Cardiac toxicity of the (R-)CHOP regimen

a systematic review and meta-analysis in the era of cardio-oncology

UMC Utrecht

M Linschoten, JAM Kamphuis, A van Rhenen, LP Bosman, MJM Cramer, PA Doevendans, AJ Teske, FW Asselbergs

Background

(R-)CHOP ((rituximab), cyclophosphamide, doxorubicin, vincristine, prednisone) has since decades been the first-line treatment for aggressive Non-Hodgkin's Lymphomas (NHL). Albeit both doxorubicin and cyclophosphamide are considered to be highly cardiotoxic, the incidence of cardiovascular adverse events (CVAE) in patients that receive this regimen is still poorly defined.

Methods

We performed a systematic literature search in PubMed, EMBASE, and the Cochrane Library. All studies reporting on the incidence of CVAEs and cardiovascular mortality were included. Meta-analyses of one-sample proportions were performed for the reported incidence of grade 3+4 (severe/life-threatening) CVAEs and heart failure. Subgroup analysis was performed on aggregate data to determine the influence of the total number of cycles, cycle interval, age and sex on the incidence of CVAEs.

Results

Of 2,314 studies assessed for eligibility, 138 studies were included (**Figure 1**) with a median follow-up of 38.4 months [IQR 25.0-52.8]. The majority of patients were treated for diffuse large B-cell lymphoma. The pooled proportion of grade 3+4 CVAEs (77 studies, n=14,362 patients) was 2.35% [95% CI 1.81-2.93]. In the subgroup analysis, female sex and older age (>65 years) were independently associated with an increased risk of severe and life-threatening CVAEs **(Figure 2**). The pooled proportion for heart failure (38 studies, n=5,936 patients) was 4.62% [95% C.I. 2.25 – 7.65%], with a significant increase from 1.63% [95% CI 0.82-2.65] to 11.72% [95% CI 3.00-24.53] when cardiac function was actively monitored (p = 0.0166)(**Figure 3**)**.**

Conclusion

If cardiac function is screened actively, cardiac dysfunction can be detected in >10% of patients, implying that this AE is common in patients treated with (R-)CHOP. Early identification of cardiac dysfunction can facilitate prompt initiation of heart failure treatment and thereby improve cardiac outcome. Active cardiac monitoring should especially be considered in patients at higher risk of CVAEs including females and the elderly (>65 years).

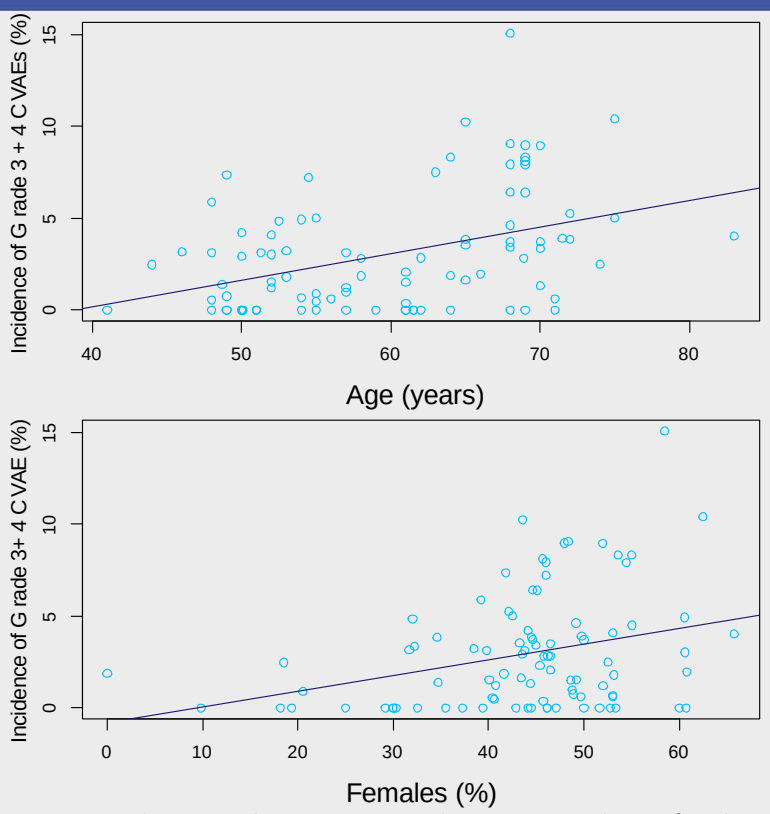

Figure 2. Subgroup analysis on aggregate data. Upper: Incidence of grade 3+4 CVAEs related to age, RR 3.18 in patients >65 years. Lower: gender, expressed as % of female patients in the study.

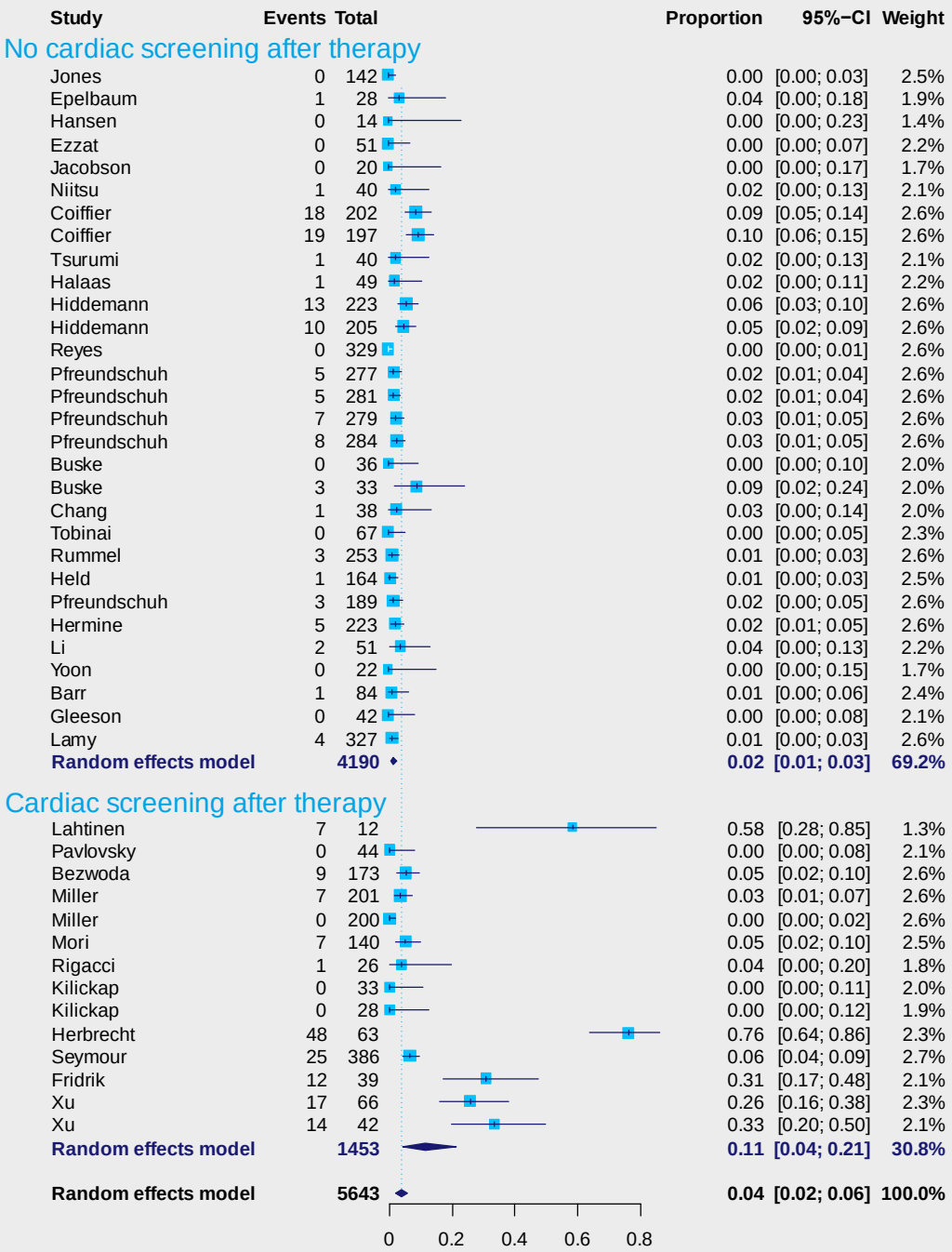

Figure 3. Forest plot of the pooled proportions of overall heart failure, sorted on if active monitoring of cardiac function was performed (lower) or not performed (upper).

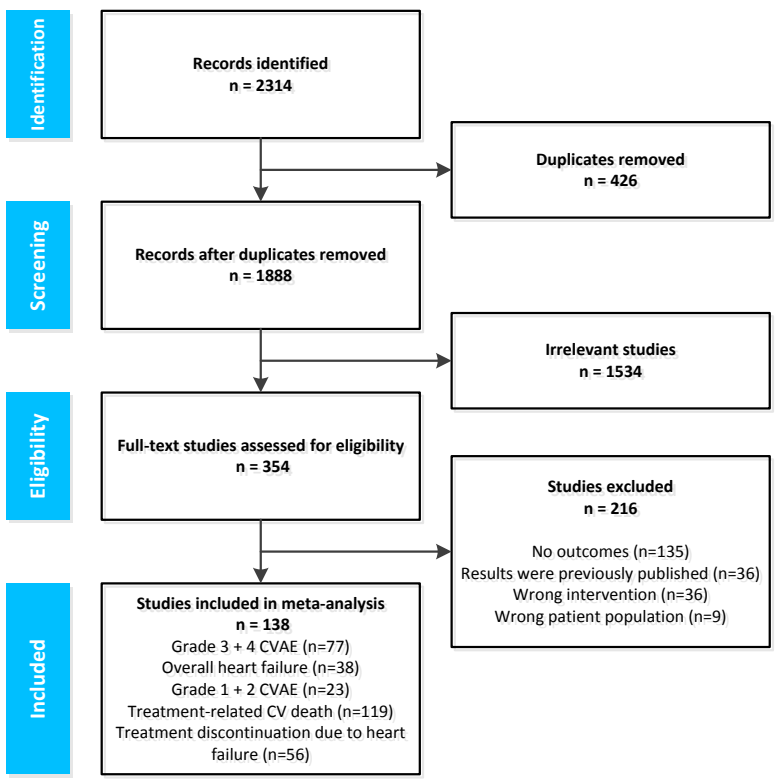

Figure 1. Flowchart of study selection process.

Contact: m.p.m.linschoten@umcutrecht.nl

University Medical Center Utrecht

Dr. Linschoten is supported by the Alexandre Suerman Stipend of the University Medical Center (UMC) Utrecht.
Dr. Asselbergs is supported by the University College London Hospitals, National Institute for Health Research Biomedical Research Center.