

Prevalence and assessment tools of cancer-related cognitive impairment in lung cancer survivors: A systematic review and proportional meta-analysis

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ABSTRACT

Purpose Cancer-related cognitive impairment (CRCI) is a significant risk factor influencing the quality of life in lung cancer survivors. No absolute assessment tool has been confirmed to assess CRCI in lung cancer survivors. This review was undertaken to pool the overall prevalence of CRCI and to summarize the assessment tools in assessing CRCI among lung cancer survivors.

Methods PubMed, Cochrane Library, Embase, CINAHL, and CNKI were searched to retrieve articles reported CRCI prevalence. Summary prevalence estimates were pooled using a random effects model, along with corresponding 95% prediction intervals (PIs). The Freeman-Tukey double arcsine transformation of proportions was incorporated in the analysis. Additionally, subgroup analysis, meta-regression, and leave-one-out analysis were performed.

Results A total of 12 studies, involving 1934 survivors, were included in the review. All of these studies were found to have a low risk of bias in terms of their methodological quality. Four studies (33.3%) utilized the International Cognition and Cancer Task Force (ICCTF) criteria to identify CRCI through neuropsychological tests. The pooled prevalence rate of CRCI was found to be 26% (95% PI, 16–37%), $I^2 = 95.97%$. The region in which the studies were conducted was identified as a significant factor contributing to this heterogeneity ($p = 0.013$). No indication of small-study effects was found (Egger's test: $p = 0.9191$).

Conclusion This review provides an overview of CRCI prevalence and assessment tools in lung cancer survivors. The findings can serve as epidemiological evidence to enhance clinicians' and researchers' understanding of early detection and assessment.

INTRODUCTION

There are insufficient research on cognitive changes among lung cancer surviving patients, cancer-related cognitive impairment (CRCI) remains a crucial missing piece of the puzzle that requires further investigation.

The cognitive function of cancer survivors can be influenced not only by the progression of the disease itself but also by the treatments administered to combat it. And survivors are not fully aware of the cognitive functioning decline caused by the cancer treatments; clinical recognition and psychoeducation about CRCI are likely the most crucial aspect of its management.

Various risk factors have been identified for CRCI, including advanced age, lower levels of cognitive functioning prior to undergoing cancer treatments such as chemotherapy, surgery, radiation therapy, and combined therapy, cancer-related symptoms, and physical inactivity.

The aim of this review is to pool the overall prevalence of CRCI and to summarize the assessment tools in assessing CRCI among lung cancer survivors.

METHODS AND MATERIALS

DESIGN: This systematic review and proportional meta-analysis adhered to the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines to ensure accurate and transparent reporting of the findings. The review protocol was registered in PROSPERO ID: CRD42023403279.

SEARCH METHODS: The search for relevant studies encompassed five electronic databases, namely PubMed, Cochrane Library, Embase, CINAHL, and CNKI, from their inception until May 2023.

INCLUSION AND EXCLUSION CRITERIA: The inclusion criteria for articles in this review were as follows: (1) publication in a peer-reviewed journal in the English language, (2) reporting of cases related to cancer-related cognitive impairment, and (3) focusing on lung cancer survivors.

SYNTHESIS: a random effects model was employed to pool the summary prevalence estimates, presented in percentages (%), along with their corresponding 95% prediction intervals (PIs) and confidence intervals (CIs). Subgroup analysis, meta-regression, and leave-one-out analysis were also performed.

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RESULTS

The prevalence of cancer-related cognitive impairment varied widely across the included studies, ranging from 6 to 84.4%. Figure 2 displays the forest plot, which presents the pooled prevalence estimates of the included studies.

Our meta-regression analysis has shown that region ($p = 0.013$) was a factor associated with the heterogeneity. Figure 3 presents the bubble plot for the heterogeneity factor.

The result of the leave-one-out analysis shows that omitting study by Bartels et al. (2021) causes the overall prevalence of CRCI to decrease by 23%, while the overall prevalence of 12 studies was 26% (Figure 4). The analysis did not show any evidence of small-study effects (Egger's test: $p = 0.9191$).

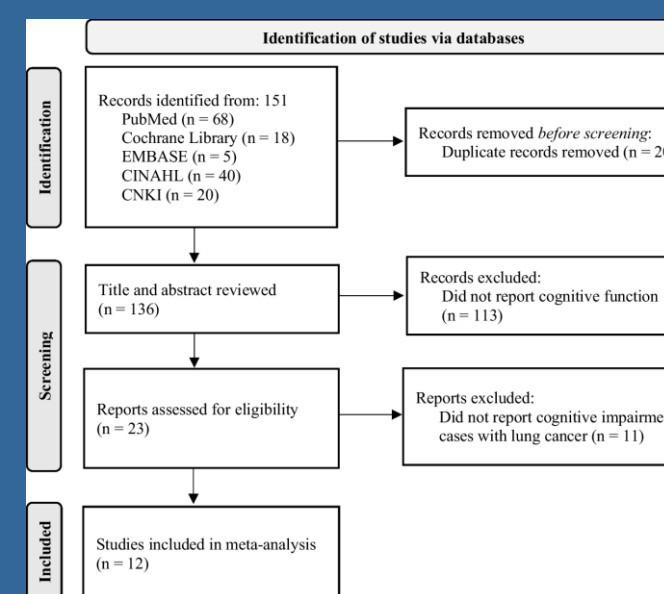


Figure 1. Flow diagram detailing the selection process

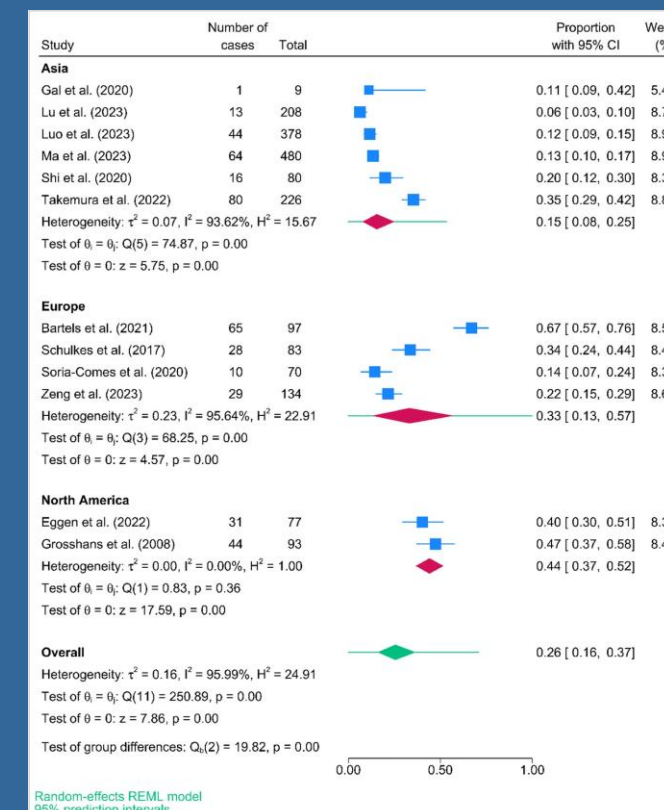


Figure 2. The forest plot of the overall pooled prevalence and study conducted in Asia, Europe, and North America reported estimates of cancer-related cognitive impairment from a random effects model

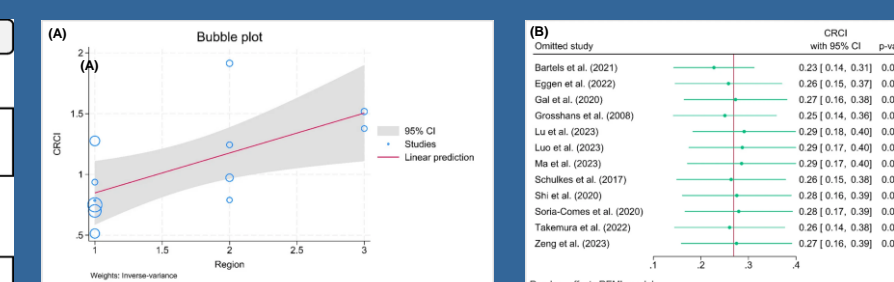


Figure 3(A). Bubble plot for region to display the result of meta-regression. Note. Region was found to be a significant factor contributing to heterogeneity ($p = 0.017$). CRCI, cancer-related cognitive impairment

Figure 3(B). Leave-one-out analysis to identify the outlier and its impact. Note. Omitting study by Bartels et al. (2021) causes the overall prevalence of CRCI to decrease by 23% (overall prevalence of 12 studies was 26%). CRCI, cancer-related cognitive impairment

Table 1. Summary of cognitive function assessment in lung cancer survivors

Assessment	Domain	Description
Objective	Neuro-psychological tests/ Neurocognitive function tests	Verbal Learning and Memory Test HVLT-R Verbal Selective Reminding Test COWA Token Test
	Visuospatial memory	Rey-Osterrieth Complex Figure test Benton Visual Retention Test
	Working memory	CANTAB (Cambridge Stockings) Digit span forward and backward Arithmetic subtests of the WAIS-R
	Attention	Test of Attentional Performance
	Executive function	TMT Part B Wisconsin Card Sorting Number of perseverative errors
	Processing speed and visual attention	TMT Part A Digit Symbol subtest of the WAIS-R
	Mental flexibility	TMT Part B
	Verbal and visual reasoning	Similarities and Block Design subtests of the WAIS-R
	Motor coordination	Grip strength Grooved pegboard test Finger tapping
	MMSE	Orientation
Repetition		Repeating named prompts
Verbal recall		Repeating named prompts recall Serial sevens
SPMSQ	Language	Naming a pencil and a watch Visual construction Varies, involving drawing figure shown
	Memory	Short-term and long-term memory
	Information	Orientation to surroundings Information about current events Serial mathematical tasks Capacity to perform serial mathematical tasks
Subjective	CogPCI	Perceived cognitive impairment Functional assessment of cancer therapy-cognitive scale
	FACT-Cog	Perceived cognitive impairment Perceived cognitive abilities Concerns from others Impact on quality of life
EORTC QLQ-C30 cognitive function subscale	Perceived cognitive function (memory and attention)	Have you had difficulty concentrating on things like reading a newspaper or watching television? (attention) Have you had difficulty remembering things? (Memory)

Abbreviations. COWA, Controlled Oral Word Association; HVLT-R, Hopkins Verbal Learning Test-Revised; CANTAB, Cambridge Neuropsychological Test Automated Battery; WAIS-R, Wechsler Adult Intelligence Scale-Revised; TMT, Trail Making Test; MMSE, Mini-Mental State Examination; CogPCI, Perceived Cognitive Impairment subscale; SPMSQ, Short Portable Mental State Questionnaire; FACT-Cog, Functional Assessment of Cancer Therapy; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire.

DISCUSSION

This meta-analysis represents the first attempt to summarize the overall prevalence of cognitive-related cancer-related impairment (CRCI) among lung cancer survivors. The result indicates the prevalence of CRCI in lung cancer survivors was 26%, which is similar to breast cancer survivors (around 15–25%).

Of 12 studies involving 1934 lung cancer survivors, 33.3% reported that CRCI was assessed by neuropsychological tests using the ICCTF criteria, 25% applied the MMSE, and 8.3% reported the application of the SPMSQ.

As for the subjective assessments measuring perceived cognitive impairment for CRCI, three studies applied subjective assessments including CogPCI subscale and EORTC QLQ-C30 cognitive function subscale.

Further, in the subgroup analysis, we pooled the subgroup prevalence according to region (Asia/Europe/North America) and types of assessment (objective/subjective). Studies conducted in Asia (15%) shows lower prevalence of CRCI than in Europe (33%) and North America (44%).

The meta-regression analysis revealed that the study region was a source of heterogeneity in this meta-analysis.

CONCLUSIONS

In this meta-analysis, which included a total of 12 studies, it was found that the combined prevalence of CRCI among lung cancer survivors was estimated to be 26%.

The analysis also highlighted the significant impact of study region on the observed heterogeneity. There is a need for evidence-based interventions and policies that focus on preventing and reducing the prevalence of CRCI.

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