Aspetti nutrizionali: Sarcopenia e prevenzione della perdita di massa magra

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EASOCOM
EASO Collaborating Centre for Obesity Management

IFSO European Chapter
Bariatric and Centre of Excellence Metabolic Surgery
European Accreditation Council

- **Possiamo misurare la massa magra nel paziente operato?**
- **Il calo ponderale ha effetto sulla massa magra?**
- **La perdita di massa magra ha effetto sulla prognosi?**
- **Possiamo prevenire la perdita di massa magra?**

- **Possiamo misurare la massa magra nel paziente operato?**
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- **Possiamo prevenire la perdita di massa magra?**

- **Metodi**
  - **Densitometria (DEXA)**
  - **Impedenziometria (BIA)**

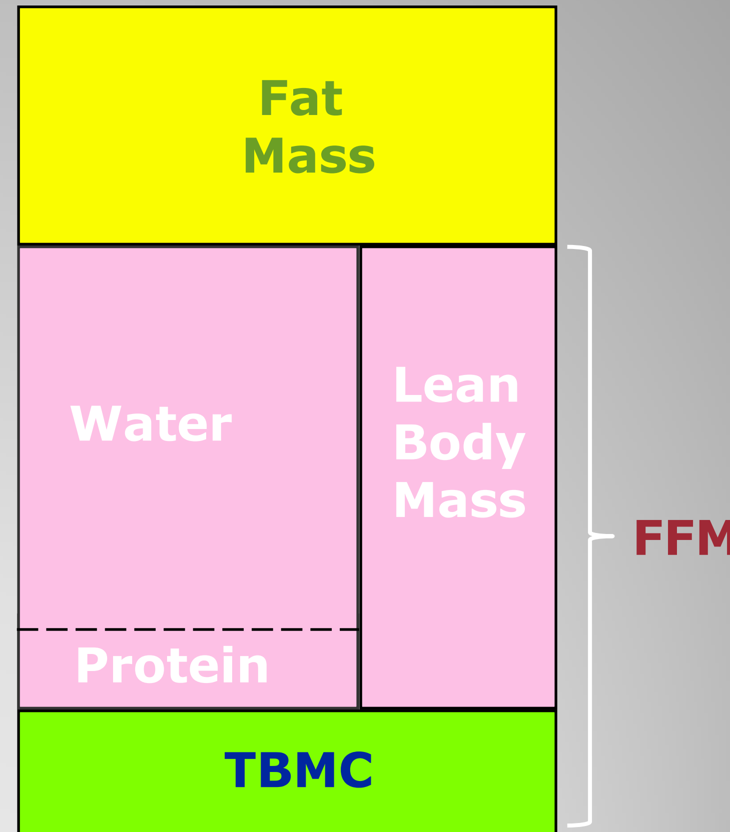
Composizione corporea nell’obesità

- **Vantaggi**

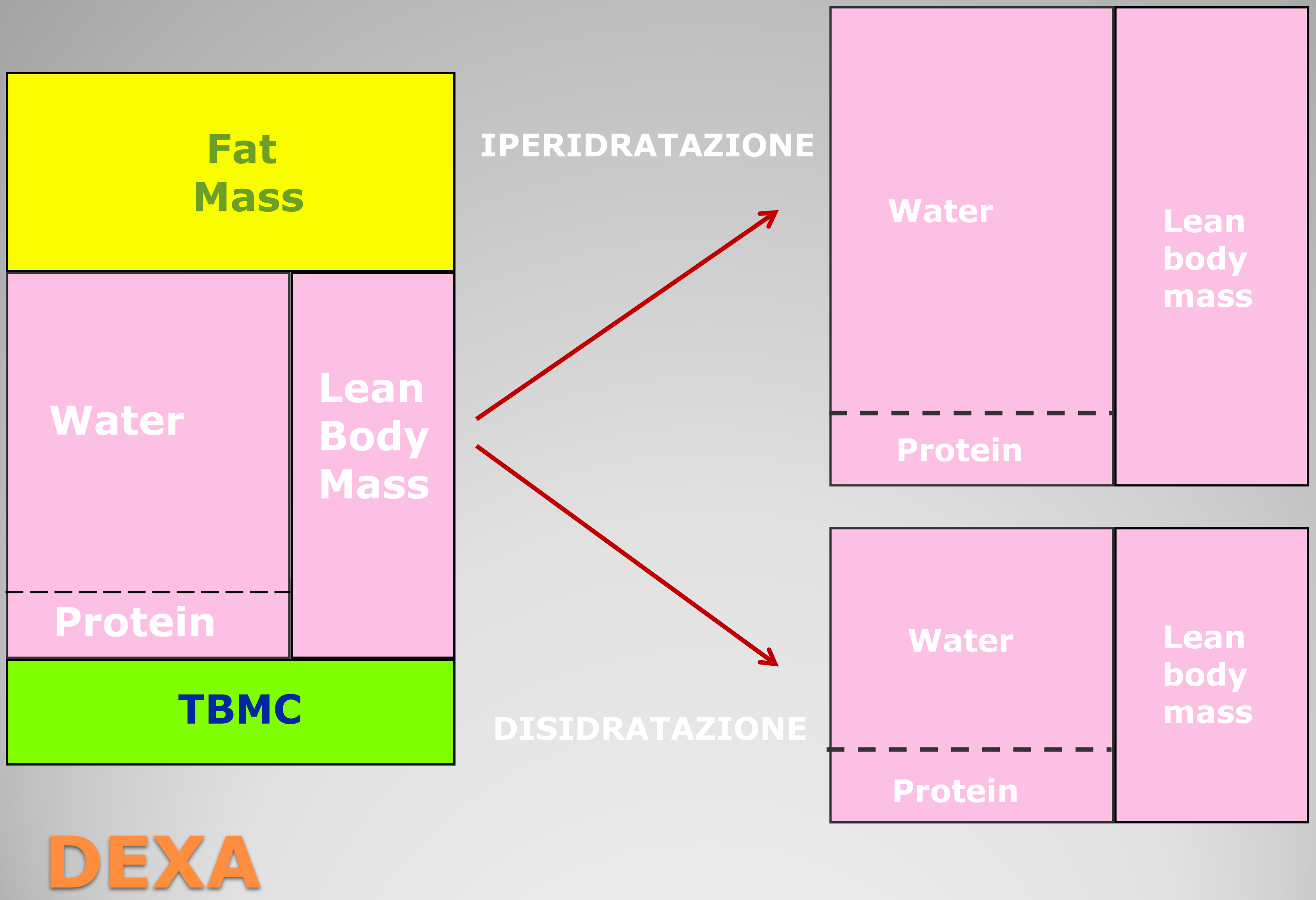
1. Consente la valutazione di sotto-regioni
2. E’ rapido
3. Estremamente diffuso
4. Utilizzato nei grandi trials
5. Non invasivo
6. Molto preciso e riproducibile

- **Svantaggi**

1. Relativamente costoso
2. Non trasportabile
3. Esposizione radiante
4. Limiti di peso e dimensioni



DEXA



Fat Mass
Water
Protein
Lean Body Mass
TBMC
IPERIDRATAZIONE
Water
Protein
Lean body mass
DISIDRATAZIONE
Water
Protein
Lean body mass
DEXA

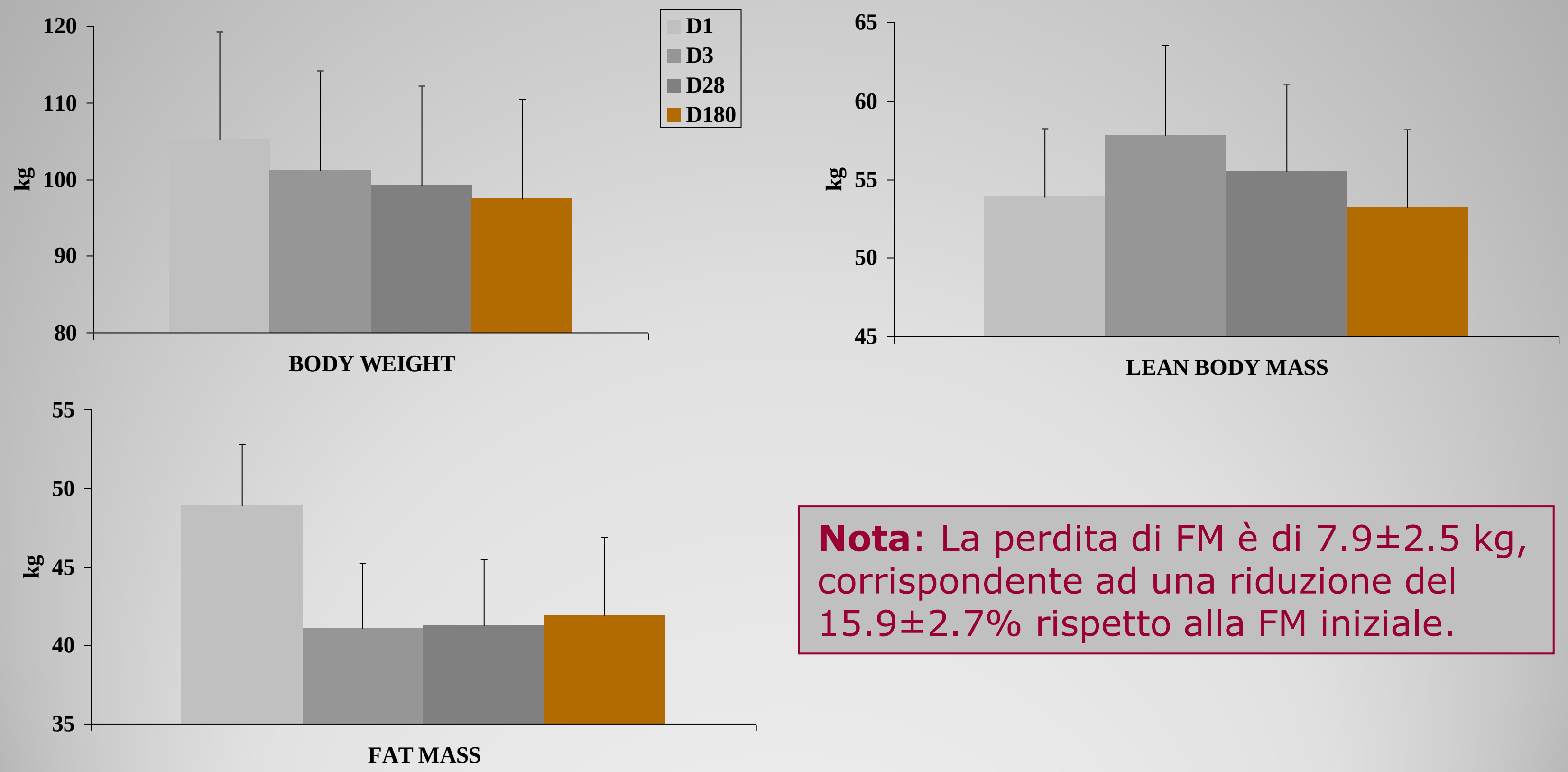
The effects of the surgical removal of subcutaneous adipose tissue on energy expenditure and adipocytokine concentrations in obese women






Busetto et al. NM&CVD 2008;18:112.

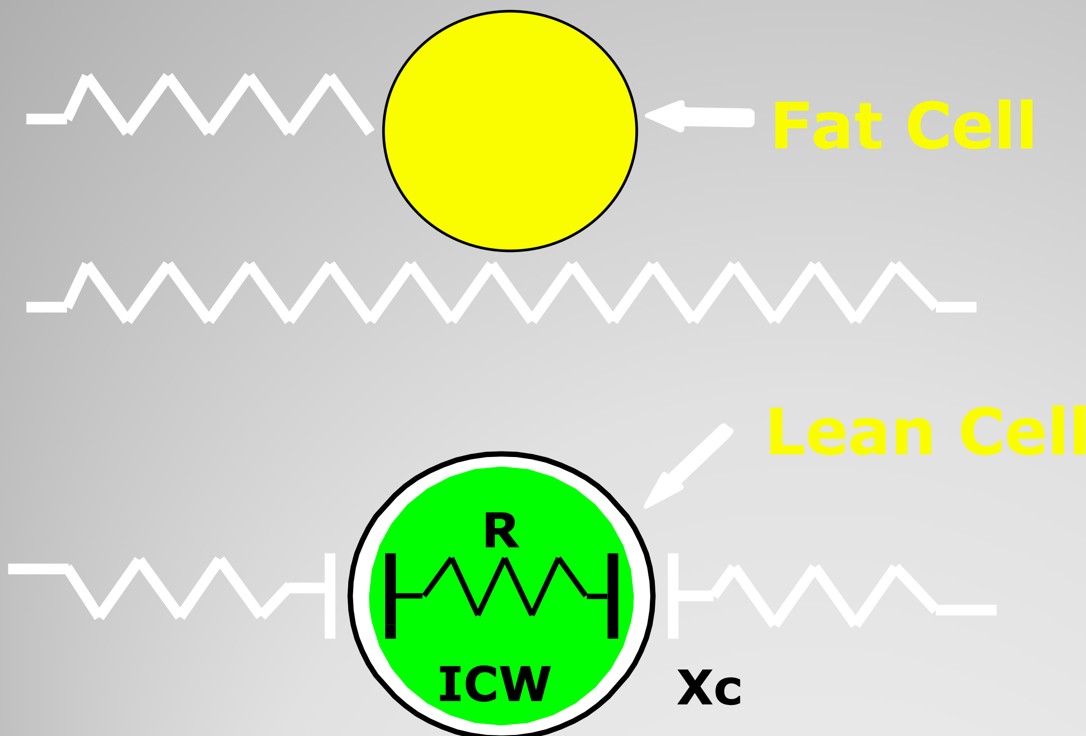
The effects of the surgical removal of subcutaneous adipose tissue on energy expenditure and adipocytokine concentrations in obese women

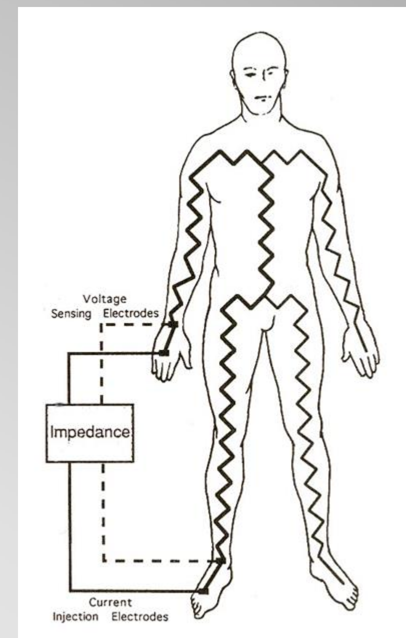


Nota: La perdita di FM è di 7.9±2.5 kg, corrispondente ad una riduzione del 15.9±2.7% rispetto alla FM iniziale.

Busetto et al. NM&CVD 2008;18:112.

Teoretical Model

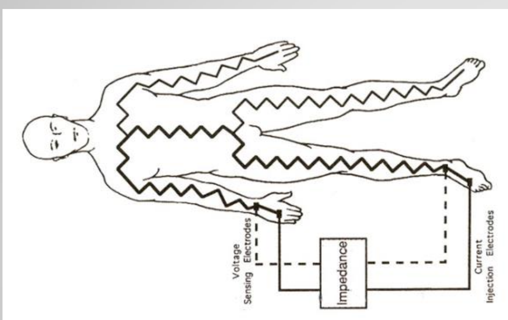




BIA

- Misure primarie (± dirette)

- Z= impedenza totale (cellule + fluidi)
- R= resistenza elettrica (fluidi)
- Xc= reattanza (cellule)
- Pa= angolo di fase (rapporto ICW/ ECW)
- C= capacità corporea (cellule)
- Zh/Zl= Impedance Ratio (icw/ecw)



- Stime indirette

- TBW
- BCM
- MM
- BMR

- ECW
- ICW
- FFM
- FM

Costanti biologiche
Equazioni predittive

BIA

1. Errore intrinseco strumentale (1-2% a 50 kHz)

2. Errori di regressione lineare (SEE rispetto ai reference method)

3. Errori dei metodi di riferimento (3-6% diluizione isotopica)

4. Errori su modello elettrico del corpo (anisotropia, non-cilynder)

5. Variabilità biologica (composizione individuale + geometria)

Errors with BIA prediction equations:

1 + 2 + 3 + 4 + 5

BIA

FAT-FREE MASS Errors

Table 1 Bioelectrical impedance analysis equation reported in the literature since 1990 for fat-free mass (FFM) classified according to subject category (adult, elderly, overweight) and standard error of the estimate (SEE).

Population	Source	n	Criterion measure	Equation	r^2	SEE*	BIA instrument
Adults							
Healthy subjects, 18–94 yr	Kyle et al.[74]	343	DXA	$-4.104 + 0.518\,\mathrm{Ht}^2/R_{50} + 0.231$ weight $+0.130\,\mathrm{Xc} + 4.229$ sex	0.97	1.8	Xitron
Healthy adults, 18–29 yr	Lohman[75]	153	Densitometry[85,†]	Women $= 5.49 + 0.476\,\mathrm{Ht}^2/R_{50}$ $+0.295$ weight	NR	2.1	Valhalla
Healthy adults, 30–49 yr	Lohman[75]	122	Densitometry[85,†]	Women $= 11.59 + 0.493\,\mathrm{Ht}^2/R_{50}$ $+0.141$ weight	NR	2.5	Valhalla
Healthy, ethnic divers	Kotler et al. SF parallel[58]	126	DXA	Women $= +0.07 + 0.88\,(\mathrm{Ht}^{1.97}/Z_{50}^{0.49})$ $(1.0/22.22) + 0.081$ weight	0.71	6.56% (≈ 2.6)	RJL-101
Healthy subjects, >16 yr	Deurenberg et al.[76]	661	Multi-C,[87] densitometry[86,‡]	$-12.44 + 0.34\,\mathrm{Ht}^2/R_{50} + 0.1534$ height $+0.273$ weight $- 0.127$ age $+ 4.56$ sex	0.93	2.6	RJL-101
Healthy subjects, 12–71 yr	Boulier et al.[6]	202	Densitometry	$6.37 + 0.64$ weight $+ 0.40\,\mathrm{Ht}^2/Z_{1\,\mathrm{MHz}} - 0.16$ age -2.71 sex (men $= 1$, women $= 2$)	0.92	2.6	IMP BO-1
Women 18–60 yr	Stolarczyk et al.[77]	95	Multi-C[§]	$20.05 - 0.04904\,R_{50} + 0.001254\,\mathrm{Ht}^2$	0.75	2.6	Valhalla

BIA

ESPEN Working Group. Clin Nutr 2004;23:1226–1243

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- **La perdita di massa magra ha effetto sulla prognosi?**
- **Possiamo prevenire la perdita di massa magra?**

Table 2 Summary of the effects of dietary, behavioral and pharmaceutical weight loss interventions on the %FFML (16 studies with 26 time points)

Author	*Year*	*Intervention*	*Study type*	*Weight loss (kg)*	*%FFML*	*Duration (wks)*	*N*	*Sex*	*Initial BMI*	*Method*
Gower *et al.*[26]	2002	LCD	Obs	13.1	5.9	10	18	F	29.2	DEXA
Due *et al.*[23]	2004	LCD	RCT	10.2	11.8	52	20		30.8	DEXA
Leenan *et al.*[24]	1993	LCD	RCT	11.7	12.0	13	40	F	30.9	DEXA
Gotfredsen *et al.*[25]	2001	LCD	RCT	10.2	11.8	52	16		36.9	UWW
Gower *et al.*[26]	2002	LCD	Obs	12.7	12.0	10	19	F	28.7	DEXA
Due *et al.*[23]	2004	LCD	RCT	15.6	13.5	52	21		35.0	DEXA
Kockx *et al.*[27]	1999	LCD	Obs	11.4	14.0	13	25	F	31.3	UWW
Tchernof *et al.*[28]	2002	LCD	Obs	14.5	18.6	13.9	25	F	35.2	DEXA
Purnell *et al.*[29]	2000	LCD	Obs	10.0	20.0	13	21	M	31.0	UWW
Leenan *et al.*[24]	1993	LCD	Obs	12.6	22.2	13	38	M	30.5	UWW
Kockx *et al.*[27]	1999	LCD	Obs	12.1	24.8	13	25	M	30.5	UWW
Tchernof *et al.*[30]	2000	LCD	Obs	14.1	25.5	56	13	F	35.4	DEXA
Shadid and Jensen[31]	2003	LCD+ex	RCT	11.7	4.3	20	39		32.1	DEXA
Okura *et al.*[32]	2003	LCD+ex	RCT	10.2	21.6	14	33	F	29.4	DEXA
Gotfredsen *et al.*[25]	2001	LCD+Orl	RCT	11.2	11.6	52	16		36.9	DEXA
Kamel *et al.*[33]	2000	LCD+Sib	Obs	10.6	31.1	26	19	F	33.3	UWW
Berube-Parent *et al.*[34]	2001	LCD+Sib	Obs	10.7	38.3	13	8	M	35.0	DEXA
Pronk *et al.*[35]	1992	VLCD	CCT	20.8	23.0	13	40	F	35.0	DEXA
Hoie *et al.*[36]	1993	VLCD	Obs	11.1	23.4	9	86	F	30.0	UWW
Hoie *et al.*[36]	1993	VLCD	Obs	14.2	31.0	9	47	M	30.0	UWW
Eston *et al.*[37]	1992	VLCD	Obs	11.5	37.4	6	10	F	35.0	UWW
Pronk *et al.*[35]	1992	VLCD+ex	CCT	22.1	14.8	13	23	F	35.0	DEXA
Goodpaster *et al.*[38]	1999	VLCD+ex	CCT	12.2	17.2	17	17	F	34.0	UWW
Pronk *et al.*[35]	1992	VLCD+ex	CCT	20.6	22.5	13	23	F	35.0	UWW
Pronk *et al.*[35]	1992	VLCD+ex	CCT	21.5	24.1	13	23	F	35.0	DEXA
Goodpaster *et al.*[38]	1999	VLCD+ex	CCT	17.6	26.1	17	15	M	34.5	DEXA

Abbreviations: CCT, clinical controlled trial; DEXA, dual energy X-ray absorptiometry; F, female; LCD+ex, low calorie diet+exercise; LCD+orl, low calorie diet+orlistat; LCD+Sib, low calorie diet+sibutramine; M, male; Obs, observational study; RCT, randomized controlled trial; UWW, under water weighing; VLCD+ex, very low calorie diet+exercise.

Changes in fat-free mass during significant weight loss: a systematic review

Chaston TB et al. Int J Obes 2007;31:743

Table 4 Summary of the effects of surgical weight loss interventions on the %FFML

Author	Year	Intervention	Study type	FFM loss (%Weight loss)	Weight loss (kg)	Duration (wks)	n	Sex	Initial BMI	Method
Vettor *et al.*[42]	2003	BPD	Obs	17.5	43.5	78	10		49.8	TBW
Tacchino *et al.*[43]	2003	BPD	Obs	19.2	31.7	26	101	F	45.5	DEXA
Gniuli *et al.*[44]	2005	BPD	Obs	20.0	47.6	104	10		45.3	TBW
Tacchino *et al.*[43]	2003	BPD	Obs	20.1	43.3	52	101	F	45.5	DEXA
Tacchino *et al.*[43]	2003	BPD	Obs	22.0	46.0	104	101	F	45.5	DEXA
Mingrone *et al.*[45]	2002	BPD	RCT	25.1	35.1	52	31	F	48.3	DEXA
Fabris *et al.*[46]	2004	BPD	Obs	26.2	48.6	78	10		49.0	TBW
Mingrone *et al.*[45]	2002	BPD	RCT	27.8	52.1	52	15	M	48.4	DEXA
Valera-Mora *et al.*[47]	2005	BPD	Obs	29.1	55.0	104	85	F	48.9	TBW
Benedetti *et al.*[48]	2000	BPD	CCT	31.5	60.4	130	14		48.1	DEXA
Greco *et al.*[49]	2002	BPD	CCT	48.5	33.0	26	8		49.4	DEXA
Valera-Mora *et al.*[47]	2005	BPD	Obs	52.7	55.0	104	22	M	48.1	TBW
Das *et al.*[50]	2003	RYGB	Obs	21.2	53.4	61	30		50.1	TBW
Carey *et al.*[51]	2006	RYGB	Obs	29.3	12.3	4	19		48.7	UWW
Carey *et al.*[51]	2006	RYGB	Obs	33.2	39.7	26	19		48.7	UWW
Carey *et al.*[51]	2006	RYGB	Obs	36.3	25.9	13	19		48.7	UWW
Coupaye *et al.*[52]	2005	LAGB	Obs	12.7	23.7	52	36	F	47.2	DEXA
Pugnale *et al.*[53]	2003	LAGB	Obs	14.1	27.7	52	31	F	43.6	DEXA
Sergi *et al.*[54]	2003	LAGB	Obs	14.1	17.0	26	6	F	42.8	DEXA
Gasteyger *et al.*[55]	2006	LAGB	Obs	16.4	39.6	104	36	F	43.8	DEXA
Giusti *et al.*[56]	2005	LAGB	Obs	16.9	29.5	52	37	F	43.7	DEXA
Giusti *et al.*[57]	2004	LAGB	Obs	17.4	27.6	52	31	F	43.6	DEXA
Gasteyger *et al.*[55]	2006	LAGB	Obs	17.5	29.7	52	36	F	43.8	DEXA
Pugnale *et al.*[53]	2003	LAGB	Obs	17.8	18.5	26	31	F	43.6	DEXA
Giusti *et al.*[56]	2005	LAGB	Obs	17.9	39.1	104	37	F	43.7	DEXA
Giusti *et al.*[57]	2004	LAGB	Obs	18.7	18.7	26	31	F	40.5	DEXA
Giusti *et al.*[56]	2005	LAGB	Obs	19.3	19.2	26	37	F	43.7	DEXA
Gasteyger *et al.*[55]	2006	LAGB	Obs	19.7	19.3	26	36	F	43.8	DEXA
Garrapa *et al.*[58]	2005	LAGB	Obs	23.6	23.3	26	15		42.2	DEXA

Abbreviations: BPD, biliopancreatic diversion; CCT, clinical controlled trial; DEXA, dual energy X-ray absorptiometry; LAGB, laparoscopic adjustable gastric banding; Obs, observational; RCT, randomized controlled trial; RYGB, roux en Y gastric bypass; TBW, total body water.

Changes in fat-free mass during significant weight loss: a systematic review

Chaston TB et al. Int J Obes 2007;31:743

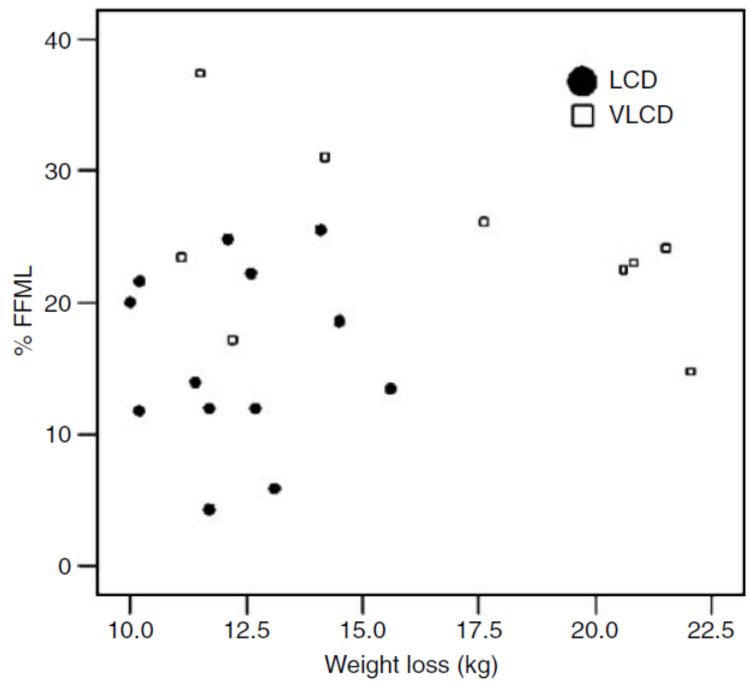

Figure 1 Weight loss and the %FFML after LCD and VLCD. There is significantly greater weight loss and %FFML with VLCDs.

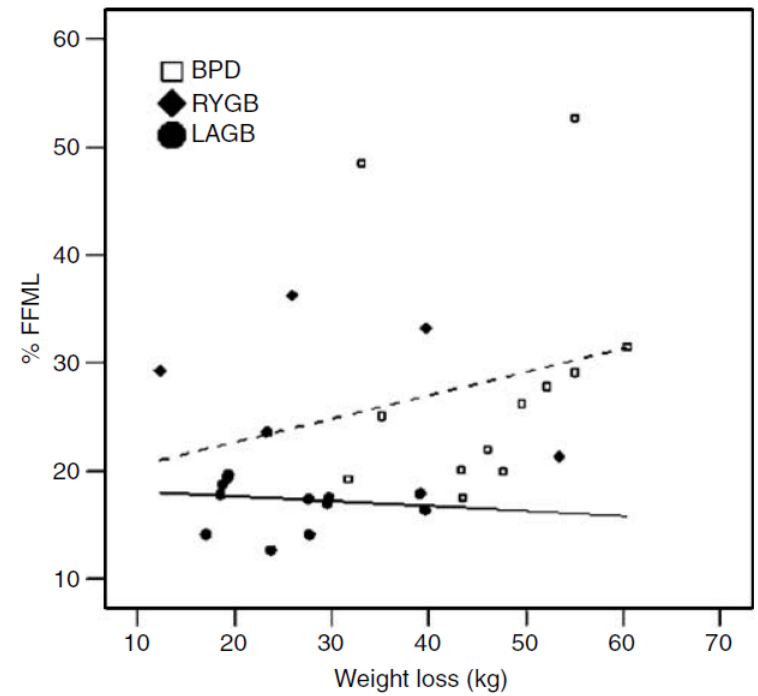

Figure 2 Weight loss and the log of the proportion of weight lost as FFM after BPD, RYGB and LAGB. Lines indicate trends between %FFML and weight loss for BPD (dashed) and LAGB (solid).

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Pooled Mean %FFM using medical therapy: 27% in Men and 20% in Women.

Table 5 Percentage of cohort time points of each intervention reporting greater %FFML loss than average

Intervention	*Number with %FFML < average*	*Number with %FFML > average*	*% cohorts with %FFML > average*
LCD	11	1	8%
LCD+exercise	2	0	0%
VLCD	0	4	100%
VLCD+exercise	3	2	40%
LAGB	12	1	8%
RYGB	0	4	100%
BPD	3	9	75%

Abbreviations: BPD, biliopancreatic diversion; %FFML, percentage of weight lost as fat-free mass; LAGB: laparoscopic adjustable gastric banding, LCD: low calorie diet, RYGB: roux en Y gastric bypass; VLCD: very low calorie diet.

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- **Possiamo prevenire la perdita di massa magra?**

- Heart Failure
- End-Stage Renal Disease
- Coronary Artery Disease
- Non-bariatric Surgery

Obesity Paradox

- **In most of the studies, patients with higher BMI were much younger than their normal weight counterparts.**
- **Obese patients tend to present earlier and this are investigated and treated earlier.**
- **Data regarding patients with BMI>35 have been minimal.**
- **BMI may not the most accurate index of obesity.**
- **The obesity paradox may just be an overrepresentation of cachexia.**

Obesity Paradox: pitfalls

Morse SA et al. Curr Hyptertens Rep 2010;12:120

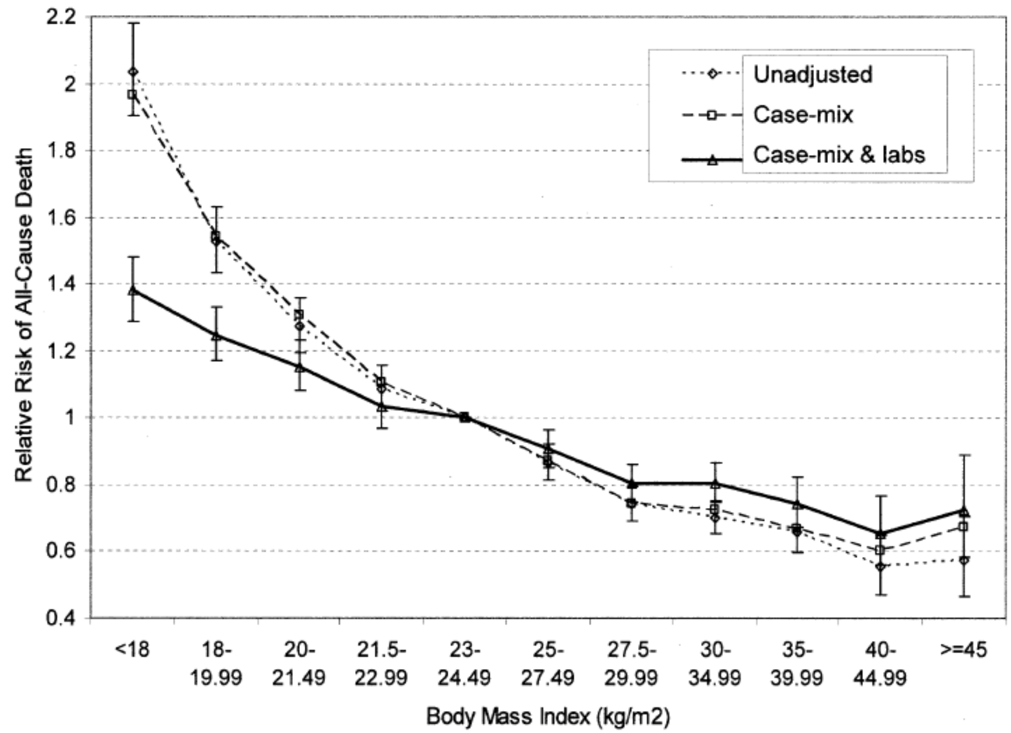
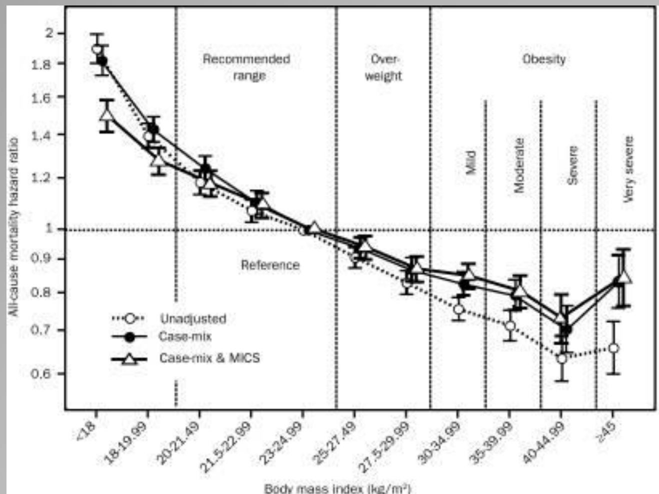
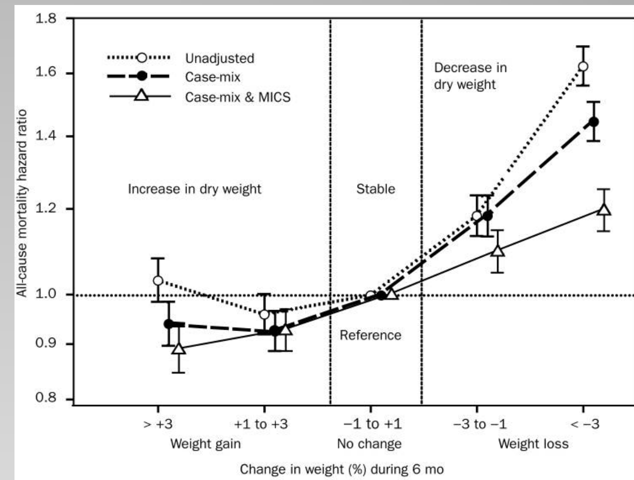


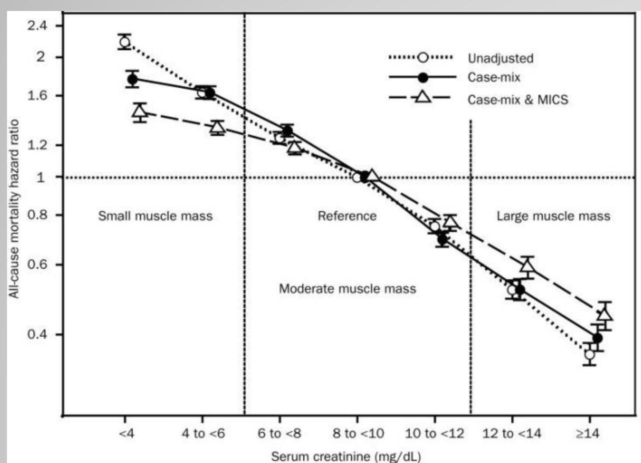
Fig 1. Time-dependent association between BMI and 2-year all-cause mortality in 54,535 MHD patients (95% confidence interval bars are not shown for the case-mix–adjusted group to enable better distinction of confidence intervals for other 2 groups).

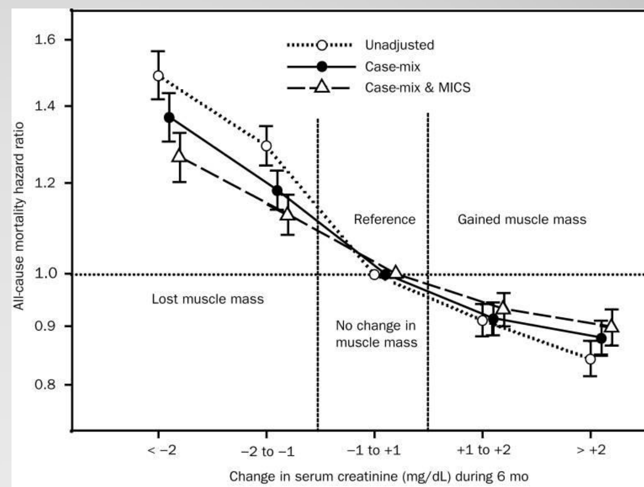
BMI and survival in hemodialysis patients

Kalantar-Zadeh K et al. Am J Kidney Dis 2005;46:489









BMI and survival in hemodialysis patients

Kalantar-Zadeh K et al. Mayo Clin Proc 2010;95:991

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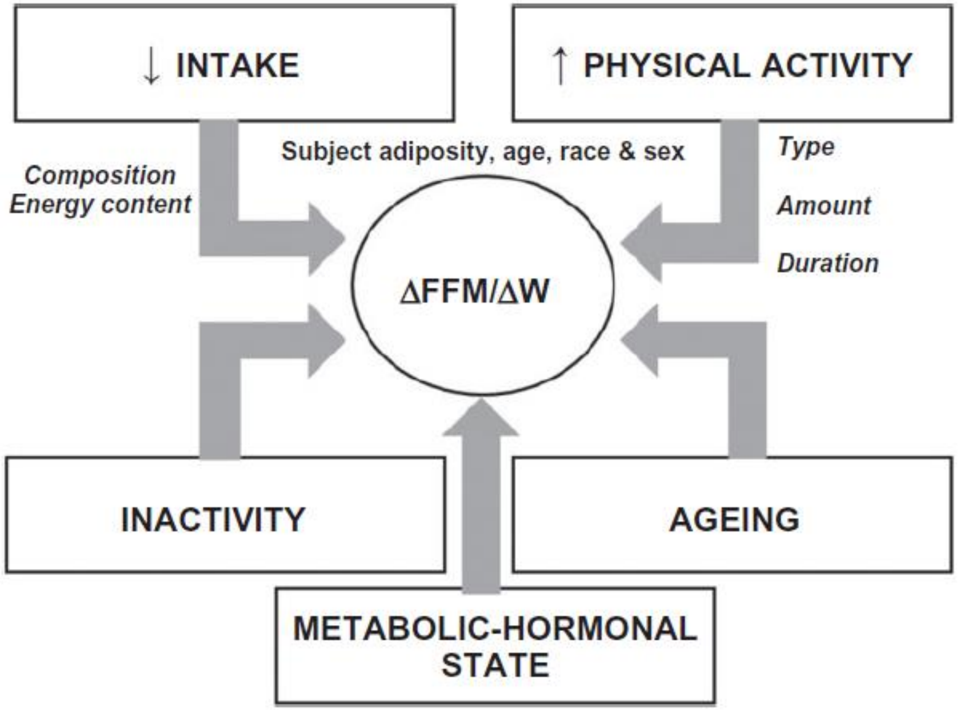
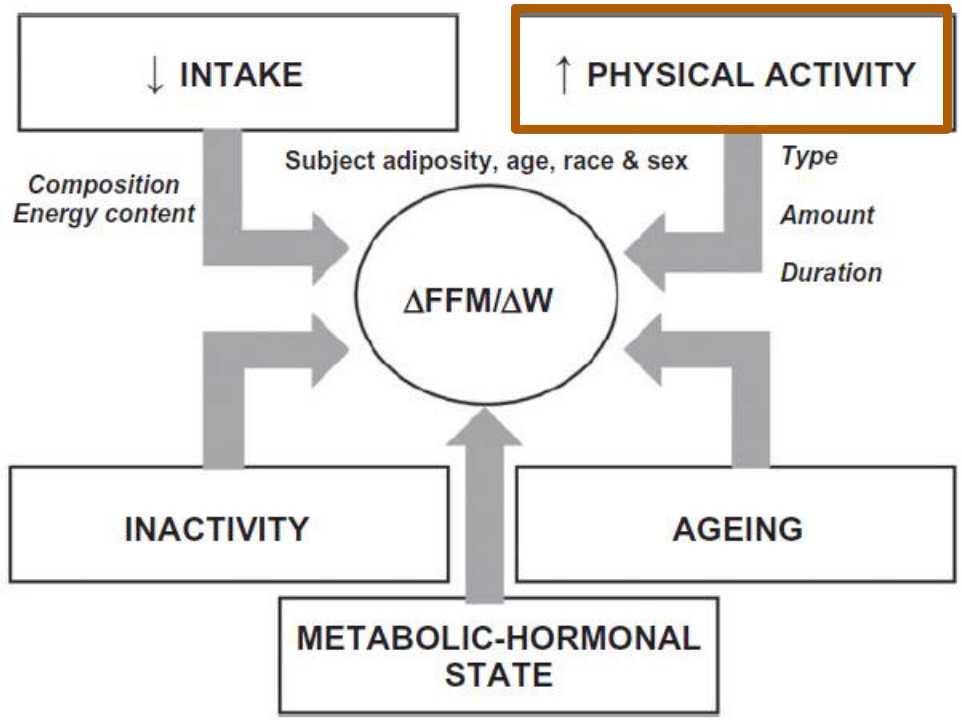


Figure 2 The main recognized or potential contributing factors that influence the fractional loss of FFM (ΔFFM/ΔW) with dieting.

Heymsfield SB et al. Obes Rev 2014



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Changes in fat-free mass during significant weight loss: a systematic review

Chaston TB et al. Int J Obes 2007;31:743

Janssen I, Fortier A, Hudson R, Ross R. Effects of an energy-restrictive diet with or without exercise on abdominal fat, intermuscular fat, and metabolic risk factors in obese women. *Diabetes Care* 2002; **25**: 431–438.
Janssen I, Ross R. Effects of sex on the change in visceral, subcutaneous adipose tissue and skeletal muscle in response to weight loss. *Int J Obes Relat Metab Disord* 1999; **23**: 1035–1046.
Rice B, Janssen I, Hudson R, Ross R. Effects of aerobic or resistance exercise and/or diet on glucose tolerance and plasma insulin levels in obese men. *Diabetes Care* 1999; **22**: 684–691.

Table 3 Three RCT's comparing FFM loss on a LCD, LCD+aerobic exercise and LCD+resistance exercise using multi slice whole body MRI

Author	*Year*	*Intervention*	*Weight loss (kg)*	*%FFML*	*Weeks*	*N*	*Sex*	*Initial BMI*
Janssen and Ross[40]	1999	LCD	11.7	35.9	16	10	M	31.6
Janssen and Ross[40]	1999	LCD+aerobic	11.4	17.5	16	10	M	33.0
Janssen and Ross[40]	1999	LCD+resistance	12.7	18.9	16	10	M	33.6
Janssen and Ross[40]	1999	LCD	10.7	23.4	16	10	F	34.5
Janssen and Ross[40]	1999	LCD+aerobic	11.5	8.7	16	10	F	35.5
Janssen and Ross[40]	1999	LCD+resistance	10.0	13.0	16	10	F	32.5
Rice *et al.*[41]	1999	LCD	12.1	29.7	16	9	M	31.9
Rice *et al.*[41]	1999	LCD+aerobic	11.5	15.6	16	10	M	32.3
Rice *et al.*[41]	1999	LCD+resistance	13.6	20.6	16	10	M	33.8
Janssen *et al.*[39]	2002	LCD	10.0	22.0	16	13	F	33.7
Janssen *et al.*[39]	2002	LCD+aerobic	11.1	10.8	16	11	F	36.0
Janssen *et al.*[39]	2002	LCD+resistance	10.0	14.0	16	14	F	31.6

Abbreviations: FFM, fat-free mass; %FFML, percentage of weight lost as fat-free mass; LCD; low calorie diet; MRI, magnetic resonance imaging; RCT, randomized controlled trial.

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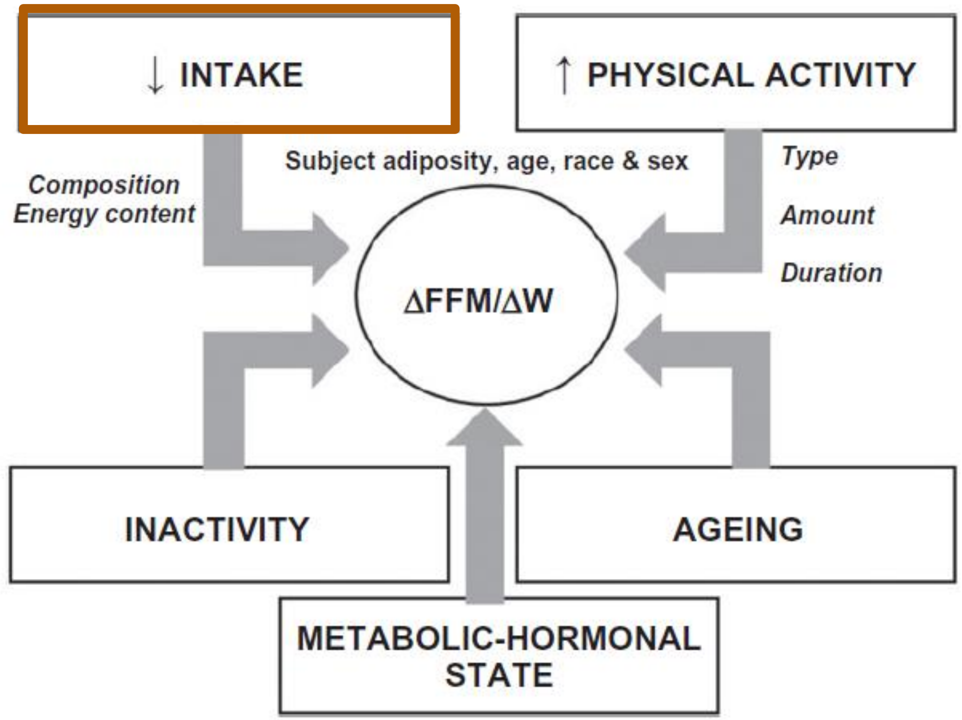
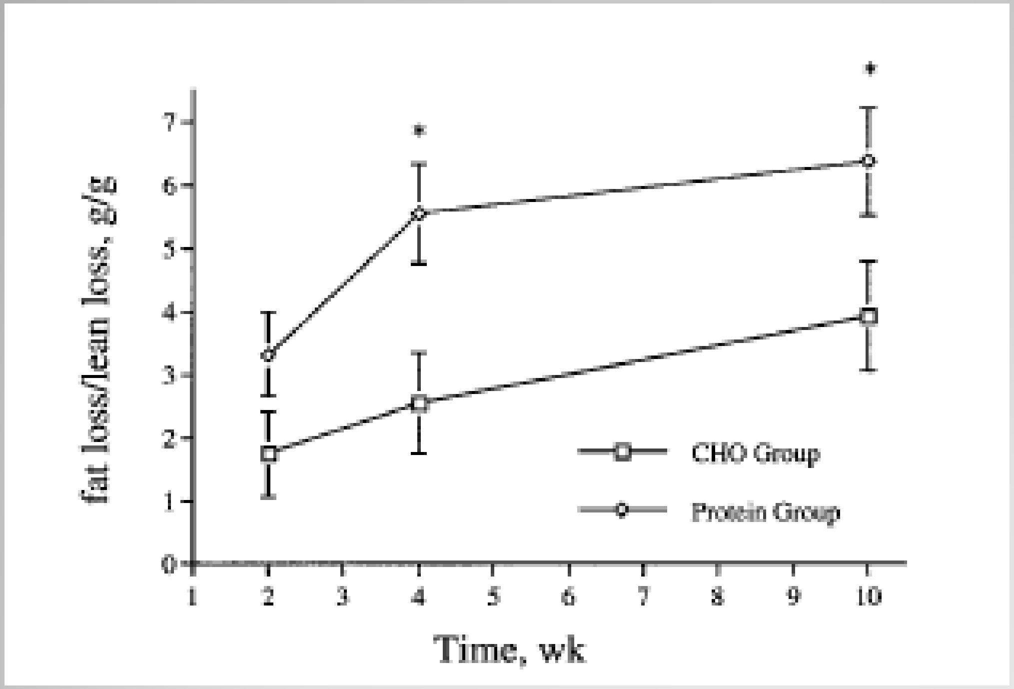


Figure 2 The main recognized or potential contributing factors that influence the fractional loss of FFM (ΔFFM/ΔW) with dieting.

Heymsfield SB et al. Obes Rev 2014

12 F. 1700 kcal/d diet with dietary protein 0.8 g/kg/d
12 F. 1700 kcal/d diet with dietary protein 1.4 g/kg/d



A Reduced Ratio of Dietary Carbohydrate to Protein Improves Body Composition and Blood Lipid Profiles during Weight Loss in Adult Women[1,2]

Lyman DK et al. J Nutr 2003;133:411

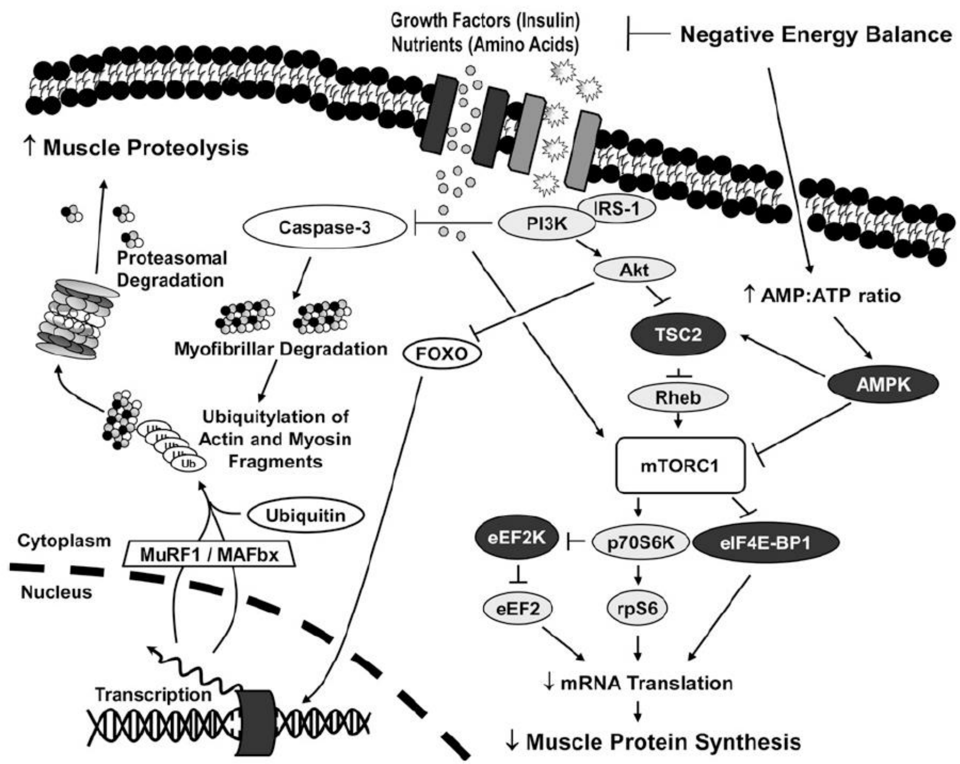
Protein intake should be individualized, assessed, and guided by an RD, in reference to gender, age, and weight **(Grade D)**. A minimal protein intake of 60 g/d and up to 1.5 g/kg ideal body weight per day should be adequate; higher amounts of protein intake—up to 2.1 g/kg ideal body weight per day—need to be assessed on an individualized basis **(Grade D)**.

Recommendations for protein intake are variable but studies suggest higher protein levels (80-90 g/d) are associated with reduced loss of lean body mass (267 [EL 4, NE]; 268 [EL 2, PCS]; 269 [EL 3, SS]). Protein intake is generally reduced following surgery (270 [EL 2, PCS]) and adequate intake can be facilitated through the use of protein supplements, though a causal effect of protein supplement use and favorable body composition change has not been demonstrated (271 [EL 2, PCS]).

AACE/TOS/ASMBS Guidelines

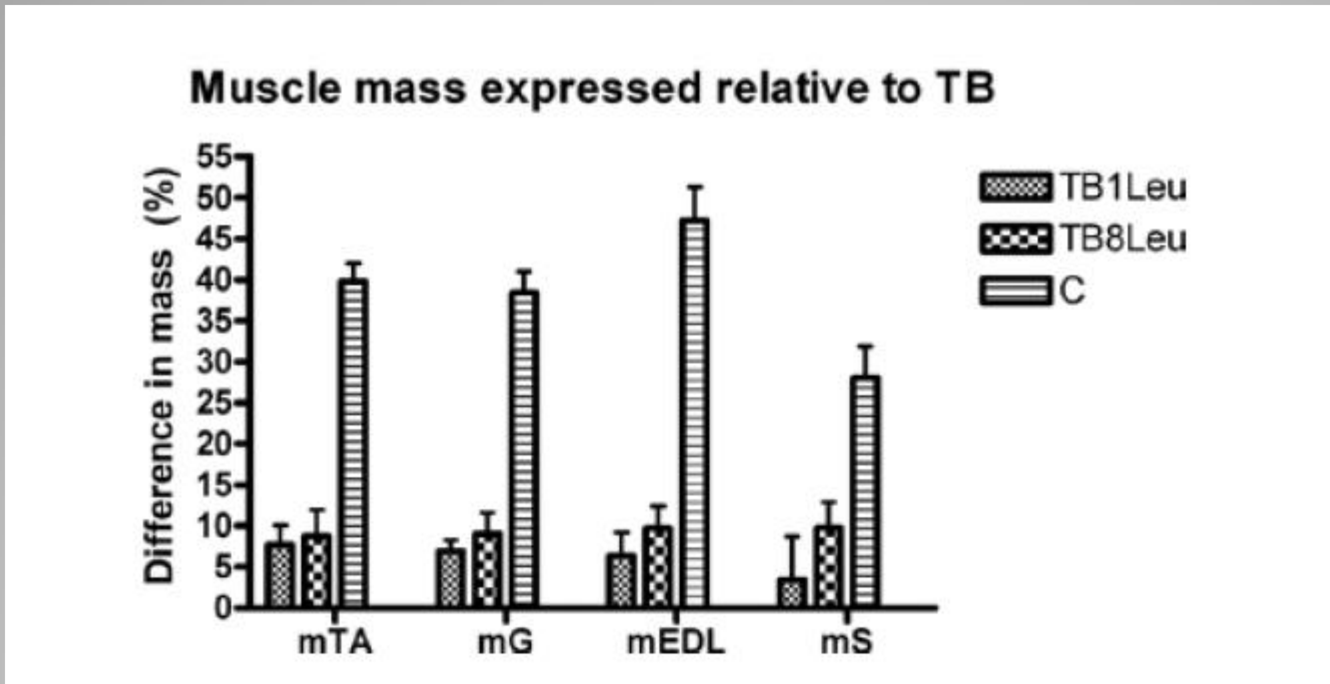
Obesity 2013;21:S1

Figure 1 In response to negative energy balance, mRNA translation and muscle protein synthesis may be down-regulated as a result of decreased nutrient and growth factor availability, causing reduced mTORC1 activation. Decreased mTORC1 activation and subsequent decreases in muscle protein synthesis, coupled with increased FOXO nuclear localization, increased transcription of atrophy-related genes, with up-regulated caspase 3 activation and muscle protein ubiquitylation provide a possible mechanism contributing to skeletal muscle loss in response to periods of negative energy balance. Synthetic stimulators are depicted in gray, whereas inhibitors of synthesis are shown in black. Akt, protein kinase B; AMPK, AMP-activated protein kinase; eEF2, eukaryotic elongation factor 2; eEF2K, eukaryotic elongation factor 2 kinase; eIF4E-BP1, eukaryotic translation initiation factor 4E-binding protein 1; FOXO, forkhead box O; IRS-1, insulin receptor substrate 1; MAFbx, muscle atrogin F-box protein; mTORC1, mammalian target of rapamycin complex 1; MuRF1, muscle RING-finger protein 1; p70S6K, 70-kDa S6 kinase; PI3K, phosphatidylinositol 3-kinase; Rheb, ras homolog enriched in brain; rpS6, ribosomal protein S6; TSC, tuberous sclerosis complex; Ub, ubiquitin.



Skeletal Muscle Responses to Negative Energy Balance: Effects of Dietary Protein[1,2]

Carbone JW et al. Adv Nutr 2012;3:119



Dose-dependent effects of leucine supplementation on preservation of muscle mass in cancer cachectic mice

Peters SJ et al. Oncol Rep 2011;26:247

Grazie per l'attenzione