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ORIGINAL RESEARCH

Metabolic Modulation for Cancer Pain Relief: A Retrospective Pilot Study

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Purpose: Cancer pain, as a common symptom in patients with advanced cancer, seriously affects quality of life. A metabolism-based therapeutic strategy involving glucose metabolic regulation (hereafter pragmatically referred to as Warburg therapy) may offer clinical benefits for cancer pain management. This study aimed to evaluate the analgesic potential of this metabolic modulation strategy in patients with advanced cancer.

Methods: This was a single-institution retrospective pre-post cohort study involving 71 patients with advanced cancer treated with Warburg therapy. The primary endpoint was the change in pain intensity from baseline to the end of treatment, assessed using the Verbal Rating Scale (VRS). Secondary endpoints included changes in opioid consumption, calculated as oral morphine milligram equivalents (MME), and NSAID use. Changes in tumor marker levels and overall survival were analyzed as exploratory outcomes.

Results: After treatment, the median VRS pain score decreased from 4 (IQR: 3–4) at baseline to 2 (IQR: 2–4) following the final treatment course (Wilcoxon signed-rank test, $p<0.0001$), and 80.3% of patients experienced at least a 20% reduction in pain scores. Among the 50 patients receiving opioids before treatment, 10 discontinued opioid use entirely (7 transitioned to celecoxib). Exploratory analyses demonstrated decreases in tumor markers among a subset of patients.

Conclusion: Warburg therapy significantly improved pain symptoms in patients with advanced cancer and was associated with reduced analgesic medication use in a subset of patients. Exploratory analyses also suggested potential treatment-related changes in selected tumor markers and imaging findings; however, these observations require further validation in prospective studies.

Keywords: advanced cancer, Warburg effect, cancer pain, opioids, metabolic therapy

Introduction

Cancer is a major public health concern that threatens human health. According to the International Agency for Research on Cancer (IARC), there were 19.976 million new cancer cases and 9.7 million cancer-related deaths worldwide in 2022.[1] Cancer pain, particularly in the advanced stages, is characterized by prolonged, persistent, and often intractable pain, which severely affects the survival quality of patients.[2,3] According to the World Health Organization's (WHO) three-step approach to analgesia, the management of cancer pain is typically categorized into three stages, progressively increasing the intensity of treatment from non-opioids (eg, NSAIDs) to weak opioids (eg, tramadol) to strong opioids (eg, morphine)[4] Clinical studies have shown that 92% of patients receiving the full WHO three-step therapy eventually required conversion to strong opioids due to inadequate pain relief[5] Current clinical pain management for patients with advanced cancer, primarily relying on opioids, can alleviate pain but is associated with adverse effects, such as nausea, vomiting, dizziness, and respiratory depression. The long-term or excessive use of opioids may lead to dependency and addiction, limiting their clinical utility.[6,7] Experimental and observational studies[8] suggest that opioids may promote tumor growth and increase infection risk via the hypothalamic–pituitary–adrenal axis, potentially reduce the efficacy of

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immunotherapy, and even shorten patient survival. Moreover, the severity of cancer-related pain and the corresponding opioid requirements have been associated with lower survival rates in patients with advanced cancer.[9,10] Therefore, there is an urgent need for novel therapeutic approaches to alleviate cancer pain, without the adverse effects of traditional analgesics.

The Warburg effect hypothesis, proposed by Nobel laureate Otto Warburg in 1927, which posits that tumor cells preferentially utilize glycolysis for energy production, even in the presence of oxygen, and that the proliferation of cancer cells can be effectively inhibited by restricting or modifying the uptake of glucose.[11–13] A metabolism-based anticancer strategy has been developed to regulate glucose metabolism through insulin-induced hypoglycemia combined with low-dose anticancer treatment. Because this therapeutic regimen was designed based on principles related to tumor metabolic vulnerability and the Warburg effect hypothesis, the term "Warburg therapy" is used throughout this manuscript for descriptive convenience rather than as a standardized therapeutic category.

During the administration of Warburg therapy, insulin will be utilized to induce short-term hypoglycemic states in patients and combined with low-dose chemotherapeutic agents to inhibit tumor proliferation. Over the past decade, this therapeutic approach has demonstrated its safety and clinical feasibility across multiple clinical centers within China through studies and applications involving a substantial number of patients.[14–16] Clincially, cancer pain is usually caused by tumor growth and associated treatments. As tumors increase in size, they may exert compressive forces on surrounding tissues and nerves. Additionally, chemotherapeutic agents, while targeting tumor cells, can inadvertently damage healthy cells, resulting in inflammatory responses and pain.[2,17,18] Therefore, therapeutic strategies capable of influencing tumor-associated metabolic processes or reducing treatment-related burden may contribute to symptom improvement. Although Warburg therapy has been suggested to influence tumor metabolism, its specific analgesic effects have not been widely investigated. Therefore, the primary objective of this study was to evaluate the analgesic potential of Warburg therapy through a retrospective analysis of 71 patients with advanced cancer, thereby providing exploratory clinical insights into cancer pain management.

Methods

Study Design and Patient Inclusion Criteria

This retrospective analysis included 71 patients with advanced cancer treated at Wuxi People's Hospital and its medical consortium from October 2023 to May 2025. The study was approved by the Ethics Committee of Wuxi People's Hospital (KY23149; KY24137) and registered on ClinicalTrials.gov (NCT06404528). Informed consent was obtained from all participants.

Inclusion Criteria: (1) Patients diagnosed with stage III-IV malignant tumors confirmed by pathology or clinical diagnosis; (2) Patients exhibited a distinct pain site and the Verbal Rating Scale (VRS) score of ≥ 3 upon admission. Exclusion Criteria: (1) Patients with cognitive impairment or mental illness; (2) Patients allergic to the drugs used in the study; (3) Patients with severe dysfunction of vital organs such as the heart, liver, or kidneys. The cohort included 34 males and 37 females, aged 29–89 years, with 16 different types of advanced cancers, predominantly digestive system tumors (53.52%), and 66 patients (92.96%) were diagnosed with stage IV disease. The majority of patients experienced intermittent pain (52.6%), and most of the pain was located in the abdominal region (70.42%). (Table 1).

Table 1 Demographics and Clinical Characteristics of Patients

Characteristic	No. of Patients (n=71)	Percent (%)
Sex		
Male	34	47.89
Female	37	52.11

(*Continued*)

Table 1 (Continued).

Characteristic	No. of Patients (n=71)	Percent (%)
Age, years		
≤ 50	12	16.90
51–70	41	57.75
≥ 71	18	25.35
Cancer Type		
Respiratory system tumors	10	14.09
Digestive system tumors	38	53.52
Head and neck tumors	18	25.35
Urogenital system tumors	5	7.04
Cancer Stage	5	7.04
III	66	92.96
IV		
The nature of pain	33	46.48
Dull pain	13	18.31
Sharp pain	25	35.21
Intermittent pain		
Number of treatments per patient		
≤4	18	25.35
5-10	38	53.52
≥11	15	21.13

Treatment Regimen

All the patients underwent Warburg therapy. Prior to treatment, patients fasted overnight to stabilize their blood glucose levels. Subsequently, regular insulin was administered intravenously to induce a hypoglycemic state, typically reducing the blood glucose level to approximately 2 mmol/L. The initial dose of regular insulin was typically set at 10–12 IU, which was further individualized and titrated dynamically based on the patient's baseline blood glucose levels, insulin sensitivity, and real-time blood glucose changes. Blood glucose was monitored at 10 minute intervals, and when non-diabetic patients reached < 2.8 mmol/L or diabetic patients reached < 3.8 mmol/L, a subconventional dose of fluorouracil (250 mg) and cyclophosphamide (200 mg) was administered intravenously. Thirty minutes after administration, patients were provided with food or intravenous glucose to restore normal blood glucose levels (Figure 1). Patients received daily treatment for 7 days, followed by a 1–2 month rest period before the subsequent cycle. Vital signs, including pulse, ECG, temperature, and blood pressure, were continuously monitored throughout the treatment. Among the 71 patients, 38 (53.52%) underwent 5–10 treatment cycles, and 15 (21.13%) underwent more than 11 cycles, with one patient receiving up to 23 cycles (Table 1). Pain intensity was recorded at the end of each treatment cycle, and the last completed cycle was used as the post-treatment endpoint for analysis.

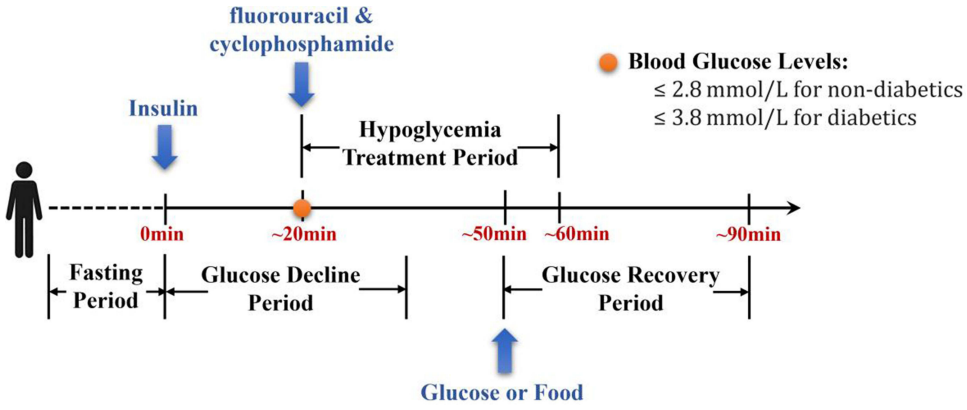

Figure 1 The Protocol for the Warburg therapy.

Outcome Measures

The primary endpoint of this study was the change in pain intensity from baseline to the end of treatment. Secondary endpoints included changes in opioid consumption and NSAID use. Tumor marker changes and overall survival were evaluated as exploratory outcomes.

A verbal rating scale (VRS) was utilized to assess the pain intensity of patients prior to treatment and following the completion of the final course of treatment, with scores ranging from 0 = no pain, 1 = mild discomfort, 2 = discomfort, 3 = comparatively painful/uncomfortable, 4 = very painful, and 5 = painful to extreme.[19,20]

Opioid usage before and during the final course of treatment was obtained by reviewing medical records, and opioid usage amounts were converted to daily oral morphine milligram equivalents (MME) for comparison, with conversion factors of 3, 0.1, 0.3, 0.37, 1.5, and 2.4 for intravenous morphine, oral tramadol, intravenous tramadol, intravenous Dezocine, oral oxycodone, and, fentanyl patch respectively.[21] As some patients also used NSAIDs (celecoxib) for adjunctive analgesia, the dosage of NSAIDs before and after treatment was also compared.

Available serum tumor marker data obtained before treatment initiation and following treatment completion were retrospectively reviewed to explore changes in tumor marker levels. Serum tumor markers were comprehensively evaluated based on standard clinical guidelines tailored to each specific malignancies. Depending on the primary tumor type and clinical indications determined by the attending oncologists, relevant biomarkers—including but not limited to carcinoembryonic antigen (CEA), carbohydrate antigen 19–9 (CA19-9), carbohydrate antigen 125 (CA125), and alpha-fetoprotein (AFP)—were routinely monitored at baseline and post-treatment. Imaging examinations performed during follow-up as part of routine clinical assessment were descriptively reviewed as exploratory observations. Radiological assessments were primarily performed using conventional computed tomography (CT) or magnetic resonance imaging (MRI) scans according to standard institutional guidelines.

Statistical Analysis

Normality was assessed using the Shapiro–Wilk test. As the analyzed variables were not normally distributed, continuous variables were presented as median with interquartile range (IQR), and paired comparisons were performed using the Wilcoxon signed-rank test.

A two-sided p value < 0.05 was considered statistically significant. Statistical analyses were performed using GraphPad Prism 9.

Results

Pain Management and Patient Outcomes

Figure 2 depicts the patients' pain improvement, with the median VRS pain score decreasing from 4 (IQR: 3–4) at baseline to 2 (IQR: 2–4) after treatment. This reduction in VRS scores following the final treatment course compared to

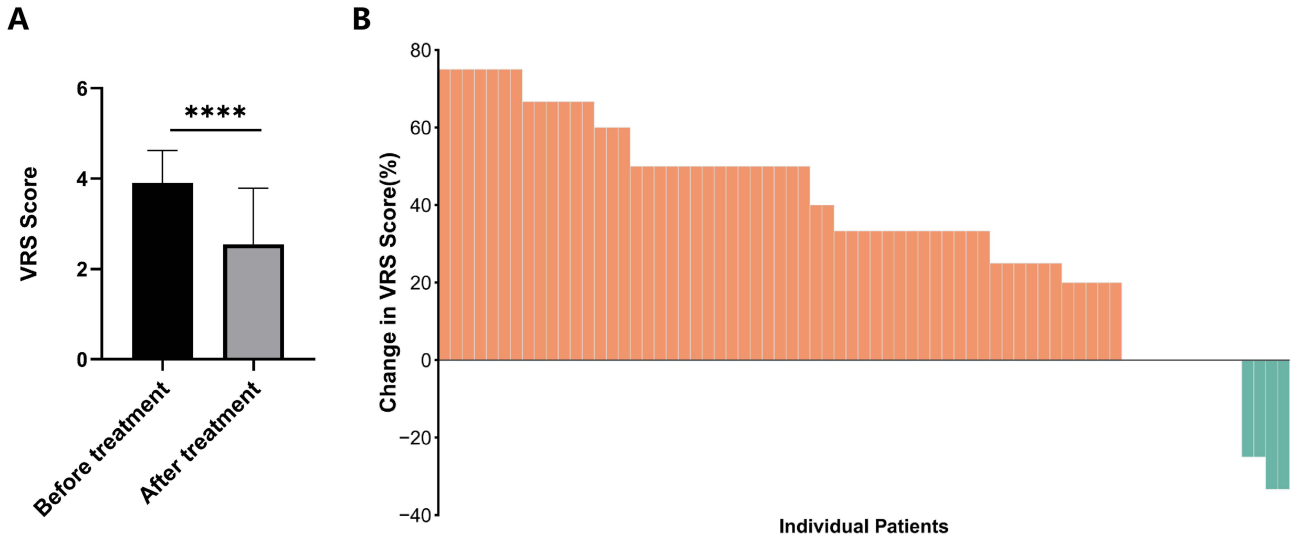

Figure 2 Changes in Pain Scores and Individual Pain Relief After Treatment (n=71). (**A**) Comparison of pain scores before and after treatment. Pain scores are presented as median with IQR. Statistical comparisons were performed using the Wilcoxon signed-rank test. ****P < 0.0001. (**B**) Waterfall plot showing individual percentage changes in pain relief based on VRS scores after treatment. Positive values indicate pain reduction, whereas negative values indicate worsening pain symptoms.

the pre-treatment baseline was statistically significant (Wilcoxon signed-rank test, $p < 0.0001$; 95% confidence interval [CI]: −1.605 to −1.099). Among the study population, 80.3% of patients experienced pain relief after treatment. Specifically, 43.7% (n = 31) achieved ≥ 50% pain reduction, 36.6% (n = 26) experienced pain reduction between 20% and 50%, and 19.7% (n = 14) showed minimal pain reduction (< 20%), including 10 patients with no change in pain intensity and 4 patients whose pain worsened after treatment.

Further analysis of pain variation across treatment cycles showed that among the 57 patients who experienced pain relief, 54 patients (94.7%) maintained a stable pain status without rebound in VRS scores for at least three months after first treatment, while 3 patients (5.3%) exhibited a gradual increase in VRS due to tumor progression in the later stages of treatment, though their pain levels remained lower than those before treatment. These findings suggest that the analgesic effect of the treatment was generally stable and sustained during the treatment period, with most patients maintaining pain relief without rebound.

Among the 71 patients followed up until November 2025, 43 (60.6%) had died, 26 (36.6%) were still alive, and 2 (2.8%) were lost to follow-up. Overall survival (OS) ranged from 1 to 26 months, with a median OS of 9 months. Notably, 25 patients (35.2%) survived for 12 months or longer.

Safety and Adverse Events During Treatment

As shown in Table 2, treatment-related adverse events were predominantly transient hypoglycemia-related symptoms, including drowsiness, dizziness, weakness, palpitations, and sweating/warmth sensation. Palpitations and sweating/warmth sensation were the most frequently observed manifestations during treatment, while some patients additionally experienced drowsiness, weakness, or dizziness.

Following treatment completion and subsequent oral intake or intravenous glucose administration, blood glucose levels gradually recovered, and all observed hypoglycemia-related symptoms resolved without persistent sequelae. Treatment interruption or postponement was primarily related to changes in patients' clinical conditions rather than severe hypoglycemia-related events. Throughout all treatment sessions, no severe hypoglycemia-related complications, including seizures, severe arrhythmias, or intensive care unit transfer, were observed. No treatment-related deaths occurred.

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Table 2 Treatment-Related Adverse Events

Adverse Event	No. of Patients (n=71)	Percent (%)
Sleepiness/Drowsiness	49	69.01%
Dizziness	10	14.08%
Weakness	17	23.94%
Palpitations	62	87.32%
Sweating/warmth sensation	63	88.73%
Seizure	0	0.00%
Arrhythmia	0	0.00%
ICU transfer	0	0.00%

The Opioid Use of Patients

Among the 71 patients, 2 patients did not take any analgesic medication throughout the treatment, and 19 received only NSAIDs as adjuvant analgesia. As shown in Figure 3, there was no statistically significant difference in morphine consumption before and after treatment. The median daily morphine milligram equivalent (MME) was 10 mg/day (IQR: 0–20) at baseline and 10 mg/day (IQR: 3–20) during the final treatment cycle (Wilcoxon signed-rank test, $p = 0.8217$; 95% confidence interval [CI]: −9.992 to 9.362). Although no significant reduction in overall opioid consumption was observed, 26 of the 50 patients receiving opioids at baseline (52%) demonstrated reduced or stable opioid requirements after treatment. Overall, 10 discontinued opioid use entirely after treatment, and 12 achieved a ≥50% reduction in MME.

In addition, 67 patients used NSAIDs (celecoxib) as adjuvant analgesia before and after treatment. The median daily NSAID dose decreased from 400 mg/day (IQR: 0–400) at baseline to 0 mg/day (IQR: 0–400) during the final treatment cycle (Wilcoxon signed-rank test, $p < 0.0001$; 95% confidence interval [CI]: −184.6 to −78.10). Among these patients, 7 switched to oral NSAIDs for pain control after discontinuing morphine.

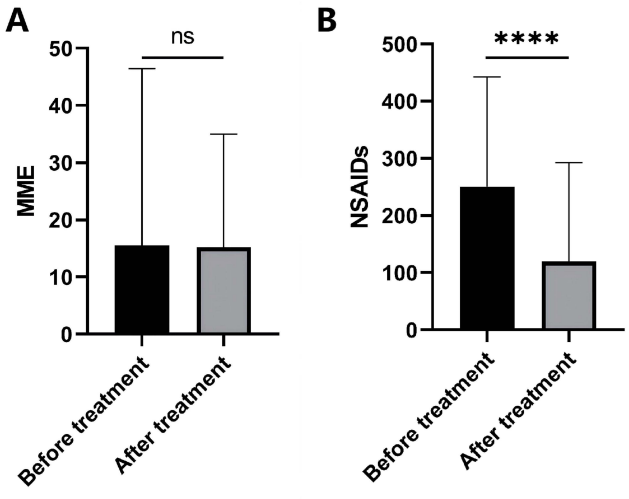

Figure 3 Changes in analgesic medication use before and after treatment. (**A**) Changes in daily opioid consumption measured as morphine milligram equivalents (MME) (n=50); (**B**) Changes in daily NSAID consumption (n=67). Data are shown as median with IQR. Statistical comparisons were performed using the Wilcoxon signed-rank test. ns, no significant difference; ****P < 0.0001.

Serum Tumor Marker Changes During Treatment

To explore changes associated with treatment, alterations in measurable peripheral blood tumor markers were analyzed. Among the 71 enrolled patients, 16 lacked complete pre- and post-treatment samples, and 8 maintained tumor marker levels within the normal range throughout treatment. The remaining 47 patients presented with at least one elevated tumor marker. Given the heterogeneity of testing items among patients (eg, CA125, CEA, CA19-9, CA15-3, etc), the marker showing the highest pre-treatment elevation in each patient was selected as the representative indicator for efficacy assessment Given the heterogeneity of baseline tumor marker levels and marker types across patients, a variation within ± 5% was pragmatically defined as indicating relative stability for descriptive purposes.

Results showed that in 23 patients (48.94%), the representative tumor marker decreased after treatment, with 10 patients (21.28%) exhibiting a reduction greater than 50% (Figure 4). Seven patients (14.89%) showed minimal or no change, while 17 patients (36.17%) demonstrated increased marker levels. Overall, these findings suggest that reductions in selected tumor markers were observed in a subset of patients; however, due to marker heterogeneity and the absence of standardized radiologic response assessment, tumor marker analyses should be considered exploratory and hypothesis-generating.

Representative Imaging Findings in Selected Patients

To provide descriptive examples of radiologic changes observed during treatment, representative imaging findings from two selected patients are presented below. These cases are presented to illustrate imaging changes observed during treatment rather than to provide a standardized assessment of tumor progression or treatment response across the entire cohort.

As shown in Figure 5, Patient P1 was diagnosed with lung cancer in December 2022 after presenting with recurrent chest tightness. The patient initially received six cycles of chemotherapy combined with immunotherapy but discontinued due to severe fatigue and poor appetite, and was switched to oral apatinib therapy. In November 2023, follow-up CT revealed multiple hepatic metastases. After six cycles of second-line chemotherapy, disease progression was observed. The patient subsequently began Warburg therapy in June 2024. Baseline CT demonstrated multiple hepatic metastatic lesions. After four months of treatment, most liver lesions had disappeared, and after five months, only two to three small residual nodules remained (Figure 5A–C).

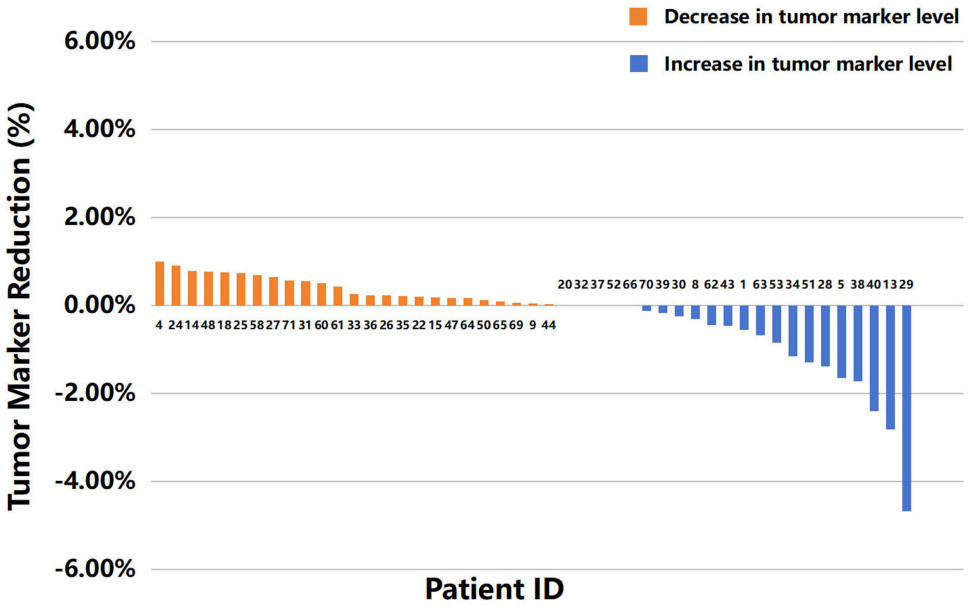

Figure 4 Tumor markers were measured before and after treatment. (n=47). Each bar represents one patient (Patient ID). Orange bars indicate decreased tumor marker levels, whereas blue bars indicate increased tumor marker levels.

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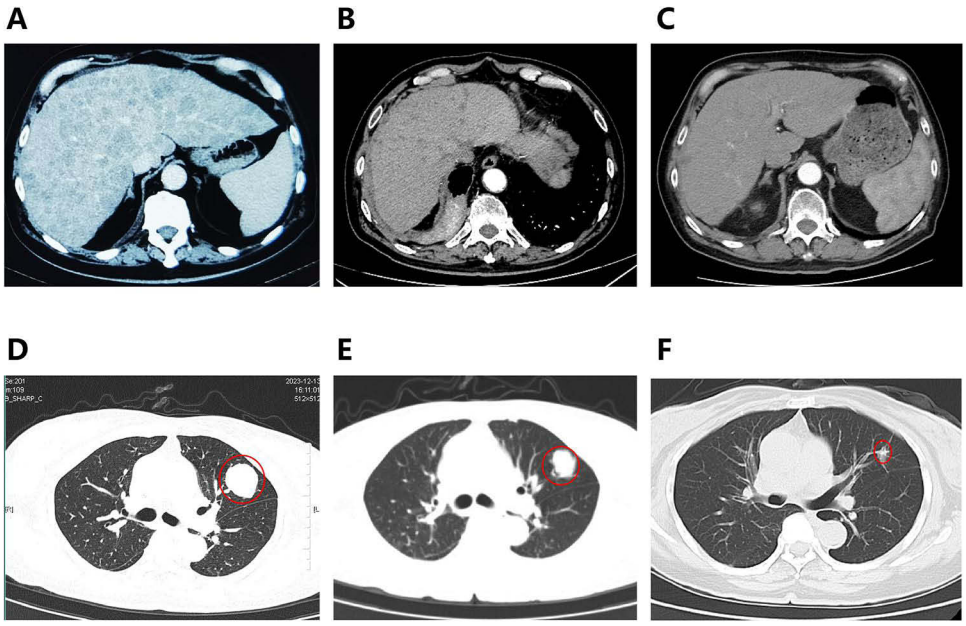

Figure 5 Representative imaging changes in two patients treated with Warburg therapy. (**A–C**) Patient P1: CT scans showing multiple hepatic metastases at baseline (**A**) marked regression after 4 months (**B**) and only 2–3 small residual lesions after 5 months (**C**). (**D–F**) Patient P2: CT scans showing a left lung metastatic lesion (3 × 3 cm) at baseline (**D**) decreased in size after 3 months (**E**) and reduced to 1×0.8 cm after 11 months (**F**). The red encircled regions highlight the changes in the lung metastatic lesion.

Patient P2 was diagnosed with adrenocortical carcinoma of the left adrenal gland in 2021 and underwent laparoscopic adrenalectomy. In 2022, follow-up PET–CT revealed a hypermetabolic nodule in the posterior segment of the left upper lung lobe. Thoracoscopic wedge resection was performed, and pathology confirmed metastatic adrenocortical carcinoma. Postoperative treatment with mitotane and etoposide was discontinued due to severe nausea, vomiting, and fatigue. The patient began Warburg therapy in December 2023. At baseline, the left lung metastatic lesion measured approximately 3×3 cm. After several treatment cycles, CT in March 2024 showed a marked reduction in lesion size, and by November 2024, only a small residual nodule (approximately 1×0.8 cm) remained (Figure 5D–F).

Discussion

Malignant cancer has consistently been the primary disease that significantly threatens human health, with cancer-related pain being the most prevalent complication. Untreated or inadequately managed cancer pain can exacerbate the condition, severely impacting patients' quality of life. Currently, chemotherapy remains the primary modality for cancer treatment. Although high doses of chemotherapeutic agents can, to a certain extent, inhibit tumor growth and prolong survival, the adverse effects that occur during chemotherapy can exacerbate the patient's discomfort. The theoretical basis of the Warburg effect is rooted in the dependence of tumor cells on a high-glucose environment. Some researches have demonstrated that more than 70% of patients with solid tumors exhibit abnormal glucose uptake in 18F-FDG PET examination, indicating that altered glucose metabolism represents a significant target for cancer therapy.[22,23] Presently, a number of in vitro and clinical studies have demonstrated that insulin pretreatment significantly enhances the inhibitory effects of various cytotoxic drugs. On one hand, insulin administration can induce a pharmacological hypoglycemic state and reduce glucose uptake in tumor cells by limiting glucose availability.[24] On the other hand, under glucose-deprived conditions, tumor cells may fail to obtain sufficient energy to express multidrug resistance–related proteins.[15,25] This mechanism is hypothesized to markedly enhance tumor cell sensitivity to chemotherapeutic agents and consequently improve treatment efficacy.[26] Cyclophosphamide is a broad-spectrum antineoplastic agent with potent immunostimulatory effects, and compared with other chemotherapeutics, fluorouracil has a shorter half-life and is more easily metabolized.[27,28] Therefore, we have employed the use of insulin to induce short term hypoglycemia in the Warburg therapy protocol. The induced hypoglycemia limits the supply of blood glucose creating a hypoglycemic period during which chemotherapy drugs are administered. Its safety has been demonstrated in prior observational reports.[14]

In this study, we retrospectively analyzed 71 patients with advanced cancer who received Warburg therapy, focusing on changes in pain intensity, analgesic consumption, and exploratory tumor-related outcomes before and after treatment. The results demonstrated that the patients' pain scores were significantly reduced compared to those before treatment.

Analysis of opioid and NSAID consumption showed that patients' morphine use remained stable, while NSAID (celecoxib) consumption significantly decreased, and 10 patients successfully transitioned from opioids to NSAIDs for pain control, without any reported withdrawal symptoms. In our patient population, three cases exhibited MME/day > 50 mg prior to treatment, and in the final course of treatment, MME/day was reduced to conventional doses (≤ 30 mg) in two of these cases. In addition, after the final treatment course, 12 patients (30%) achieved more than a 50% reduction in opioid dosage, which may reduce the potential adverse effects and risks associated with long-term opioid dependence. Although the mean opioid dose did not show a statistically significant decrease across the entire cohort, the successful de-escalation from potent opioids to NSAIDs in specific patients highlights a potential role for this protocol as an adjunctive strategy in multimodal cancer pain management, warranting further prospective evaluation.

According to the WHO's three-step analgesic ladder, the demand for analgesics in patients with advanced cancer generally increases as the disease progresses. Non-steroidal and weak opioid analgesics exhibit a "ceiling effect," where escalating doses fail to enhance analgesic efficacy but instead increase drug-related adverse reactions. In contrast, opioids provide potent analgesia without a ceiling effect. However, the long-term use of opioids, particularly at escalating doses, may induce various adverse effects and dependence.

In 2022, the Centers for Disease Control and Prevention (CDC) issued guidelines for prescribing opioids for chronic pain, emphasizing that the risks of adverse effects and mortality are dose dependent. Compared with conventional doses, when higher opioid doses are administered (ie, MME/day > 50 mg), the risk of overdose increases by 19 to 4.6 times, encompassing but not limited to addiction, gastrointestinal reactions, cardiotoxicity, respiratory depression, and mortality.[29]

Despite their established role in cancer pain management, real-world data suggest that opioid tapering is uncommon once treatment is initiated. In a palliative care study[30] reported that among 145 cancer patients, only 25 (17%) were able to taper and discontinue opioids, with 3 (12%) experiencing withdrawal symptoms during the process. Similarly, a large retrospective study,[31] only 1.3% of non-cancer patients maintained stable opioid intake during long-term follow-up.

Beyond pain control, growing evidence has suggested that opioid exposure may be associated with broader clinical implications. Previous research[30] has reported that while opioid use is effective for pain relief, increasing opioid requirements for cancer-related pain do not necessarily correlate with improved survival. In addition, a meta-analysis[32] indicated that opioid use was associated with significantly reduced overall survival (OS) and progression-free survival (PFS) in patients receiving immune checkpoint inhibitor (ICI) therapy.

From a metabolic perspective, tumor cells rely heavily on glycolysis for energy production, and interventions targeting glucose availability may alter tumor metabolic dynamics. By depriving tumor cells of glucose—the key substrate required for high glycolytic flux—Warburg therapy reduces lactate accumulation and mitigates extracellular acidification, which may consequently alleviate acid-induced nociception.[33] In addition, it is also plausible that such metabolic modulation may influence signaling pathways involved in tumor-induced bone pain, including RANKL-mediated mechanisms,[34] however, these potential mechanisms remain hypothetical and warrant further investigation in future studies.

This study also has several limitations. First, the retrospective, single-center, pre–post cohort design without a control group precludes causal inference; observed improvements in pain scores may be influenced by placebo effects, regression to the mean, or natural disease fluctuations rather than the specific effects of Warburg therapy. Furthermore, the cohort included heterogeneous tumor types with different pain mechanisms and disease trajectories, limiting the generalizability of the findings and precluding robust subgroup analyses. In addition, the relatively small sample size and single-center setting further limit statistical power and external validity.

Second, pain intensity and opioid use were assessed only at baseline and at the end of treatment, without longitudinal follow-up measurements, which may not fully capture temporal changes in pain dynamics or treatment-related fluctuations. Outcome assessment time points also varied across patients due to differences in treatment cycles and follow-up duration, introducing additional variability in exposure and disease status at evaluation.

Finally, the proposed mechanisms underlying the observed analgesic effects, such as metabolic reprogramming or altered RANKL signaling, remain speculative and require further experimental validation.

Therefore, future large-scale, multicenter prospective studies incorporating dynamic pain monitoring and mechanistic biomarkers are warranted to validate these findings and elucidate the biological pathways through which Warburg therapy may modulate tumor-associated pain.

Conclusion

In summary, this single-center retrospective cohort study of patients with advanced cancer suggests that Warburg therapy, a metabolism-based therapeutic strategy, may reduce cancer-related pain and is associated with decreased analgesic requirements. While preliminary, these data suggest that Warburg therapy represents a potential adjunctive strategy for multimodal cancer pain management, though further validation in large-scale prospective studies remains necessary.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of the Wuxi People's Hospital (ethical approval number: KY23149; KY24137), and registered on ClinicalTrials.gov (NCT06404528). All patients included in the study provided informed consent. All experiments were performed in accordance with local ethics standards and Helsinki Declaration of 1976.

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Disclosure

Michael Pennington reports patenting is planned that would be broadly relevant but not directly involved with the current publication. The authors declare no other conflicts of interest.

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