Studi Validitas dari Coefficient-of-Variation sebagai Alat Ukur Goodness-of-Fit Test Menggunakan Metode Variance-Based Sensitivity Analysis (Sobol' Method) pada Radioterapi Molekuler = Study of the Validity of Coefficient-of-Variation as a Measure of Goodness-of-Fit Test Using Variance-Based Sensitivity Analysis (Sobol' Method) in Molecular Radiotherapy

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Abstrak

Estimasi yang akurat dari time-integrated activity coefficient (TIAC) ginjal diperlukan untuk optimisasi terapi. Berdasarkan penelitian sebelumnya, prosedur seleksi model berbasis populasi terbukti baik untuk estimasi ini. Penelitian ini menerapkan uji sensitivitas untuk melihat validitas dari persen coefficient-of-variation (%CV) yang digunakan sebagai alat ukur goodness-of-fit (GoF) pada tahapan seleksi model untuk kasus radioterapi molekuler. Data farmakokinetik populasi dari 63 pasien terapi radioligand 177Lu-PSMA-617 digunakan.
Dilakukan fitting untuk 12 fungsi sums of exponential (SOE) dengan pemodelan NLME terhadap data seluruh pasien. Seleksi model dilakukan dengan uji GoF (inspeksi visual dan %CV) serta pembobotan Akaike. Uji Variance-Based Sensitivity Analysis (VBSA) dijalankan untuk model setiap fungsi dengan Fourier Amplitude Sensitivity Test (FAST) sebagai pembanding.
Hasil VBSA dan FAST sama-sama menunjukkan signifikansi statistik pada arah hubungan yang positif antara indeks sensitivitas dan %CV parameter pada fungsi f6d (gradien = 4,86×10-5 (± 0,91×10-5)) dan f7a (gradien = 3,00×10-2 (± 0,30×10-2)). Hasil tersebut mendukung seleksi model. Model final terbaik yang diperoleh adalah fungsi f6a(t) = A1 exp(-(1 + phys)t) +A2 exp(-(2 + phys)t) A3 exp(-(3 + phys)t) (A1 + A2 A3) exp(-(bc + physt). Didapatkan estimasi TIAC ginjal (54,62 ± 23,62) menit. Dengan demikian, penggunaan %CV dalam seleksi model menunjukkan validitas yang didukung oleh uji sensitivitas.
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Accurate estimation of the kidney time-integrated activity coefficient (TIAC) is required for therapy optimization. Based on previous studies, a population-based model selection procedure has proven to be good for this estimation. This study applied a sensitivity test to see the validity of the percent coefficient-of-variation (%CV) used as a goodness-of-fit (GoF) measure in the model selection process for molecular radiotherapy cases. Population pharmacokinetic data from 63 patients treated with the radioligand 177Lu-PSMA-617 were used.
The fitting of 12 sums of exponential (SOE) functions with NLME modeling was performed on all patients' data. Model selection was performed using the GoF test (visual inspection and %CV) and the Akaike weighting. The Variance-Based Sensitivity Analysis (VBSA) was run for each function model with Fourier Amplitude Sensitivity Test (FAST) as a comparison.
Both VBSA and FAST results showed statistical significance of positive correlation between sensitivity indices and %CVs of parameters in function f6d (slope = 4.86×10-5 (± 0.91×10-5)) and function f7a (slope = 3.00×10-2 (± 0.30×10-2)). The results here supported the model selection. The best final model found was the function f6a(t) = A1 exp(-(1 + phys)t) + A2 exp(-(2 + phys)t) A3 exp(-(3 +phys)t) (A1 + A2 A3) exp(-

(bc + phys)t). From this model, an estimated kidney TIAC of (54.62 ± 23.62) minutes was obtained. Thus, the use of %CV in model selection shows validity supported by the sensitivity test.