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META-ANALYSIS ARTICLE

Serum ferritin as a prognostic biomarker in CAR-T therapy for multiple myeloma: A meta-analysis

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ABSTRACT

Serum ferritin, a marker of systemic inflammation and iron metabolism, has been implicated in the outcomes of patients with relapsed/refractory multiple myeloma (R/R MM). However, its prognostic significance in R/R MM patients undergoing chimeric antigen receptor-modified T-cell (CAR-T) therapy remains unclear. This meta-analysis aimed to evaluate the association between pre-infusion serum ferritin levels and survival outcomes in R/R MM patients treated with CAR-T therapy. We systematically searched PubMed, Embase, and Web of Science for relevant studies. Studies reporting progression-free survival (PFS) and/or overall survival (OS) based on serum ferritin levels were included. Hazard ratios (HRs) with 95% confidence intervals (CIs) were pooled using a random-effects model.
Eight retrospective cohort studies, encompassing 1,077 patients, met the inclusion criteria. High pre-infusion serum ferritin levels were significantly associated with worse PFS (HR: 2.15, 95% CI: 1.74–2.66, $p < 0.001$) and OS (HR: 2.86, 95% CI: 2.20–3.72, $p < 0.001$), with mild heterogeneity ($I^2 = 9\%$ for PFS and 0% for OS). Sensitivity analyses, conducted by excluding one study at a time, confirmed the robustness of these findings. Subgroup analyses showed consistent results across different CAR-T product sources (commercial vs. academic), ferritin cutoffs, and follow-up durations (p for subgroup differences all > 0.05).
In conclusion, elevated serum ferritin levels before CAR-T infusion predict poorer survival outcomes in R/R MM patients. These findings highlight the potential prognostic value of ferritin and its role in optimizing patient selection and management strategies in CAR-T therapy.

Keywords: Multiple myeloma; chimeric antigen receptor-modified T cells; CAR-T; ferritin; survival; progression

INTRODUCTION

Relapsed/refractory multiple myeloma (R/R MM) is a challenging hematologic malignancy characterized by the persistence or recurrence of disease despite standard therapies (1, 2). This aggressive condition accounts for a substantial proportion of morbidity and mortality in multiple myeloma patients (3). The prognosis of R/R MM

remains poor, with limited therapeutic options, particularly for patients who have failed multiple lines of treatment (4). In recent years, chimeric antigen receptor T-cell (CAR-T) therapy has emerged as a promising option, offering targeted and durable responses by redirecting a patient's immune cells to attack malignant plasma cells expressing the B-cell maturation antigen (BCMA) (5, 6). However, despite its efficacy, the outcomes of CAR-T therapy vary significantly among patients, necessitating a deeper understanding of prognostic factors to improve patient selection and treatment outcomes (7, 8).

Ferritin, a ubiquitous iron-storage protein, plays a dual role as a key regulator of iron homeostasis and an acute-phase reactant (9). Elevated serum ferritin levels are often associated with systemic inflammation, oxidative stress, and immune dysregulation (10, 11), which are common in advanced malignancies and intensive therapies like CAR-T. In the context of R/R MM, ferritin's role extends beyond its biochemical properties, potentially serving as a biomarker of disease activity and treatment outcomes (12). Previous studies have indicated that elevated ferritin levels may correlate with adverse clinical outcomes, including reduced survival, but evidence specific to patients undergoing CAR-T therapy remains sparse (13, 14). The potential mechanisms linking high serum ferritin levels to poor prognosis in CAR-T-treated R/R MM patients are multifaceted. Elevated ferritin may reflect a pro-inflammatory milieu that exacerbates treatment-related toxicities such as cytokine release syndrome (CRS) (15) and immune effector cell-associated neurotoxicity syndrome (ICANS) (16), which are critical determinants of CAR-T outcomes. Additionally, ferritin's association with iron overload and oxidative stress may impair immune cell functionality, reducing the effectiveness of CAR-T cells and fostering an immunosuppressive tumor microenvironment (17). Despite these insights, the prognostic value of serum ferritin in CAR-T therapy for R/R MM remains poorly defined, with most available evidence stemming from small, heterogeneous studies (18-25). In view of this knowledge gap, we performed a meta-analysis in this study to comprehensively evaluate the association between pre-infusion serum ferritin levels and survival outcomes in patients with R/R MM treated with CAR-T therapy.

MATERIAL AND METHODS

Study design and data sources

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (26, 27) and the Cochrane Handbook for Systematic Reviews and Meta-analyses (28). The protocol of the meta-analysis has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration identifier CRD42025636605. We systematically searched PubMed, EMBASE, and Web of Science databases from database inception to January 3, 2025. The search strategy included terms related to "ferritin," "CAR-T therapy," and "relapsed/refractory multiple myeloma", with the combination of ("ferritin" OR "ferritins") AND ("myeloma" OR "multiple myeloma") AND ("Chimeric Antigen Receptor" OR "Chimeric Antigen Receptors" OR "Chimeric T Cell Receptors" OR "Chimeric T-Cell Receptors" OR "Chimeric Antigen Receptor T Cell" OR "CAR-T" OR "Artificial T Cell Receptors" OR "Artificial T-Cell Receptors" OR "chimeric immunoreceptors" OR "Axicabtagene ciloleucel" OR "Axi-cel" OR "KTE-C19" OR "KTEC19" OR "CTL-019" OR "CTL019" OR "Yescarta" OR "Lisocabtagene" OR "maraleucel" OR "Liso-cel" OR "JCAR-017" OR "JCAR017" OR "Breyanzi" OR "Brexucabtagene" OR "autoleucel" OR "Brexu-cel" OR "KTE-X19" OR "KTEX19" OR "Tecartus" OR "Tisagenlecleucel" OR "Tisa-cel" OR "Kymriah" OR "ART-19" OR "CART19" OR "Axicabtagene" OR "ciloleucel" OR "Idecabtagene" OR "vicleucel" OR "Ciltacabtegene" OR "autoleucel"). Reference lists of relevant original and review articles were also reviewed to identify potentially relevant studies. Only studies published in English were considered. The detailed search strategy for each database is shown in **Supplemental File 1**.

Inclusion and exclusion criteria

The inclusion criteria for potential studies were defined according to the PICOS framework:

P (patients): Adults (≥18 years old) diagnosed with R/R MM who were treated with CAR-T.

I (exposure): A high serum ferritin level before the infusion of CAR-T was considered as exposure. The cutoffs for defining a high level of serum ferritin were consistent with the values used in the original studies.

C (comparison): Patients with a low level of serum ferritin before the infusion of CAR-T were considered as controls.

O (outcome): Evaluated the median progression-free survival (PFS) and/or overall survival (OS) following CAR-T therapy by comparing R/R MM patients with high versus low serum level of ferritin and reported the data of the hazard ratio (HR) and 95% confidence interval (CI) for these outcomes. In general, PFS was defined as the time from CAR-T infusion to relapse, disease progression, all-cause mortality, or the last follow-up, while OS was defined as the time from CAR-T infusion to all-cause mortality or the last follow-up.

S (study design): Observational studies with longitudinal follow-up, such as cohort studies, nested case-control studies, and post-hoc analyses of clinical trials.

Review, editorial, meta-analyses, preclinical studies, studies not limited to patients with MM, without serum ferritin level as exposure, or studies did not report the outcomes of interest were excluded. If two or more studies had overlapping populations, the study with the largest sample size was included in the meta-analysis.

Study quality evaluation and data extraction

The literature search, study identification, quality assessment, and data extraction were conducted independently by two authors, with any disagreements resolved through discussion and consensus between the two authors. Study quality was evaluated using the Newcastle–Ottawa Scale (NOS) (29), which assesses the selection, control of confounders, and outcome measurement and analysis, with scores ranging from 1 to 9 and with 9 indicating the highest quality. Selection criteria included representativeness of the cohort (1 point if patients were consecutively or randomly selected), ascertainment of exposure (1 point if standard laboratory assays were used), and baseline disease status (1 point if outcome was not present at baseline). Comparability was scored based on adjustments for age, sex (1 point), and other key confounders (1 point). Outcome assessment included adequate follow-up duration (1 point if ≥12 months), completeness of follow-up (1 point if ≤20% loss to

follow-up), and reliable outcome assessment (1 point if based on medical records or registries). The data collected for analysis included the study details (author, year, country, and design), patient characteristics (diagnosis, sample size, mean age, and sex), CAR-T products used for therapy, timing of serum ferritin measuring and the cutoff values for defining a high serum ferritin level, follow-up duration, outcomes reported, and variables adjsuted when the association between serum ferritin level and survival outcomes were reported.

Statistical analyses

The associations between serum ferritin and PFS/OS of patients with R/R MM on CAR-T were presented as HRs and 95% CIs. Data of HRs and standard errors were calculated based on the 95% CIs or p values, followed by a logarithmical transformation to ensure stabilized variance and normalized distribution (28). The significance of heterogeneity was evaluated with the Cochrane Q test (28). The I^2 statistic was also calculated, and an I^2 value of 0% indicates no observed heterogeneity, while values of 25%, 50%, and 75% correspond to low, moderate, and high heterogeneity, respectively (30). A random-effects model was used to pool HRs and 95% CIs to account for potential variability among studies (28). Although statistical heterogeneity was low (I^2 = 9% for PFS and 0% for OS), we opted for a random-effects model as a more conservative approach, considering possible differences in study populations, ferritin cutoffs, and other unmeasured confounders. When heterogeneity is minimal, the results of a random-effects model are generally similar to those of a fixed-effects model, ensuring robust and generalizable findings (28). Via excluding individual studies sequentially, a sensitivity analysis was performed to evaluate the robustness of the findings. Predefined subgroup analyses were performed according to the source of CAR-T product (commercial or academic), cutoffs of defining a high serum ferritin, and follow-up durations. The medians of the continuous variables were selected as the cutoff values for defining subgroups. Publication bias was evaluated using funnel plots and visual inspection for asymmetry, supplemented by Egger's regression test (31). Analyses were performed using RevMan (Version 5.1; Cochrane Collaboration, Oxford, UK) and Stata software (version 12.0; Stata Corporation, College Station, TX, USA).

RESULTS

Study inclusion

The study inclusion process is illustrated in **Figure 1**. Initially, 227 potentially relevant records were identified from the three searched databases and citations of related articles, with 59 initially excluded due to duplication. A subsequent screening of the titles and abstracts led to the further exclusion of 145 articles, primarily because they did not align with the objectives of the meta-analysis. The full texts of the remaining 23 records were reviewed by two independent authors, resulting in the exclusion of 15 more records for various reasons, as detailed in **Figure 1**. Finally, eight articles remained and were deemed appropriate for inclusion in the quantitative analysis (18-25).

Overview of the study characteristics

Table 1 shows the summarized characteristics of the available studies included in the meta-analysis. These studies were all retrospective cohort studies, published between 2023 and 2025, and performed in the United States, China, Spain and Israel. Overall, 1077 patients with R/R MM were included, with the mean ages ranging from 57.0 to 64.0 years and the proportion of men varying from 44.0 to 62.5%. Commercial BCMA-directed CAR-T cell therapies including Idecabtagene Vicleucel and Ciltacabtagene Autoleucel were used in six studies (19-21, 23-25), while academic anti-BCMA CAR-T cells were used in the other two studies (18, 22). Serum ferritin levels were all measured before CAR-T infusion among the included studies. The cutoff values for defining a high serum ferritin were based on the medians in two studies (19, 24), the upper limit of normal (ULN) in five studies (20-23, 25), and the upper quartile of serum ferritin in another study (18). The median follow-up durations varied from 7.0 to 32.0 months. The outcome of PFS was reported in seven studies (18, 20-25), while the outcome of OS was reported in all the eight studies (18-25). For seven studies (18-23, 25), multivariate analyses were performed to evaluate the association between serum ferritin and survival outcomes, with the adjustment of age, sex, extramedullary disease (EMD), and performance status etc. to a varying degree. For another study (24), the univariate analysis was used. The NOS scores of the

included studies were six to eight, suggesting an overall moderate to good study quality (**Table 2**).

Meta-analysis for the outcome of PFS

Overall, seven studies (18, 20-25) reported the association between pre-infusion serum ferritin and PFS of R/R MM patients who were treated with CAR-T. A mild heterogeneity was observed among the studies (I^2 = 9%). Poole results with a random-effects model showed that patients with a high serum ferritin before CAR-T infusion were associated with a poor PFS (HR: 2.15, 95% CI: 1.74 to 2.66, p < 0.001; **Figure 2A**). Further sensitivity analysis by excluding one dataset at a time did not significantly change the results (HR: 1.98 to 2.35, p all < 0.05). Specifically, excluding the only study with univariate analysis (24) showed similar results (HR: 2.08, 95% CI: 1.70 to 2.55, p < 0.001; I^2 = 0%). Subsequent subgroup analyses indicated that the association between pre-infusion serum ferritin and poor PFS were not significantly different between studies with commercial and academic CAR-T (p for subgroup difference = 0.52; **Figure 2B**), among studies with different cutoffs of serum ferritin (p for subgroup difference = 0.78; **Figure 3A**), or between studies with follow-up durations > or ≥ 12 months (p for subgroup difference = 0.06; **Figure 3B**).

Meta-analysis for the outcome of OS

The pooled results with eight studies (18-25) showed that a high serum ferritin level before CAR-T infusion was associated with poor OS in R/R MM patients during follow-up (HR: 2.86, 95% CI: 2.20 to 3.72, p < 0.001; **Figure 4A**) with no significant heterogeneity (I^2 = 0%). Sensitivity analyses by omitting one study at a time showed similar results (HR: 2.78 to 2.98, p all < 0.05). The results were also consistent by excluding the only study (24) with univariate analysis (HR: 2.82, 95% CI: 2.16 to 3.68, p < 0.001; I^2 = 0%). Further subgroup analyses according to the source of CAR-T products (p for subgroup difference = 0.86; **Figure 4B**), cutoffs of serum ferritin (p for subgroup difference = 0.85; **Figure 5A**), and median follow-up durations (p for subgroup difference = 0.64; **Figure 5B**) also showed consistent results.

Publication bias

The funnel plots for the meta-analyses of the association between pre-infusion serum ferritin and the survival outcomes of patients with R/R MM are shown in **Figure 6A**

and 6B. The plots are symmetrical on visual inspection, suggesting a low risk of publication bias. Further results of Egger's regression analyses also showed a low risk of publication bias ($p = 0.42$ for the outcome of PFS and $p = 0.51$ for the outcome of OS).

DISCUSSION

The findings of this meta-analysis demonstrate a significant association between high pre-infusion serum ferritin levels and poor survival outcomes in patients with R/R MM treated with CAR-T therapy. Specifically, patients with elevated ferritin levels before CAR-T infusion exhibited a markedly increased risk of shorter PFS and OS. These findings remained robust across sensitivity analyses, subgroup analyses by CAR-T product source, ferritin cutoffs, and follow-up durations, with low or no heterogeneity detected. These results underscore the prognostic significance of serum ferritin in this clinical setting, providing a potential biomarker for risk stratification.

The mechanisms linking elevated ferritin levels to poor survival in CAR-T-treated R/R MM patients are complex and multifactorial. Pathophysiologically, ferritin reflects systemic inflammation and oxidative stress, both of which are prominent in advanced malignancies (32). Elevated ferritin is associated with increased levels of pro-inflammatory cytokines such as interleukin-6, which can exacerbate CAR-T-related toxicities, including CRS and ICANS (16). These adverse events are critical determinants of survival, and their severity may be amplified in patients with high baseline ferritin levels (33). Clinically, high ferritin levels may indicate an immunosuppressive tumor microenvironment and impaired CAR-T cell functionality, potentially reducing the therapy's efficacy (34). Furthermore, elevated ferritin has been linked to increased risks of infections (35), cardiac events (36), cytopenia (37), and delayed platelet recovery (38) in patients with R/R MM on CAR-T therapy, all of which can compromise patient outcomes after CAR-T therapy. Collectively, these findings support the role of high pre-infusion serum ferritin as a predictor of poor survival of patients with R/R MM on CAR-T therapy.

The results of the sensitivity analyses highlight the robustness of the findings, as excluding individual studies or focusing on multivariate analyses did not significantly alter the association between high ferritin levels and poor survival. Moreover, sensitivity analysis by excluding the only study with univariate analysis showed

consistent results, which suggests that the association between a high ferritin and poor survival in these patients may be independent of factors such age, sex, presence of EMD, and performance status. Subgroup analyses further reinforced the consistency of these results, with no significant differences observed across CAR-T product sources (commercial vs. academic), ferritin cutoffs, or follow-up durations. These findings suggest that the prognostic impact of ferritin is broadly applicable across diverse patient populations and treatment settings, providing additional confidence in its clinical relevance.

This meta-analysis has several strengths. It represents an extensive and systematic evaluation of the most up-to-date evidence, including a comprehensive literature search and rigorous adherence to PRISMA guidelines. The focus on pre-infusion ferritin levels ensures that the findings are clinically actionable, as this biomarker can be readily assessed before therapy initiation. Moreover, the use of multiple sensitivity and subgroup analyses enhances the robustness of the results, providing a nuanced understanding of the factors that may influence the association between ferritin and survival outcomes.

However, several limitations should be acknowledged. All included studies were retrospective in design, which may introduce recall and selection biases (39). Accordingly, the results should be validated in prospective cohorts. Besides, our systematic literature search was restricted to PubMed, Embase, and Web of Science. While these databases are comprehensive, relevant studies indexed in other sources, such as the Cochrane Library or ClinicalTrials.gov may have been missed. Future systematic reviews could expand the search scope to include additional databases and grey literature to ensure a more exhaustive identification of relevant studies. Despite multivariate adjustments in most studies, unmeasured confounding factors may still have influenced the observed associations. In addition, the study-level data used in this meta-analysis precludes an evaluation of individual patient characteristics, such as comorbidities, functional status, or genetic factors, which may modulate the prognostic role of ferritin. For instance, patient comorbidities (e.g., cardiovascular disease, chronic infections, and liver dysfunction) could contribute to elevated ferritin levels independently of disease severity and systemic inflammation (40). Functional status and frailty are also important factors, as more frail patients may have higher baseline inflammation and poorer tolerance to CAR-T therapy (20). Additionally, genetic and molecular characteristics of multiple myeloma, such as high-risk

cytogenetics (e.g., del(17p), t(4;14)) or TP53 mutations, could influence both ferritin levels and disease prognosis (41). Another key limitation of this meta-analysis is that it focuses on pre-infusion ferritin levels, while dynamic changes in ferritin after CAR-T infusion were not assessed in the included studies. Monitoring ferritin kinetics over time (e.g., at day 7 and day 14 post-infusion) may provide additional prognostic insights, particularly regarding treatment-related toxicities such as CRS and ICANS. Future prospective studies should investigate whether changes in ferritin levels over time are predictive of survival outcomes in CAR-T-treated patients. Moreover, there is the lack of detailed information on the specific methods used to measure ferritin levels across studies. Differences in assay techniques may lead to variability in ferritin values, potentially affecting comparability between studies. However, as all included studies were conducted in real-world clinical settings, ferritin was likely measured using standard laboratory protocols. Future studies should report assay methodologies to ensure greater consistency and comparability of results. Finally, the observational nature of the included studies prevents the establishment of a causal relationship between elevated ferritin levels and poor survival outcomes.

Clinically, the results of this meta-analysis highlight the potential utility of serum ferritin as a prognostic biomarker in patients undergoing CAR-T therapy for R/R MM. Elevated ferritin levels may identify high-risk patients who require closer monitoring and more aggressive supportive care during treatment. However, it is essential to note that the role of ferritin is currently limited to risk stratification, and it is too early to consider it as a target for therapeutic intervention. Future research should focus on prospective studies to confirm the prognostic value of ferritin, explore its integration with other biomarkers and clinical parameters, and investigate its role in predicting and managing CAR-T-related efficacies and toxicities of patients with R/R MM. Nevertheless, future research should explore whether patients with high pre-infusion ferritin levels could benefit from enhanced prophylactic strategies, such as anti-inflammatory agents, to mitigate the risk of CRS and ICANS. While no direct evidence currently supports this approach, prospective studies incorporating ferritin-guided risk stratification may help optimize supportive care in CAR-T therapy.

CONCLUSION

In conclusion, this meta-analysis provides up-to-date evidence that elevated pre-infusion serum ferritin levels are associated with poor survival outcomes in patients with R/R MM treated with CAR-T therapy. These findings underscore the potential of ferritin as a prognostic marker and offer valuable insights into its possible clinical utility. While further research is needed to address the limitations of the current evidence and refine its applications, the results contribute to the growing body of knowledge aimed at improving patient outcomes in the era of CAR-T therapy.

Conflicts of interest: The authors declare no competing interests.

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Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Characteristics of the included studies

Author year	Country	Study design	Diagnosis	Sample size	Mean age (years)	Male (%)	CART-T treatment	Timing of ferritin measuring	Ferritin cutoff determination	Ferritin cutoff value (ng/mL)	Follow-up duration (months)	Outcomes reported	Variables adjusted
Mohty 2023	USA	RC	R/R MM	133	66	44	Idecabtagene vicleucel or Ciltacabtagene autoleucel	During lymphodepletion	Median	228	9	OS	Age, sex, CRP, CAR-T product, marrow burden, R-ISS, EMD, use of bridging therapy, and ECOG ≥2
Liu 2023	China	RC	R/R MM	109	57	59	Academic anti-BCMA CAR-T cells alone or	Within 3 days before CAR-T cell infusion	Upper quartile	882.3	32	PFS and OS	Age, sex, tumor burden, EMD, and R-ISS stage

							combined with anti-CD19 CAR-T cells						
Dima 2024	USA	RC	R/R MM	152	63	54	Idecabtagene vicleucel or Ciltacabtagene autoleucel	Before lymphodepletion and CAR-T infusion	ULN	400	12.5	PFS and OS	Age, sex, active EMD, ECOG PS, cytogenetics, penta-refractory status, prior BCMA therapy, and baseline CRP
Moreno 2024	USA	RC	R/R MM	40	64	62.5	Idecabtagene vicleucel or Ciltacabtagene autoleucel	Pre-CAR-T infusion	Median	337	13.5	PFS and OS	None
Hashmi	USA	RC	R/R MM	211	64	60	Idecabtagene	During	ULN	400	9.9	PFS and	Age, sex, prior

2024							vicleucel	lymphodepletion				OS	BCMA therapy, EMD, bridging therapy, ethnicity, and t(4;14) at infusion
Gagelmann 2024	Spain and Israel	RC	R/R MM	60	63	54	Academic CAR-T products targeting BCMA	Before lymphodepletion	ULN	400	10.7	PFS and OS	Age, sex, EMD, high-risk cytogenetics, lenalidomide refractoriness, and MyCARe risk
Davis 2024	USA	RC	R/R MM	136	62	53	Idecabtagene vicleucel or Ciltacabtagene autoleucel	Before lymphodepletion	ULN	400	7	PFS and OS	Age, sex, frailty, type of CAR-T product, HCT-CI, ECOG PS,

													EMD, high-risk cytogenetics, and penta-refractory status
Sidana 2025	USA	RC	R/R MM	236	64	57	Ciltacabtagene autoleucel	Before lymphodepletion	ULN	400	13	PFS and OS	Age, sex, prior BCMA targeted therapy, ECOG PS, EMD, and high-risk cytogenetics

BCMA: B-cell maturation antigen; CAR-T: chimeric antigen receptor T-cell; CRP: c-reactive protein; EMD: extramedullary disease; ECOG PS: Eastern Cooperative Oncology Group performance status; HCT-CI: the Hematopoietic Cell Transplantation Comorbidity Index; MyCARe: Myeloma Comorbidity and Age Risk Evaluation; OS: overall survival; PFS: progression-free survival; R-ISS: the Revised International Staging System; RC: retrospective cohort; R/R MM: relapsed/refractory multiple myeloma; ULN: upper limit of normal.

Table 2. Study quality evaluation via the Newcastle-Ottawa Scale.

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age and sex	Control for other confounding factors	Assessment of outcome	Enough long follow-up duration	Adequacy of follow-up of cohorts	Total
Mohty 2023	1	1	1	1	1	1	1	0 (< 12 months)	1	8
Liu 2023	0 (not consecutively or randomly included)	1	1	1	1	1	1	1	1	8
Dima 2024	0 (not consecutively or randomly included)	1	1	1	1	1	1	1	1	8
Moreno 2024	0 (not consecutively or randomly included)	1	1	1	0 (Univariate analysis only)	0 (Univariate analysis only)	1	1	1	6
Hashmi 2024	0 (not consecutively	1	1	1	1	1	1	0 (< 12	1	7

	or randomly included)							months)		
Gagelmann 2024	0 (not consecutively or randomly included)	1	1	1	1	1	1	0 (< 12 months)	1	7
Davis 2024	0 (not consecutively or randomly included)	1	1	1	1	1	1	0 (< 12 months)	1	7
Sidana 2025	0 (not consecutively or randomly included)	1	1	1	1	1	1	1	1	8

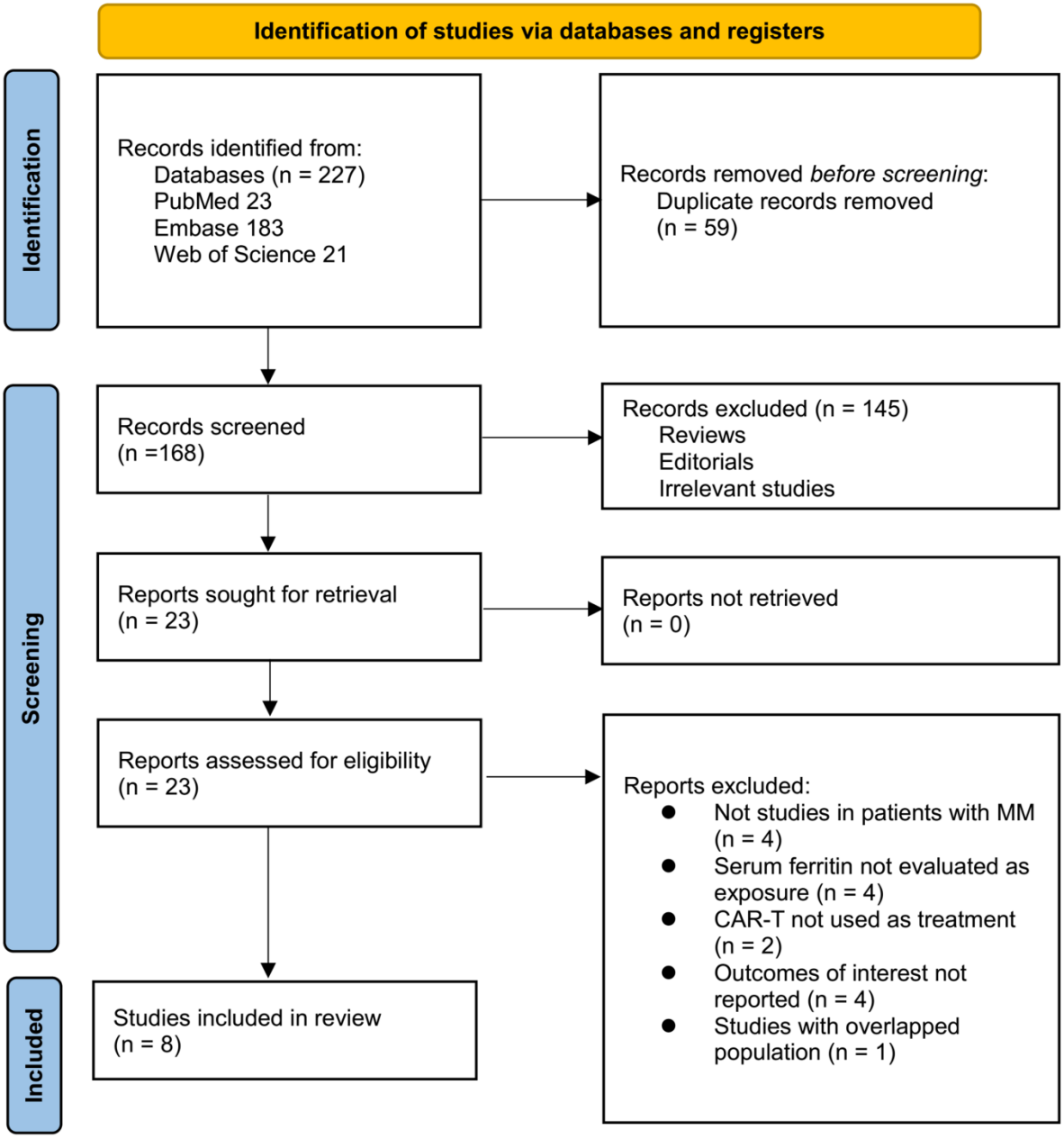

Figure 1. Flowchart of database search and study inclusion.

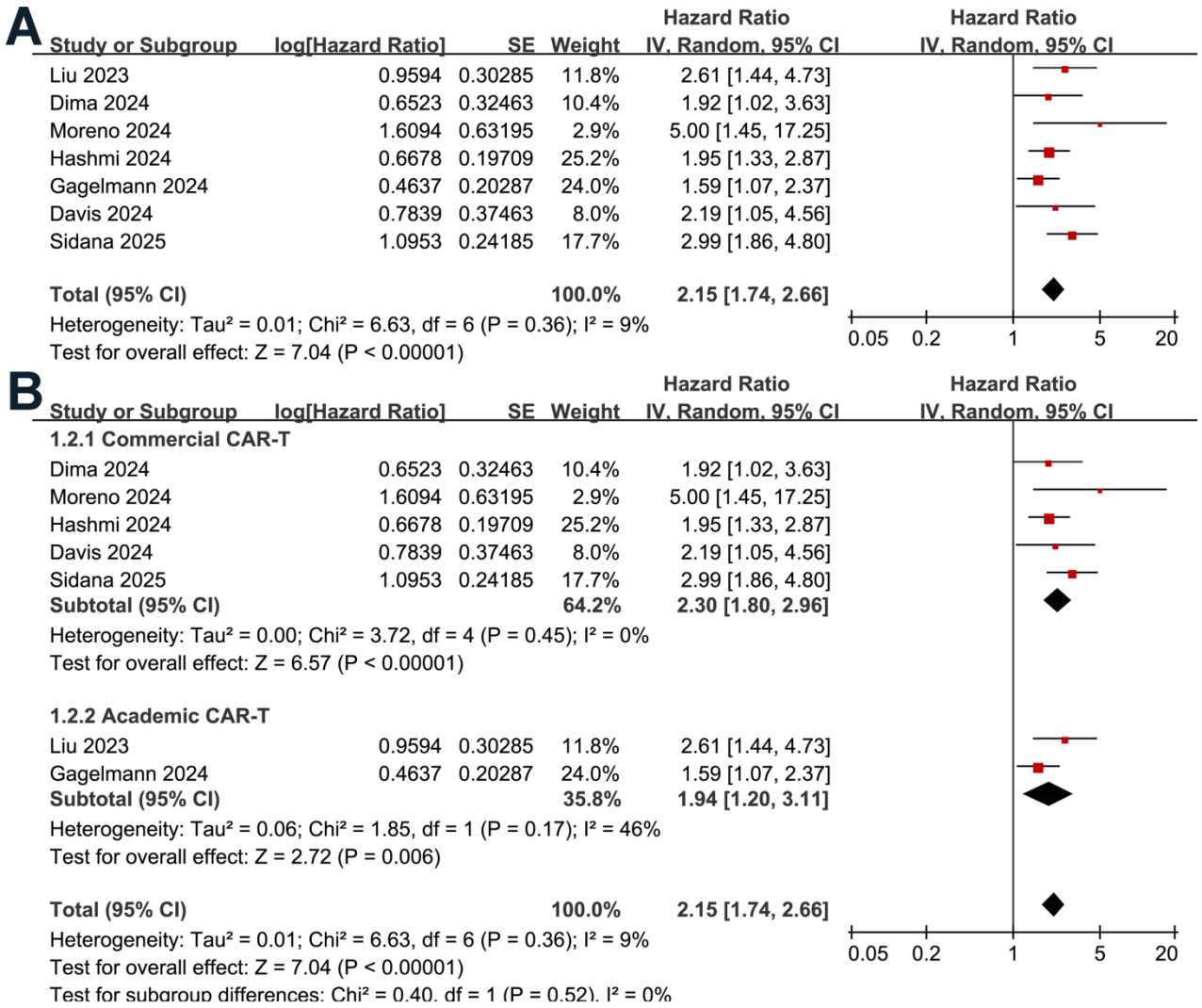

Figure 2. Forest plots for the meta-analysis of the association between pre-infusion serum ferritin and PFS of R/R MM patients on CAR-T; A, overall meta-analysis; and B, subgroup analysis according to the source of CAR-T products.

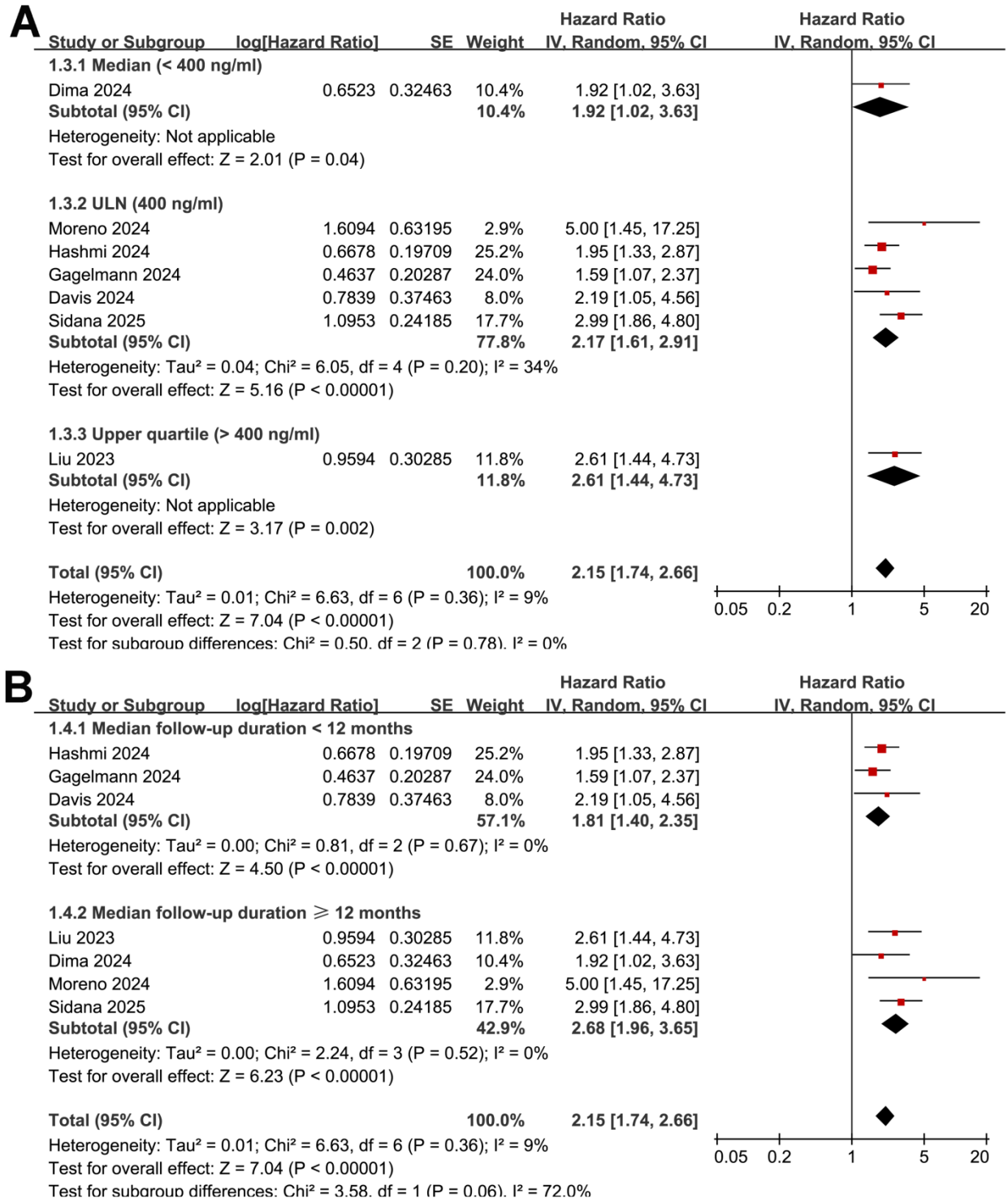

Figure 3. Forest plots for the subgroup analyses of the association between pre-infusion serum ferritin and PFS of R/R MM patients on CAR-T; A, subgroup analysis according to the cutoff of serum ferritin; and B, subgroup analysis according to the follow-up durations.

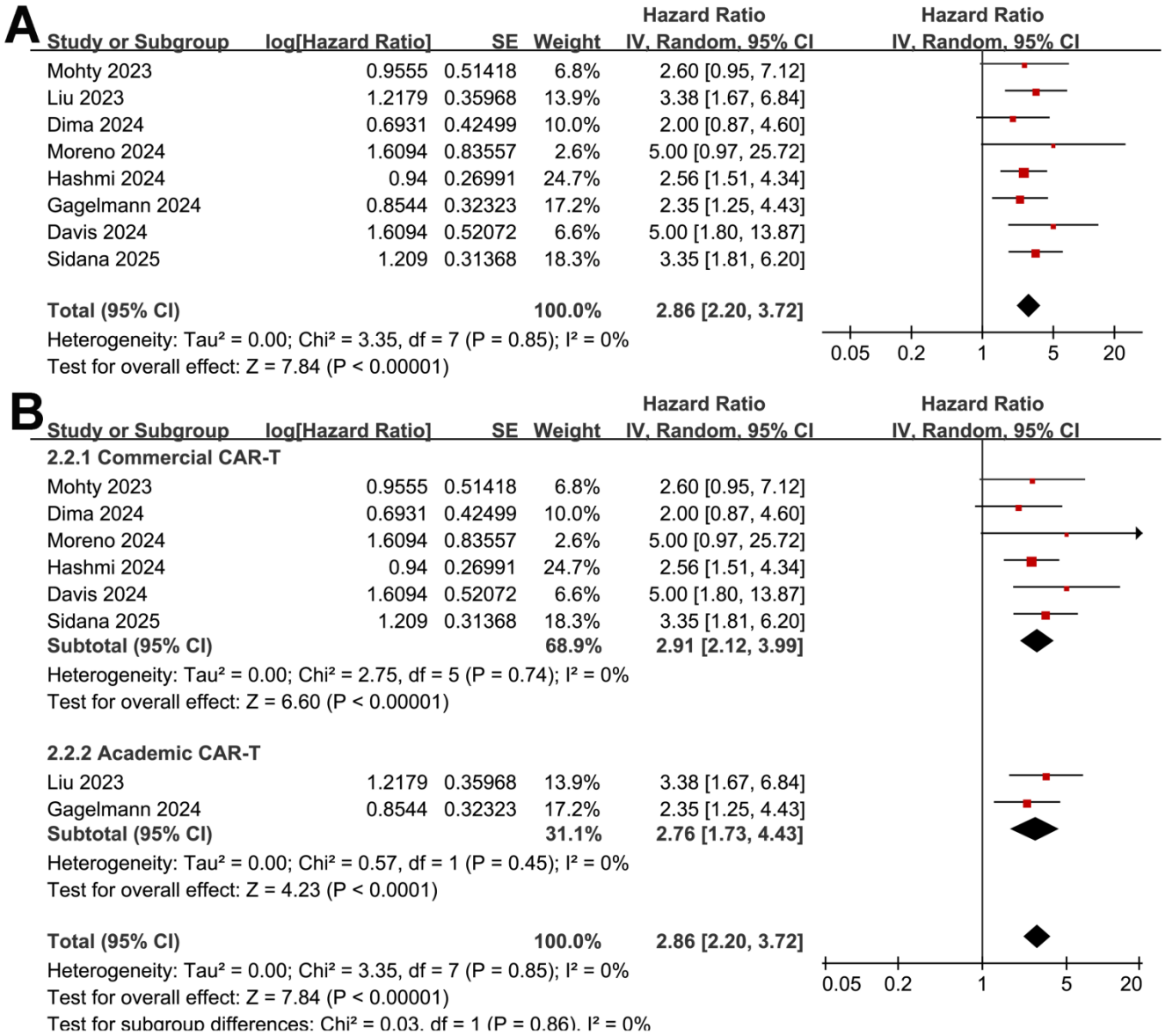

Figure 4. Forest plots for the meta-analysis of the association between pre-infusion serum ferritin and OS of R/R MM patients on CAR-T; A, overall meta-analysis; and B, subgroup analysis according to the source of CAR-T products.

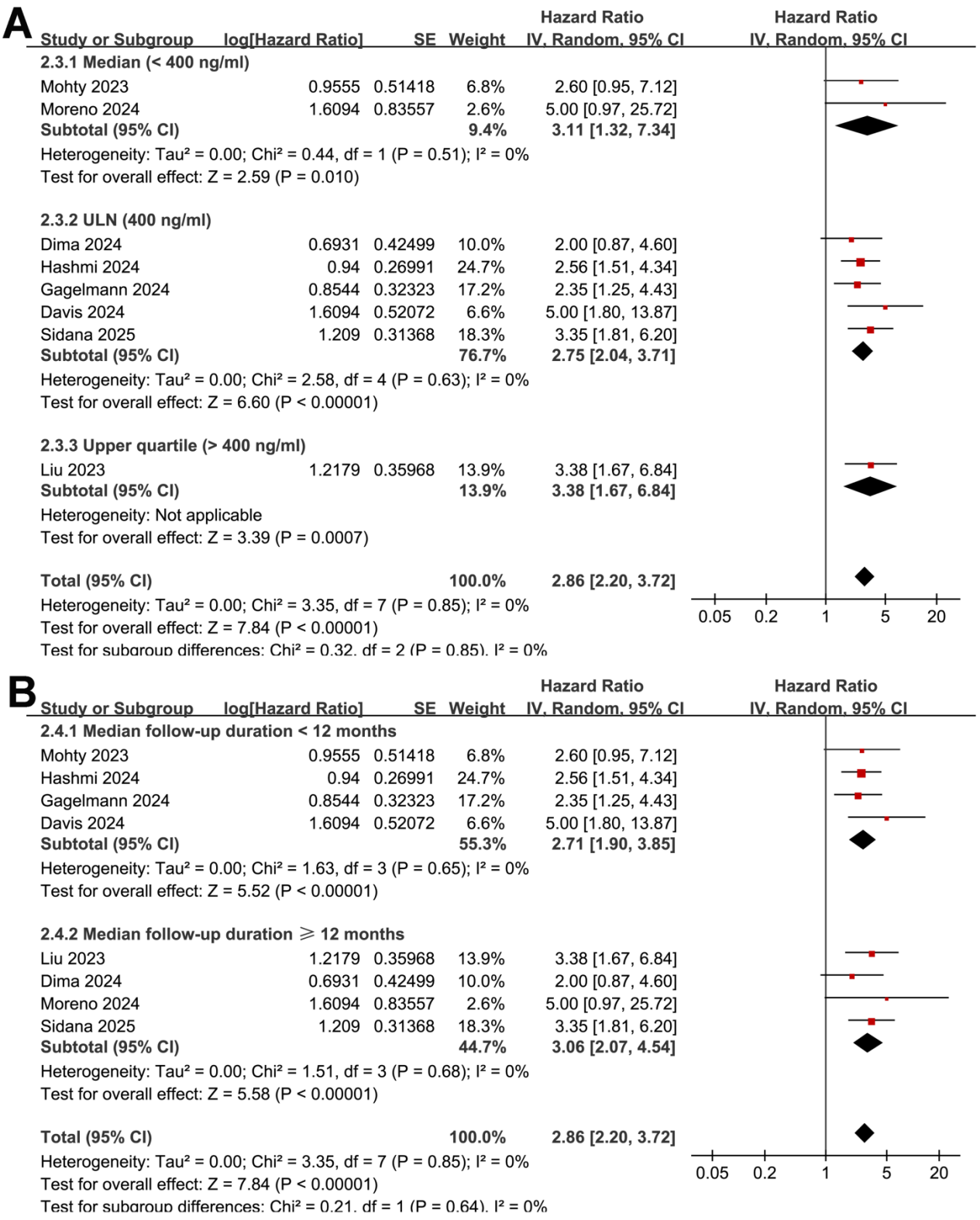

Figure 5. Forest plots for the subgroup analyses of the association between pre-infusion serum ferritin and OS of R/R MM patients on CAR-T; A, subgroup analysis according to the cutoff of serum ferritin; and B, subgroup analysis according to the follow-up durations.

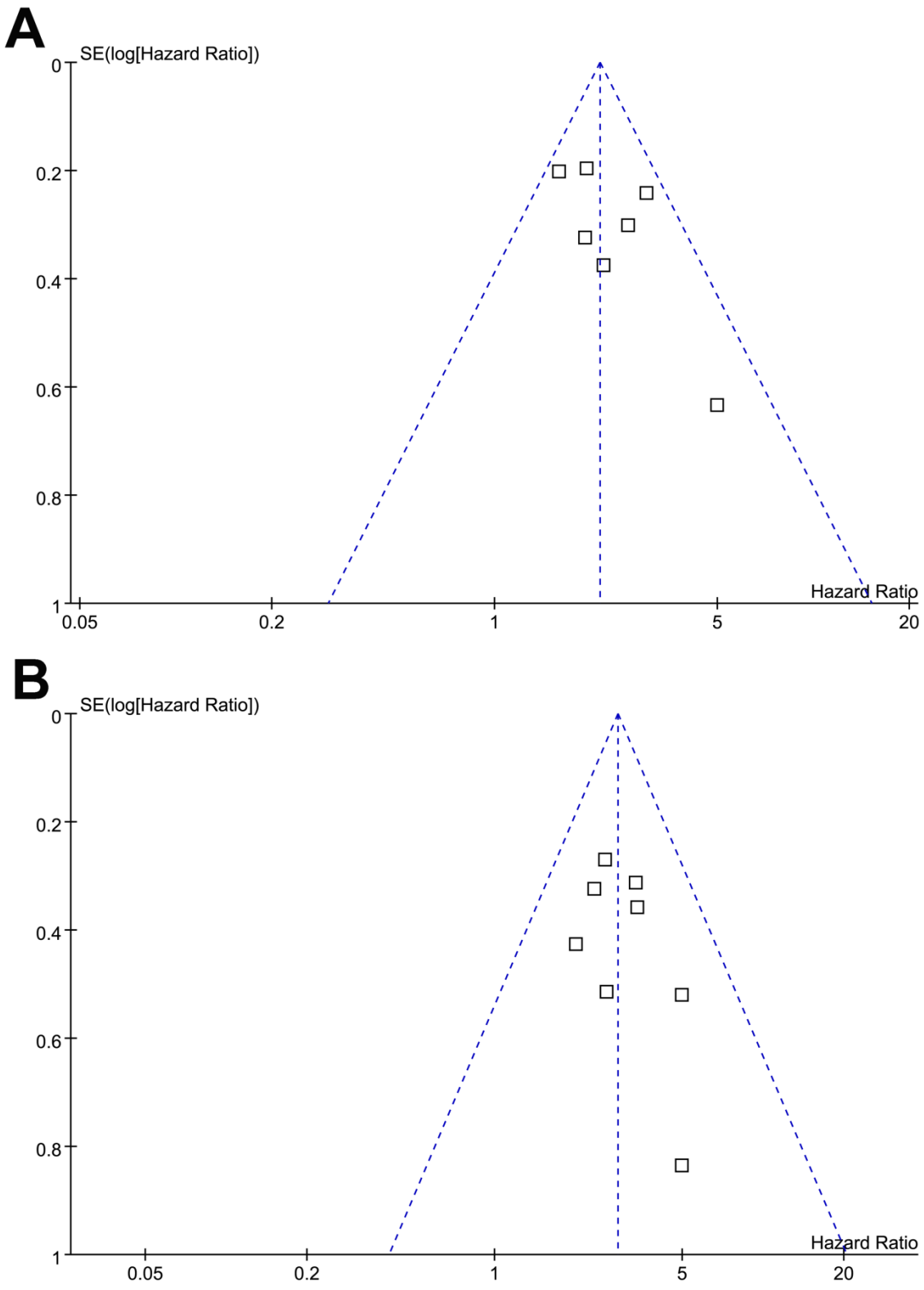

Figure 6. Funnel plots for estimating the potential publication biases underlying the meta-analyses; A, funnel plots for the meta-analysis of the association between pre-

infusion serum ferritin and PFS of R/R MM patients on CAR-T; and B, funnel plots for the meta-analysis of the association between pre-infusion serum ferritin and OS of R/R MM patients on CAR-T

SUPPLEMENTAL DATA

PubMed

("Ferritin"[Mesh] OR ferritin OR ferritins OR hyperferritinemia OR hyperferritinaemia) AND ("Multiple Myeloma"[Mesh] OR myeloma OR "multiple myeloma") AND ("Chimeric Antigen Receptor T-Cell Therapy"[Mesh] OR "Chimeric Antigen Receptor T Cells"[Mesh] OR "CAR-T" OR "chimeric antigen receptor" OR "chimeric T cell receptor" OR "artificial T cell receptor" OR "axicabtagene ciloleucel" OR "axi-cel" OR "KTE-C19" OR "CTL-019" OR "yescarta" OR "lisocabtagene maraleucel" OR "liso-cel" OR "breyanzi" OR "brexucabtagene autoleucel" OR "brexu-cel" OR "tecartus" OR "tisagenlecleucel" OR "tisa-cel" OR "kymriah" OR "idecabtagene vicleucel" OR "cilta-cel" OR "Ciltacabtagene autoleucel")

Embase

('ferritin'/exp OR ferritin OR ferritins OR hyperferritinemia OR hyperferritinaemia) AND ('multiple myeloma'/exp OR myeloma OR 'multiple myeloma') AND ('chimeric antigen receptor'/exp OR 'CAR T cell'/exp OR 'chimeric antigen receptor t cells' OR 'chimeric T cell receptor' OR 'artificial T cell receptor' OR 'axicabtagene ciloleucel' OR 'axi-cel' OR 'KTE-C19' OR 'CTL-019' OR 'yescarta' OR 'lisocabtagene maraleucel' OR 'liso-cel' OR 'breyanzi' OR 'brexucabtagene autoleucel' OR 'brexu-cel'

OR 'tecartus' OR 'tisagenlecleucel' OR 'tisa-cel' OR 'kymriah' OR 'idecabtagene vicleucel' OR 'cilta-cel' OR 'Ciltacabtagene autoleucel')

Web of Science

TS=("ferritin" OR "ferritins" OR "hyperferritinemia" OR "hyperferritinaemia") AND TS=("myeloma" OR "multiple myeloma") AND TS=("Chimeric Antigen Receptor" OR "CAR-T" OR "chimeric antigen receptor T cells" OR "chimeric T cell receptor" OR "artificial T cell receptor" OR "axicabtagene ciloleucel" OR "axi-cel" OR "KTE-C19" OR "CTL-019" OR "yescarta" OR "lisocabtagene maraleucel" OR "liso-cel" OR "breyanzi" OR "brexucabtagene autoleucel" OR "brexu-cel" OR "tecartus" OR "tisagenlecleucel" OR "tisa-cel" OR "kymriah" OR "idecabtagene vicleucel" OR "cilta-cel" OR "Ciltacabtagene autoleucel")