



INTRODUCTION & AIM

Body surface area (BSA) is used to calculate the dosage of cytostatic agents. As cytostatics are generally water soluble, the Fat Free Mass (FFM) would be a logical alternative to BSA for calculating the dosage of cytostatic agents.

We want to evaluate, if the dose of cytostatic agent¹/FFM is related to toxicity.

¹ 5-Flourouracil, Oxaliplatin, Irinotecan, Capecitabine, Gemcitabine and *Nab-Paclitaxel recieved as mono or combination therapy*

A single-center, observational and prospective study was performed on 69 colorectal and pancreatic cancer patients in systemic cytostatic treatment.

FFM was measured by bioimpedance spectroscopy (BIS-SOZO, ImpediMed) at the beginning of each treatment cycle for two-five cycles for two months. Toxicity outcomes were bone marrow depression, dose-limiting toxicity and hospitalization, patient-reported energy and protein intake (24hour recall), general health, quality of life and selected side effects (PRO-CTCAE). Toxicity was measured for two months. Analysis was performed for the individual cytostatic agents and regimens.

Table 1. Change in fa	_	· · · · ·					Table 2 Dess of extented	ing any fat from a	ness (EEM) at hesel	in a and in aid an a	a of torrigity					
		Change in FFM (kg) over 1 month from baseline (n=55)			nge in FFM (kg 1 baseline (n=37	() over 2 months	Table 5. Dose of cytosta	tics pr. fat free mass (FFM) at baseli Neutropenia (<2,0 x 10^9/L),		Thrombocytopenia (<145 x				Hospitalization, incidence		
	rł	no (95% CI)	OR (95% CI)	rho ((95% CI)	OR (95% CI)		incidence		10^9/L), incidenc		incidence				
Neutropenia ($<2,0 x$ 10 $^0/I$) incidence	1.0	0.24	-	-		-		rho (95% CI)	OR (95% CI)	rho (95% CI)	OR (95% CI)	rho (95% CI)	OR (95% CI)		OR (95% CI)	
10^9/L) incidence		-0.47-0.04), =0.085					5-FU mg/FFM kg at baseline (n=32)	-0.24 (-0.55- 0.12), p=0.18	-	0.22 (-0.15- 0.53), p=0.23	-	-0.34 (-0.62- 0.03), p=0.06	-	-0.28 (-0.57- 0.09), p=0.13	-	
Thrombocytopenia (<145 x 10^9/L)	-		-			-	5-FU mg/FFM kg at 1. cycle (n=14)	-		0.45 (-0.13- 0.80), p=0.1	1.206 (0.969- 1.502), p=0.093	-0.39 (-0.77- 0.20), p=0.17	-	-	. .	
incidence Dose-limiting toxicity	-		-			0.661 (0.425-	Oxaliplatin mg/FFM kg at baseline (n=29)	2.7.2 	2.7.1 	-0.20 (- 0.53- 0.18), p=0.29	-	0.18 (-0.21- 0.51), p=0.36	-	-		
incidence Hospitalization		0.19(-0.44-	-	-0.40) (-0.65	1.027), p=0.066 0.778 (0617-0.982),	Oxaliplatin mg/FFM kg at 1. cycle (n=12)	0.36 (-0,29- 0.78), p=0.26	· - · ·	-	-	-	-	-0.27 (-0.74- 0.37), p=0.4	-	
incidence Duration of	-(.08), p=0.16 0.22 (-0.46-	-	-0.41	l (-0.66	p=0.034* -	Irinotecan mg/FFM kg at baseline (n=25)	0.01 (-0.38- 0.41), p=0.95	-	-	-	-	-	-	-	
hospitalization (days)0.06), p=0.110.08), p=0.012*Table 1 shows Spearman/Point Biseral correlation and logistic regression between change in FFM (kg) after one or two months and incidence/duration of toxicity during two months. Correlation analysis is limited to Mann-Whitney U-test estimates on groupings of							Irinotecan mg/FFM kg at 1. cycle (n=12) Capecitabine mg/FFM kg	0.49 (-0.16- 0.84), p=0.11	128.77 (0.14- 114362.16), p=0.16	-0.26 (-0.73- 0.31), p=0.42	-	-0.31 (-0.76- 0.34), p=0.33	-			
toxicity incidence (yes/no) with able 2. Dose of cytost	L		ass (FFM) at b	paseli	ne and change	in bone marrow cells	at baseline (n=27)									
	Change in leucocyte count/L from baseline to cycle 2 (%)			Change in thrombocyte count/L from baseline to cycle 3 (%)			Capecitabine mg/FFM kg at 1. cycle (n=14)	0.42 (-0.17- 0.79), p=0.14	1.007 (0.997- 1.017), p=0.18	0.25 (-0.31- 0.70), p=0.38	-	-	-	-0.28 (-0.71- 0.31), p=0.34	-	
	n	rho (95% CI)	B (95% CI)		rho (95% CI)	B (95% CI)	Gemcitabine mg/FFM kg	-	-	0.87 (0.17-	-	-	-	-	. .	
5-FU mg /FFM kg at 1. cycle		0.08 (-0.48- 0.58), p=0.8		14	-0.62 (-0.88 0.08), p=0.018		at baseline (n=7) Nab-paclitaxel mg/FFM kg	े ः ।	2 2	0.99), p=0.012* 0.89 (-0.71-	-	-		- -		
Oxaliplatin mg /FFM kg at 1. cycle	12	-		10	-0.46 (-0.86- 0.27), p=0.18	-23.969 (-53.018-	at baseline (n=4) Mann-Whitney U-test:	Neutropeni	a (def.1/def.2/no)	0.999), p=0.11 Thrombocyto	openia (yes/no)	Dose-limitin	g toxicity	Hospitalizati	on (yes/no)	
rinotecan mg /FFM	12	-0.18 (-0.69-	- 1	12	-0.04 (-0.60-	-	EEM had DCA (m2)				1	(yes/n	10)			
kg at 1. cycle		0.44), p=0.58			0.55), p=0.9		FFM kg/BSA (m ²) FFM kg/weight kg	p>0.4 p=0.24		p>0.4 p>0.4		p>0.4 p=0.33		p>0.4 p>0.4		
Capecitabine mg	1000000	0.30(-0.29-0.72) n=0.3	-		0.28 (-0.40 - 0.76) = 0.41	-	Table 3 shows Point-Biseral correlation and logistic regression between dose of cytostatic agent divided by FFM (mg/kg) at baseline or at the first cycle and incidence of toxicity during two months. Correlation analysis is									

	(Change in FFM (kg) over 1		Change in FFM (kg) over 2 months		3	Table 3. Dose of cytostatics pr. fat free mass (FFM) at baseline and incidence of toxicity									
	1	month from baseline (n=55)			from baseline (n=37)				Neutropenia (<2,0 x 10^9/L),		Thrombocytopenia (<145 x		Dose-limiting toxicity,		Hospitalization, incidence	
	1	rho (95% CI)	OR (95% CI)	rho	(95% CI)	OR (95% CI)			incidence		10^9/L), incidenc		incidence	12		-15
Neutropenia (<2,0 x		-0.24	-	-		-			rho (95% CI)	OR (95% CI)	rho (95% CI)	OR (95% CI)	rho (95% CI)	OR	rho (95% CI)	OR
10^9/L) incidence		(-0.47-0.04),									0.00			(95% CI)	0.00 (0.55	(95% CI)
	1	p=0.085						5-FU mg/FFM kg at	-0.24 (-0.55-	-	0.22 (-0.15-	-	-0.34 (-0.62-	-	-0.28 (-0.57-	-
Thrombocytopenia		-	-	-		-		baseline (n=32)	0.12), p=0.18		0.53), p=0.23		0.03), p=0.06		0.09), p=0.13	
(<145 x 10^9/L)								5-FU mg/FFM kg at 1.			0.45 (-0.13-	1.206 (0.969-	-0.39 (-0.77-	-	T.	-
incidence								cycle (n=14)			0.80), p=0.1	1.502), p=0.093	0.20), p=0.17			
Dose-limiting toxicity	, .		-	-0.3	1 (-0.59-0-	0.661 (0.425-	- 1	Oxaliplatin mg/FFM kg at			-0.20 (- 0.53-		0.18 (-0.21-	1. T. ()	ā.	5 7 0
incidence						1.027), p=0.066		baseline (n=29)			0.18), p=0.29		0.51), p=0.36		0.05 (0.54	
Hospitalization		-0.19 (-0.44-	-		-	0.778 (0617-0.982),			0.36 (-0,29-	-	-	-	-		-0.27 (-0.74-	-
incidence		0.08), p=0.16				p=0.034*		1. cycle (n=12)	0.78), p=0.26						0.37), p=0.4	
Duration of	_	-0.22 (-0.46-			1 (-0.66	0.051		Irinotecan mg/FFM kg at	0.01 (-0.38-	-	-	-	-	-	-	-
hospitalization (days)		0.06), p=0.11	-					baseline (n=25)	0.41), p=0.95	100 55 (0.14	0.0((0.70		0.01 (0.7(
				0.08), p=0.012*			Irinotecan mg/FFM kg at	0.49 (-0.16-	128.77 (0.14-	-0.26 (-0.73-	-	-0.31 (-0.76-	-	-	-	
Table 1 shows Spearman/Point Biseral correlation and logistic regression between change in FFM (kg) after one or two months and incidence/duration of toxicity during two months. Correlation analysis is limited to Mann-Whitney U-test estimates on groupings of						1. cycle (n=12)	0.84), p=0.11	114362.16), p=0.16	0.31), p=0.42		0.34), p=0.33					
toxicity incidence (yes/no) with p<0,4. Ible 2. Dose of cytostatics pr. fat free mass (FFM) at baseline and change in bone marrow cells						Capecitabine mg/FFM kg	-	-	-	-	-	-	-	-		
able 2. Dose of cytos		•		-				at baseline (n=27)	0 42 (0 17	1 007 (0 007	0.25 (0.21				0.29 (0.71	
	Change in leucocyte count/L from baseline to cycle 2 (%)		Change in thrombocyte count/L from		and the second	Capecitabine mg/FFM kg	0.42(-0.17-0.14)	1.007 (0.997-	0.25 (-0.31-	-	-	-	-0.28 (-0.71-	-		
			. ,	baseline to cycle 3 (%)				at 1. cycle (n=14)	0.79), p=0.14	1.017), p=0.18	0.70), p=0.38				0.31), p=0.34	
	n	rho (95% CI)	B (95% CI)	n	rho (95% CI)	B (95% CI)		Gemcitabine mg/FFM kg			0.87 (0.17-	`т.		3 .		1.70
FU mg /FFM kg at	14	0.08 (-0.48-	-	14	-0.62 (-0.88	-2.041 (-3.654		at baseline (n=7)			0.99), p=0.012*					
. cycle		0.58), p=0.8			0.08), p=0.018	* 0.428) p=0.019*		Nab-paclitaxel mg/FFM kg			0.89 (-0.71-	-			T.	-
Oxaliplatin mg /FFM	12	0.11 (-0.46-		10	-0.46 (-0.86-	-23.969 (-53.018-		at baseline (n=4)		() () () ()	0.999), p=0.11		D 11 14	,		
g at 1. cycle		0.68) p=0.61			0.27), p=0.18	5.081), p=0.087		Mann-Whitney U-test: Neutropenia (def.1/def.2/no)		Thrombocytopenia (yes/no)		Dose-limiting toxicity		Hospitalization (yes/no)		
rinotecan mg /FFM	12	-0.18 (-0.69-		12 -0.04 (-0.60								(yes/n	0)		-	
g at 1. cycle		0.44), p=0.58			0.55), p=0.9			FFM kg/BSA (m ²)	p>0.4		p>0.4		p>0.4		p>0.4	
Capecitabine mg	14	0.30 (-0.29-	-	11	0.28 (-0.40-	-	1	FFM kg/weight kg	p=0.24		p>0.4		p=0.33		p>0.4	
FFM kg at 1. cycle		0.72) p=0.3			0.76), p=0.41			Table 3 shows Point-Biseral correlationlimited to Mann-Whitney U-test estimation		• • • •	• • •		-	• •	-	-

Table 2 shows Spearman correlation and linear regression between change in leucocyte and thrombocyte count in the cycle where they had the most noticeable change from baseline and the dose of cytostatic agent divided by FFM (mg/kg) at baseline. Regression analysis is limited to *correlation with rho>0,4.*

The relationship between fat free mass and toxicity of cytostatics in cancer patients

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METHOD

(kg/kg) in groups of neutropenia (def. 1=<1,0x10^9/L, def. 2=<2,0x10^9/L and no=>2,0x10^9/L), thrombocytopenia (yes/no=</>145x10^9/L), dose-limiting toxicity (yes/no) and hospitalization (yes/no) during two months.

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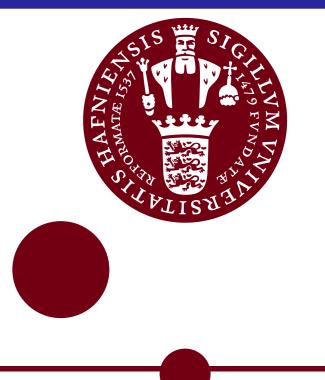
RESULTS

No significant change in FFM was found after one or two months of treatment. Median (min-max) relative change in FFM after one and two months was -0.16 % (-11.5-13.0) and 1.48 % (-10.8-13.2) respectively. After adjusting for age and gender, a one unit increase in relative FFM was associated with reduced odds for hospitalization (OR=0.778 (95 % CI 0.617-0.982), p=0.034). Change in FFM was negatively correlated with length of hospitalization (r=-0.41 (95 % CI -0.655- -0.08), p=0.012). Other associations were non-significant after adjustment.

A one unit increase in baseline 5-Fluorouracil mg/FFM was related to a 2.04 % reduction in thrombocyte count/L from cycle 1 - 3 (95 % CI - 3.65 - 0.428, p=0.019) after adjusting. Other dose/FFM and toxicity estimates were nonsignificant or deemed inconclusive.

The correlation between BSA and FFM was r=0.846 (95 % CI 0.745-0.909), p<0.001.

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CONCLUSIONS

An association between FFM and cytostatic induced toxicity could not be proven. It is suspected that low statistical power and the reliability of estimates by BIS may have influenced the lack of a systematic correlation between FFM, and dose/FFM, and cytotoxicity in this study. Furthermore, the correlation between FFM and BSA was stronger than expected, which may have understated the role of FFM independent of BSA.

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