Nephrotoxicity of TDM-guided amphotericin B infusions in intensive care patients

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Background

Continuous administration of conventional amphotericin B (CCAB) and therapeutic drug monitoring (TDM) may limit amphotericin B associated nephrotoxicity. Amphotericin B is used in intensive-care units (ICUs) for pre-emptive treatment of invasive fungal infections.

Methods

In a retrospective cohort study we compared ICU patients with an abdominal infection treated pre-emptively with CCAB, with ICU patients who did not receive CCAB using a multivariate linear regression analysis. ICU patients of two large teaching hospitals (OLVG Oost and Gelre Apeldoorn) were included between 2008 and 2019.

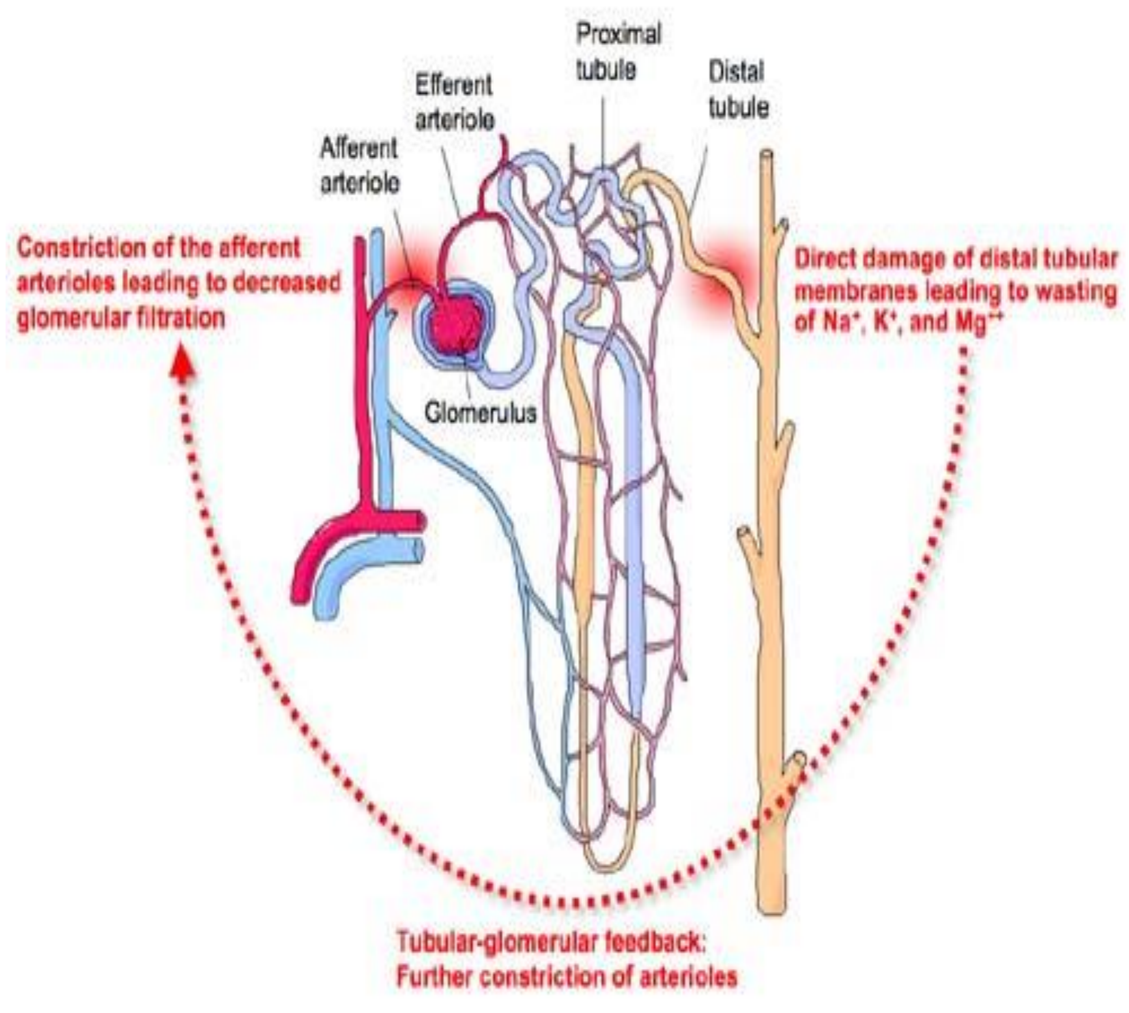
Primary endpoint	Secondary endpoint	
Creatinine	RIFLE-score	Nephrotoxicity
	Renal-SOFA	
	CVVHD	

Endpoints:
Δ mean and baseline in CCAB
versus
Δ mean and baseline in non-CCAB

Inclusion
ICU patients with abdominal sepsis
Exclusion
< 3 days IC-admission
< 3 days CCAB
Renal replacement therapy at start

Aim

To access the incidence of nephrotoxicity in critically ill patients treated with TDM-guided CCAB.



Results

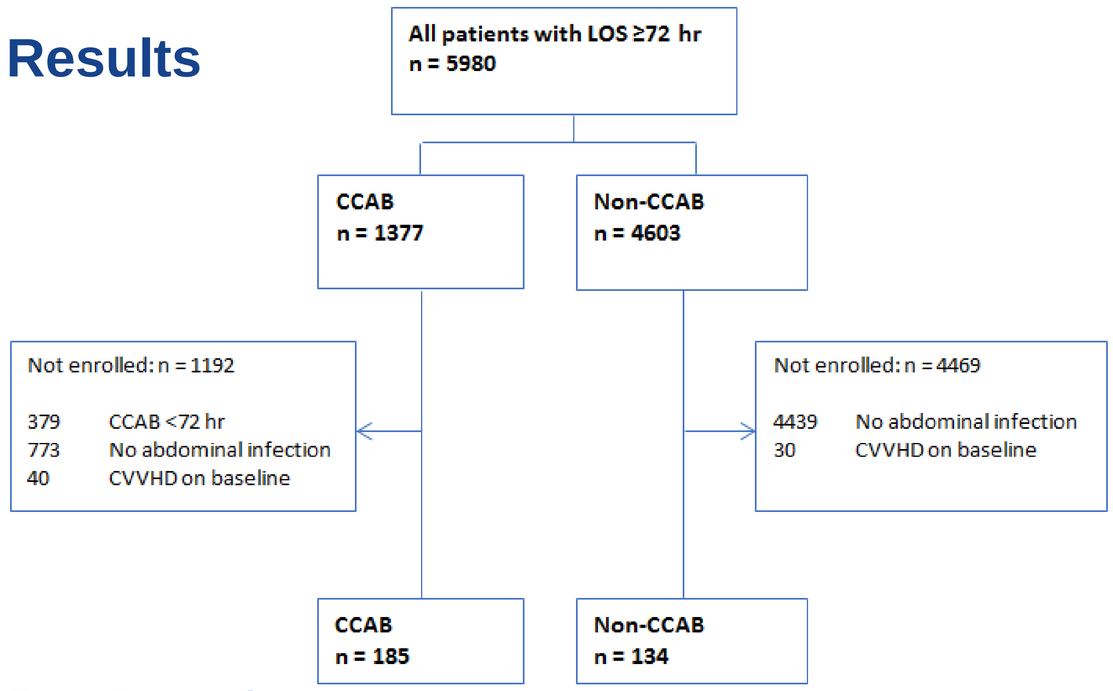


Figure 1: study flow chart.
CCAB: continuous conventional amphotericin B. LOS: length of stay.

Table 1 shows that there was no significant difference in nephrotoxicity between non-CCAB treated and CCAB treated patients. The primary endpoint, difference in mean creatinine and baseline creatinine, was -19 and -9 µmol/L for non-CCAB treated and CCAB treated patients.
Also in the multivariate linear regression analysis (table 2) there was no significant difference in nephrotoxicity between non-CCAB treated and CCAB treated patients.

Table 1. Nephrotoxicity results of 319 patients

	Non-CCAB (n=134)	CCAB (n=185)	p-value
Serum creatinine (umol/L)			
Baseline serum creatinine, median (IQR)	117 [74-188]	92 [70-153]	0,188
Difference mean creatinine and Baseline creatinine, mean (SD)	-19 (51)	-9 (54)	0,086
RenalSOFA			
Difference mean RenalSOFA and Baseline RenalSOFA, mean (SD)	-0,06 (0,67)	0,03 (0,67)	0,233
RIFLEscore			
Difference mean RIFLEscore and Baseline RIFLEscore, mean (SD)	0,21 (1,17)	0,48 (1,40)	0,072
CVVH, mean (SD)	0,08 (0,17)	0,10 (0,23)	0,358

Table 2. Multivariate linear regression analysis: difference mean creatinine and baseline creatinine

	Correlation coëfficiënt	β	p-value
CCAB vs non-CCAB	-10,4	-0,097	0,086
Corrected for confounders*	-2,5	-0,023	0,615

* baseline creatinine (1),APACHEIII score (2) age at admission (3).

Discussion

- Conventional amphotericin B instead of more expensive antifungals reduces costs
- A propensity score analysis will follow to adjust for the covariates that predict receiving CCAB

Conclusion

TDM-guided CCAB does not enhance nephrotoxicity in critically ill patients.