lung cancer?



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### KEYWORDS

Diabetes mellitus;  
Non-small cell lung  
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### Abstract

**Background:** It has been demonstrated that there are a lot of different prognostic factors which are worthy of consideration whereas diabetes mellitus (DM) has not been clearly or consistently identified as a prognostic value in advanced non-small cell lung cancer (NSCLC). The aim of this study was to investigate the prognostic significance of the characteristics of patients in advanced NSCLC. Specifically, we investigated the impact of DM for progression-free survival (PFS) and overall survival (OS) in patients receiving first-line platinum-based doublets chemotherapy.

**Methods:** We retrospectively reviewed 442 patients with advanced NSCLC. DM and other potential prognostic variables were chosen for analysis in this study. Univariate and multivariate analyses were conducted to identify prognostic factors associated with survival.

**Result:** The results of univariate analysis for OS were identified as having prognostic significance: performance status ( $p < 0.001$ ), stage ( $p < 0.001$ ), DM ( $p < 0.001$ ), liver metastasis ( $p = 0.02$ ) and brain metastasis ( $p < 0.001$ ). Stage, diabetes mellitus, and liver metastasis were identified as having prognostic significance for PFS.

Multivariate analysis showed that poor performance status, presence of DM and advanced stage were considered independent negative prognostic factors for OS ( $p < 0.001$ ,  $p < 0.001$  and  $p < 0.001$  respectively). Furthermore, DM and stage were considered independent negative prognostic factors for PFS ( $p < 0.005$  and  $p < 0.001$  respectively).

**Conclusion:** In conclusion, DM at the time of diagnosis was associated with the negative prognostic importance for PFS and OS in the advanced stage patients who were receiving first-line platinum-based doublets chemotherapy. In addition poor performance status and advanced stage were identified as negative prognostic factors.

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**PALAVRAS-CHAVE**

Diabetes mellitus;  
Carcinoma pulmonar  
de células não  
pequenas;  
Factores de  
prognóstico

## Será a diabetes mellitus um fator de prognóstico negativo no tratamento do carcinoma pulmonar de não pequenas células em estadió avançado?

**Resumo**

**Antecedentes:** Existem vários factores de prognóstico previamente estabelecidos no carcinoma pulmonar de não pequenas células (NSCLC) avançado. Até à presente data, a diabetes mellitus (DM) não foi identificada de forma consistente como potencial factor de prognóstico neste contexto. O objectivo do presente estudo é investigar o significado prognóstico das diferentes características dos doentes com NSCLC avançada. Especificamente, investigámos o impacto da DM para a sobrevivência livre de progressão (PFS) e sobrevivência global (OS) em doentes em regime duplo de quimioterapia de primeira linha à base de platina.

**Métodos:** Analisámos retrospectivamente 442 doentes com NSCLC avançado. Foram escolhidas a DM e outras potenciais variáveis de prognóstico para a análise neste estudo. Foram realizadas análises univariadas e multivariadas para identificar os factores de prognóstico associados à sobrevivência.

**Resultados:** Os resultados de análise univariada para OS identificaram como tendo significância para o prognóstico: estado geral ( $p < 0,001$ ), estadió ( $p < 0,001$ ), DM ( $p < 0,001$ ), metástases hepáticas ( $p = 0,02$ ) e metástases no cérebro ( $p < 0,001$ ). O estadió, diabetes mellitus e as metástases hepáticas foram identificadas como tendo significância de prognóstico para a PFS. A análise multivariada mostrou que um mau estado geral, a presença de DM e um estadió avançado foram considerados factores de prognóstico negativo independentes para OS ( $p < 0,001$ ;  $p < 0,001$  e  $p < 0,001$ ; respectivamente). Além disso, a DM e estadió foram considerados factores de prognóstico negativo independentes para a PFS ( $p < 0,005$  e  $p < 0,001$ ; respectivamente).

**Conclusões:** Em conclusão, a DM na altura do diagnóstico comportou-se como um fator de prognóstico negativo para a PFS e OS nos doentes em estadió avançado que estavam em regime duplo de quimioterapia de primeira linha à base de platina. Além do mau estado geral, os estádios avançados foram identificados como factor de prognóstico negativo.

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**Introduction**

Lung cancer is the most common of all cancer deaths in both men and women worldwide. NSCLC represents 80–85% of all diagnosed lung cancers cases.<sup>1</sup> Surgery is the only curative treatment option for patients with NSCLC. At the time of diagnosis, two-third of patients with lung cancer are diagnosed with locally advanced or metastatic disease. The median survival time for advanced disease is 5.8–12.6 months and the overall 5-year survival rate among this patient population is still less than 10%.<sup>2,3</sup> Systemic chemotherapy with the platinum-based doublets are currently recommended as a standard of first-line chemotherapy for treatment of NSCLC.<sup>4</sup>

An increased incidence of the NSCLC is connected with aging,<sup>5</sup> which explains why NSCLC frequently appears simultaneously with other age-related diseases such as diabetes mellitus (DM). Various studies have indicated that among patients with colorectal,<sup>6</sup> pancreatic,<sup>7</sup> breast,<sup>8</sup> or liver<sup>9</sup> cancer, existing DM was associated with a lower long-term survival. The prognostic significance of pre-existing DM in patients with lung cancer was evaluated.<sup>10–18</sup> Three studies<sup>10–12</sup> reported a decrease in survival in patients with DM compared to those without DM. On the other hand, several studies have shown that DM was associated with an equal<sup>13–15</sup> or an increased chance of survival.<sup>16–18</sup> The effect of DM on patients with NSCLC remains uncertain. In addition to this, DM has not been clearly or consistently identified

as a prognostic value for the recurrence or progression of advanced NSCLC.<sup>6,11–14</sup> The aim of this study was to investigate the impact of DM for PFS and OS on the patients receiving first-line platinum-based doublets chemotherapy.

**Methods**

We retrospectively reviewed 442 patients with histological or cytological proven NSCLC who were receiving first-line platinum-based doublets chemotherapy between August 2002 and February 2012. They had to meet the following inclusion criteria; (1) they had a histological or cytological diagnosis of locally advanced and/or metastatic NSCLC; (2) they were 18 years of age or older; (3) they had had no previous chemotherapy or radiotherapy; (4) they had to have a measurable disease, as defined by Response Evaluation Criteria in Solid Tumors RECIST.

Patients were identified as having DM on the basis of elevated fasting glucose level ( $>126$  mg/dL), and a history of DM or medication use, such as insulin or oral hypoglycemic agents. Prevalent hypertension was defined as systolic pressure  $\geq 140$  mm Hg and/or diastolic  $\geq 90$  diastolic and/or currently taking antihypertensive medications.

Twelve potential prognostic variables were chosen on the basis of previously published clinical trials.<sup>19–24</sup> The variables were divided into categories: age ( $<70$  or  $\geq 70$ ), gender (male or female), Eastern Cooperative Oncology

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