

INPLASY

INPLASY202370087

doi: 10.37766/inplasy2023.7.0087

Received: 21 July 2023

Published: 21 July 2023

Corresponding author:

Mikhail Yadgarov

mikhail.yadgarov@gmail.com

Author Affiliation:

Dmitry Rogachev National Medical
Center of Pediatric Hematology,
Oncology and Immunology,
Moscow, Russia.

Prognostic significance of 18F-FDG PET/CT-based metabolic parameters in adults and children with soft-tissue sarcoma: a meta-analysis

Yadgarov, MY¹; Berikashvili, LB²; Rakova, ES³; Kachanov, DY⁴;
Likar, YN⁵.

ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202370087

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 July 2023 and was last updated on 21 July 2023.

INTRODUCTION

Review question / Objective The aim of our study is to investigate the impact of baseline and post-therapy 18F-FDG PET/CT-based metabolic parameters on overall and event-free survival in adults and children with soft-tissue sarcoma.

(i) population: children, adolescents and adults with soft-tissue sarcomas (STS) undergoing baseline and/or post-neoadjuvant chemotherapy (NAC) 18F-FDG PET/CT

(ii) exposure: high baseline/post-NAC maximum standardized uptake value (SUVmax), high SUV ratio (SUVmax2 [post-NAC] / SUVmax1 [baseline]), high baseline metabolic tumor volume (MTV), high baseline total lesion glycolysis (TLG) values

(iii) comparator: low baseline/post-NAC SUVmax, low SUV ratio, low baseline MTV, low baseline TLG values

(iv) outcomes: event-free survival (EFS), overall survival (OS)

(v) study design: prospective and retrospective cohort studies.

Rationale Integrating additional parameters that have the potential to enhance prognostic prediction is essential, both at the onset of the disease and following neoadjuvant chemotherapy. The existing prognostic factors commonly used in oncology, such as the presence of metastases, stage, histologic subtype, and tumor volume, exhibit limited effectiveness. However, the introduction of novel parameters holds promise for improving prognostic accuracy.

While previous meta-analyses have explored the prognostic value of 18F-FDG PET/CT parameters in soft tissue sarcoma patients, recent studies have indicated a potentially diminished prognostic efficacy of these parameters in the pediatric population. Notably, these previous meta-analyses did not specifically consider the pediatric age group.

To address this gap, we have undertaken a systematic review and meta-analysis that incorporates an in-depth analysis of age subgroups, sensitivity analyses, and employs the GRADE approach to evaluate the certainty of evidence.

Through our study, we aim to provide a comprehensive understanding of the prognostic value of 18F-FDG PET/CT parameters in adults and pediatric patients with soft tissue sarcomas.

Condition being studied Various types of soft-tissue sarcomas.

METHODS

Search strategy Various types of soft-tissue sarcomas.

Participant or population Children, adolescents and adults with STS undergoing baseline and/or post-NAC 18F-FDG PET/CT.

Intervention Exposure: patients with high baseline/post-NAC SUVmax, high SUV ratio, high baseline MTV, high baseline TLG values.

Comparator Patients with low baseline/post-NAC SUVmax, low SUV ratio, low baseline MTV, low baseline TLG values.

Study designs to be included We will include prospective and retrospective cohort studies.

Eligibility criteria Inclusion criteria: cohort studies which included patients with soft tissue sarcoma and investigated the association between 18F-FDG PET-CT metabolic parameters (SUVmax, MTV, or TLG) and survival outcome (OS or EFS). Studies were excluded if they met one of the following criteria: 1) review articles, case reports; 2) other tumors (bone sarcomas, Ewing sarcomas); 3) no relevant outcomes; 4) research on animals; 5) outcomes reported for mixed groups; 6) other radiopharmaceuticals used; 7) duplicated publications.

Information sources PubMed, MEDLINE, Google Scholar, Cochrane Library.

Main outcome(s) The main study outcomes included: 1) Event-free survival. 2) Overall survival.

Quality assessment / Risk of bias analysis The internal validity and risk of bias will be assessed by two independent reviewers using the "Tool to assess risk of bias in cohort studies" contributed by the CLARITY Group at McMaster University. Publication bias and small-study effects will be assessed using Egger's test and funnel plot analysis. The certainty of evidence will be assessed with GRADE approach.

Strategy of data synthesis Data extraction was performed by two independent authors. These

data included first author, year of publication, country, journal, design, PET scanners, study period, number of centers, follow-up period, sample size, cancer type, stage of disease, histological grade, tumor location, age and sex, PET/CT time points, segmentation methods for PET/CT parameters, cut-off determination method, and effect estimates for study outcomes.

We will use STATA 17 (StataCorp LLC, Texas, US) and Cochrane tool Review Manager (RevMan version 5.3) to perform meta-analysis. Hazard ratio (HR) will be used to measure the association between 18F-FDG PET/CT metabolic parameters and survival. Univariate HR values will be extracted directly if available or calculated using Tierney et al. methodology for original studies. Meta-regression analysis using restricted-maximum likelihood (REML) random-effects model will be performed to assess whether the association between exposure and survival outcome varies by patient age, histological grade, tumor location, sex, cut-off value for metabolic parameters and study design. Results of meta-analysis will be presented using forest-plots. Statistical significance was set at 0.05 for hypothesis testing.

Subgroup analysis We will analyze the following groups of patients:

1. Children, adolescents and young adults ($\geq 75\%$ of patients are 21 y.o. and younger)
2. Adults ($\geq 75\%$ of patients are over 21 y.o.)

Sensitivity analysis Sensitivity analysis will be conducted by using two models of analysis (fixed and random effects), by analyzing HR obtained in the Cox multivariable regression analysis in the original studies and by evaluating the results of only low/moderate risk of bias studies.

Language restriction No language limitation.

Country(ies) involved Russian Federation.

Keywords PET/CT, 18F-FDG, soft-tissue sarcomas, rhabdomyosarcoma, SUVmax, MTV, TLG, survival, meta-analysis.

Contributions of each author

Author 1 - Mikhail Yadgarov - Collected the data, contributed data and analysis tools, performed the analysis, assessed risk of bias, certainty of evidence rating, wrote the paper.

Email: mikhail.yadgarov@gmail.com

Author 2 - Levan Berikashvili - Contributed data and analysis tools, assessed risk of bias, certainty of evidence rating.

Email: levan.berikashvili@mail.ru

Author 3 - Elena Rakova - Collected the data, wrote the paper.

Author 4 - Denis Kachanov - Conceived and designed the analysis, revised the manuscript, wrote the paper.

Email: kachanov78@gmail.com

Author 5 - Yury Likar - Conceived and designed the analysis, revised the manuscript, wrote the paper.

Email: likar2007@gmail.com