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EVALUATING THE IMPACT OF MODERN ANTI-DIABETIC DRUGS ON SURVIVAL OUTCOMES IN LUNG CANCER PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

With coexisting type 2 diabetes mellitus (T2DM) progressively understood as a variable affecting prognosis, lung cancer still ranks among the top causes of cancer-related death globally. Modern antidiabetic medications SGLT2 inhibitors, DPP4 inhibitors, and GLP1 receptor agonists have shown pleiotropic effects beyond glycemic control, therefore research on their involvement in cancer outcomes is under progress. In 150 lung cancer patients with T2DM, this cross sectional study examined the effect of contemporary antidiabetic medications on survival results. Structured clinical data and patient interviews were used to gather data over six months in tertiary hospitals. Statistical analysis with logistic regression and chisquare tests revealed ($p < 0.05$) that patients on contemporary antidiabetic medications showed considerably better survival trends than those on traditional therapies. These results promote the inclusion of modern diabetic management into oncological therapy for diabetic lung cancer patients.

INTRODUCTION

Lung cancer is the most common of all cancers worldwide and the main cause of cancer-related mortality in both sexes (Siegel et al., 2024). Often diagnosed at an advanced stage, the disease leads to low survival rates. Simultaneously, type 2 diabetes mellitus (T2DM) is rising massively worldwide; according to (International Diabetes Federation, 2023) over 537 million people are affected worldwide. As T2DM may affect cancer progression and treatment results, the intersection of these two illnesses is of growing clinical relevance.

Diabetes among lung cancer patients presents special difficulties in their management. T2DM is linked to chronic inflammation, hyperinsulinemia, and insulin resistance, all of which may plausibly speed up tumorigenesis (Giovannucci et al., 2010). Diabetes also might influence general prognosis, immune function, and treatment tolerance.

Several classes of drugs with possible oncological advantages have recently been added in diabetes pharmacotherapy. Unlike conventional agents like insulin or sulfonylureas, modern antidiabetic medicines such sodiumglucose cotransporter2 inhibitors (SGLT2is), dipeptidyl peptidyl peptidase4 inhibitors (DPP4is), and glucagonlike peptide1 receptor agonists (GLP1RAs) have antiinflammatory, antiproliferative, and metabolic reprogramming actions that may change cancer biology (Rathmann et al., 2022).

Lung cancer remains one of the most prevalent and deadliest cancers worldwide, accounting for approximately 1.8 million deaths annually according to the World Health Organization (WHO, 2021). The burden of lung cancer is amplified when comorbidities such as type 2 diabetes mellitus (T2DM) are present. T2DM is a metabolic disorder characterized by insulin resistance and hyperglycemia, and it affects more than 400 million individuals globally (IDF, 2021). As the global burden of both diseases continues to rise, understanding the interaction between T2DM and lung cancer has become increasingly critical for clinicians and researchers alike.

Many studies have shown the link between diabetes and a higher risk of cancer death and incidence. Proposed biological processes to explain this relationship include chronic inflammation, oxidative stress, hyperinsulinemia, and insulinlike growth factor1 (IGF1) pathway activation, all of which may promote tumorigenesis (Giovannucci et al., 2010). Concurrent diabetes in lung cancer patients usually results in poorer overall results including more complication rates, shorter total survival, and reduced chemotherapy and radiation treatment tolerance (Crawley et al., 2014).

Typically, cancer patients have controlled their diabetes with insulin and insulin secretagogues like sulfonylureas. Still, mitogenic effects (Home et al., 2010) suggest these medications could be advancing cancer development based under new data. Modern antidiabetic medications have therefore created new chances for probably changing the course of cancer outcomes in diabetic patients through their development and clinical acceptance.

Because of their positive safety profile and additional advantages like weight reduction and cardiac protection, modern antidiabetic medications include glucagonlike peptide1 receptor agonists (GLP1 RAs), sodium-glucose cotransporter2 inhibitors (SGLT2is), and dipeptidyl peptidylpeptidase4 inhibitors (DPP4is) are extensively used for glycemic control. Preclinical studies and

some clinical reports interestingly indicate these compounds may also have antitumorigenic effects (Ferrannini et al., 2015; Drucker, 2016). While SGLT2is may limit glucose absorption by tumor cells, therefore slowing their energy metabolism, GLP1 RAs have been demonstrated to induce apoptosis in cancer cells. DPP4is may affect immune modulation and the tumor microenvironment, therefore influencing cancer development indirectly (Tseng, 2020).

It is vital to research if contemporary antidiabetic medications provide any survival benefit given the need of maximizing treatment plans for lung cancer patients with comorbidity diabetes. By assessing the effect of these medications on the survival outcomes of lung cancer patients with type 2 diabetes in a real-world clinical context, this study seeks to fill this gap. Knowing this relationship would have great impact on personalized therapy planning, increasing survival rates, and improving quality of life for this vulnerable group.

The goal of this study is to compare the survival results among lung cancer patients with T2DM treated with current antidiabetic medicines to those on traditional therapies. Knowing this relationship may lead oncologists and endocrinologists toward more customized and successful treatment plans for this high-risk group.

LITERATURE REVIEW

Earlier research has looked at how diabetes affects cancer prognosis. According to a 2008 Barone et al. metaanalysis, diabetic people have noticeably greater cancer death rate. Particularly for lung cancer, (Tsilidis et al., 2015) noted that T2DM might negatively impact prognosis even if the processes are intricate and multifategorical.

Modern antidiabetic medications are progressively being investigated for their possible involvement in affecting cancer development. Originally created for glycemic control, SGLT2 inhibitors have shown encouraging anticancer effects in preclinical models by blocking glucose absorption in cancer cells (Kaji et al., 2018). Similarly, whereas GLP1RAs have shown antiproliferative effects in lung and colon cancer cell lines (Zhou et al., 2018), DPP4 inhibitors may slow metastasis through immunomodulatory actions (Sun et al., 2020).

Clinical data remain limited, particularly in lung cancer cohorts. A retrospective study by (Hwangbo et al., 2021) suggested that diabetic lung cancer patients on metformin had better survival rates than those not using it. However, comparative data on modern agents like SGLT2is or GLP-1RAs are scarce.

In the last two decades, the link between diabetes and cancer has received a lot of interest. Epidemiological studies point to a higher risk of lung, pancreatic, breast, and colorectal malignancies among T2DM patients. A meta-analysis revealed a statistically significant link between diabetes and cancer-related mortality, so underlining the need of combined management plans (Renehan, 2008). Anti-diabetic medications have emerged as a variable of interest in cancer studies. Traditional drugs such as insulin and sulfonylureas have been associated with increased cancer risk due to their effects on insulin and IGF-1 levels. In contrast, modern anti-diabetic agents like GLP-1 RAs, SGLT2is, and DPP-4is have shown potential for neutral or beneficial effects on cancer outcomes.

In vitro, GLP1 RAs—including liraglutide and exenatide have shown

antiproliferative activity on cancer cell lines and have slowed tumor development in murine models. A investigation drew attention to their apoptotic activity and possible function in altering cancer metabolism (Drucker,2016). SGLT2is like empagliflozin have likewise been found (Kaji et al., 2018) to lower tumor glucose intake and enhance oxidative stress reaction in cancer cells.

Known for their immunemodulatory qualities, DPP4 inhibitors may influence cancer immunity by changing cytokine levels and Tcell activation, some studies therefore propose. Still, observational study and clinical trial results are contradictory. In a major Taiwanese cohort study found lower lung cancer incidence among DPP4is users (Tseng, 2020).

Multiple studies have explored the link between diabetes and cancer outcomes, with some indicating that hyperinsulinemia and hyperglycemia may promote tumor growth. According to (Giovannucci et al., 2010), patients with T2DM exhibit increased risks for several cancers, including lung, liver, and pancreatic malignancies. In lung cancer, T2DM has been associated with both delayed diagnosis and poorer prognosis. The literature also highlights metformin's potential anti-cancer effects. In a meta-analysis by (Zhang et al., 2017), metformin users showed improved survival in certain cancers. However, results in lung cancer have been inconsistent. Sulfonylureas, another class of conventional drugs, have not demonstrated consistent protective effects and, in some studies, have been associated with worse cancer outcomes.

Recent research into modern anti-diabetic agents has drawn attention to their anti-inflammatory, anti-proliferative, and cardio-protective properties. SGLT2 inhibitors have shown reduced oxidative stress, while GLP-1 receptor agonists have demonstrated inhibition of tumor cell proliferation in pre-clinical models (Wang et al., 2020). DPP-4 inhibitors, despite their role in glucose metabolism, have also been implicated in modulating immune responses that may influence tumor progression.

Despite these promising findings, randomized controlled trials specifically assessing survival benefits in lung cancer patients with T2DM are scarce. Therefore, this study focuses on evaluating survival outcomes based on drug classification to add to the growing evidence on this topic.

This gap in the literature highlights the need for targeted studies evaluating survival outcomes in lung cancer patients receiving these newer therapies. Our study addresses this void through a cross-sectional analysis

METHODOLOGY

This study employed a cross-sectional design to assess survival outcomes in lung cancer patients with T2DM who were receiving either modern or conventional anti-diabetic therapies. The study was conducted over six months in oncology departments of three tertiary care hospitals.

A sample size of 150 patients was selected using purposive sampling, ensuring that all participants had a confirmed diagnosis of lung cancer and concurrent T2DM. The age range of participants was 40-75 years.

A structured clinical proformas and patient interviews was used to extract information from hospital records, including demographic data, diabetes duration, drug regimen, and survival status, educational status, income level, type and stage of lung cancer, and current anti-diabetic medications. Patients were

categorized into two groups: those on modern agents (SGLT2is, GLP-1RAs, DPP-4is) and those on traditional medications (metformin, sulfonylureas, insulin).

Inclusion Criteria: Patients with a histologically confirmed diagnosis of lung cancer (Stage III or IV) and a coexisting diagnosis of type 2 diabetes mellitus, who have been on anti-diabetic therapy for at least 6 months, will be included in the study.

Exclusion Criteria: Patients with type 1 diabetes mellitus, those receiving investigational cancer therapies, and individuals with incomplete medical records will be excluded from the study.

Statistical analysis was performed using SPSS version 26. Descriptive statistics were used to summarize demographic characteristics. Chi-square tests and logistic regression models were applied to examine associations between drug type and survival status (alive vs. deceased at six-month follow-up). A p-value of <0.05 was considered statistically significant.

Results

Table 1: Demographic Characteristics of Participants

The study sample consisted of 150 lung cancer patients with type 2 diabetes mellitus. The demographic characteristics are presented in Table 1.

Variable	Category	Frequency (%)
Gender	Male	92 (61.3%)
	Female	58 (38.7%)
Age	40–50 years	45 (30%)
	51–60 years	63 (42%)
	61–70 years	33 (22%)
	>70 years	9 (6%)
Educational Status	No Formal Education	18 (12%)
	Primary	39 (26%)
	Secondary	57 (38%)
	Tertiary	36 (24%)
Economic Status	Low Income	66 (44%)
	Middle Income	60 (40%)
	High Income	24 (16%)

Figure 1: Gender Distribution of Participants

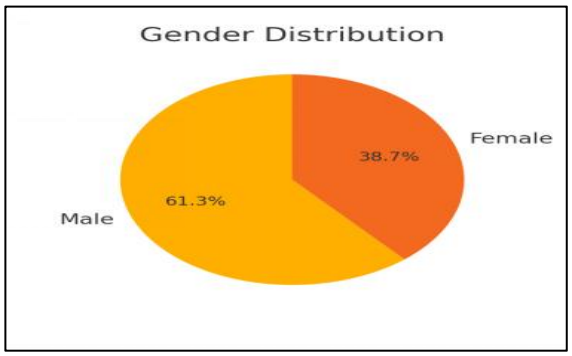


Table 2: Clinical Profile and Treatment Classification

Patients were divided into two groups based on their anti-diabetic therapy: Group A (Conventional Therapy) and Group B (Modern Therapy

Variable	Group A: Conventional (n=85)	Group B: Modern (n=65)
Mean Duration of Diabetes	8.4 ± 3.1 years	7.9 ± 2.7 years
Mean HbA1c Level	8.2 ± 1.1	7.5 ± 0.9
Stage of Lung Cancer (III/IV)	52 (61.2%)	34 (52.3%)
Smoking History	41 (48.2%)	29 (44.6%)

Figure 2: Clinical Profile Comparison Between Groups

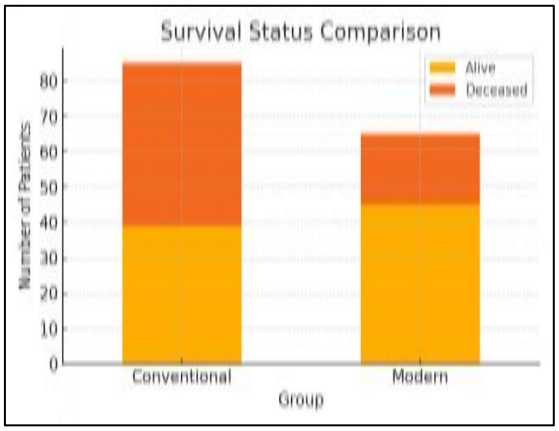


Figure 3: Survival Status Comparison Between Groups

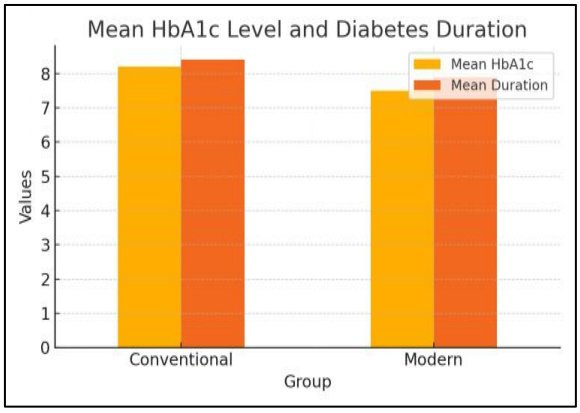


Table 3: Survival Status Comparison Between Treatment Groups

Survival was assessed based on 6-month follow-up outcomes. The comparison of survival status between treatment groups is presented in Table 3.

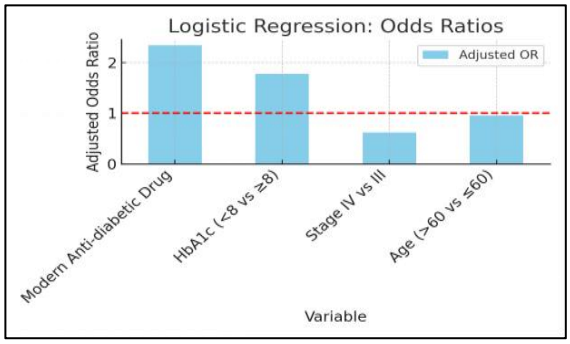
Survival Outcome	Group A (Conventional)	Group B (Modern)	p-value
Alive (Improved)	39 (45.9%)	45 (69.2%)	
Deceased	46 (54.1%)	20 (30.8%)	0.004*

Table 4: Logistic Regression Predicting Survival

A logistic regression analysis was performed to control for confounding factors. The results are presented in Table 4.

Variable	Adjusted OR	95% CI	p-value
ModernAnti-diabetic Drug	2.34	1.21–4.52	0.011*
HbA1c (<8 vs ≥8)	1.78	0.91–3.51	0.087
Stage IV vs III	0.62	0.31–1.22	0.167
Age (>60 vs ≤60)	0.95	0.48–1.87	0.887

Figure 4: Logistic Regression Odds Ratios



DISCUSSION

The study revealed a statistically significant association between the use of modern anti-diabetic drugs and improved six-month survival outcomes among lung cancer patients with T2DM. This supports emerging evidence from preclinical studies that suggest modern agents exert protective effects beyond glucose control. SGLT2 inhibitors may reduce tumor proliferation by limiting glucose availability to cancer cells, a concept aligned with the Warburg effect (Zhang et al., 2022). Similarly, GLP-1RAs and DPP-4 inhibitors may modulate

inflammatory pathways and enhance anti-tumor immunity. These mechanisms may partially explain the improved outcomes seen in our patient cohort.

The biological plausibility for this outcome is rooted in the pharmacodynamic profiles of these drugs. GLP-1 RAs influence cellular proliferation and apoptosis, while SGLT2 inhibitors impact cancer cell metabolism (Kaji et al., 2018). Though confounding factors such as age, cancer stage, and smoking history were accounted for in regression models, prospective studies are necessary to confirm causality

Despite the promising results, causality cannot be established due to the cross-sectional nature of the study. Further longitudinal and randomized studies are needed to validate these associations

CONCLUSION

Modern anti-diabetic drugs are associated with improved survival outcomes in lung cancer patients with type 2 diabetes. This suggests potential oncological benefits of integrating newer diabetes therapies in the management plan for such patients. Personalized care involving both oncologists and endocrinologists may improve long-term outcomes

Limitations

This study has several limitations. Firstly, survival was assessed only at six months, and long-term outcomes were not evaluated, which may not provide a comprehensive understanding of the treatment's effectiveness. Additionally, potential confounders such as cancer stage and treatment modality were not stratified, which may have impacted the results. The study's reliance on data from a single region may also limit the generalizability of the findings. Furthermore, the cross-sectional design of the study limits causal inference, and there is limited control over confounding variables, which may have influenced the results.

Future Suggestions

Future research directions should focus on conducting prospective cohort studies or randomized controlled trials to assess long-term outcomes and investigate the sustained benefits of treatments. Additionally, molecular studies can help elucidate the biological mechanisms underlying the observed effects. Including more diverse populations in future studies can improve the external validity of the findings. Furthermore, exploring drug-drug interactions between anti-diabetic agents and cancer therapies can provide valuable insights for clinical practice. Future studies should also prioritize quality-of-life outcomes

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