Nuove indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

Il sottoscritto Prof. LUIGI BARREA

ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

X *che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario*

❑ *che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:*

- *……*
- *……*
- *……*

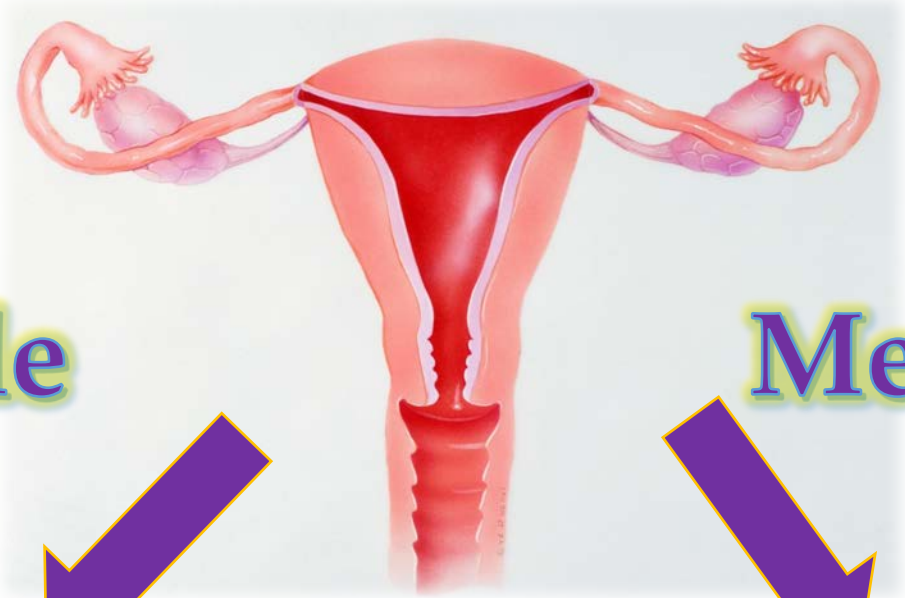
Nuove indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

KDA Ketogenic Diet ACADEMY

SINut Società Italiana di Nutraceutica



Età fertile

Menopausa

MENOPAUSE

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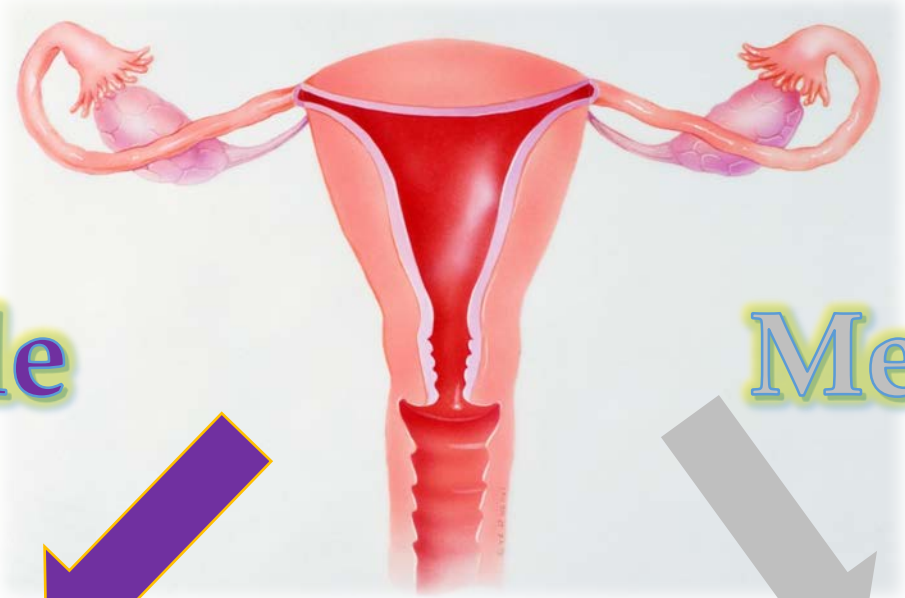


Età fertile

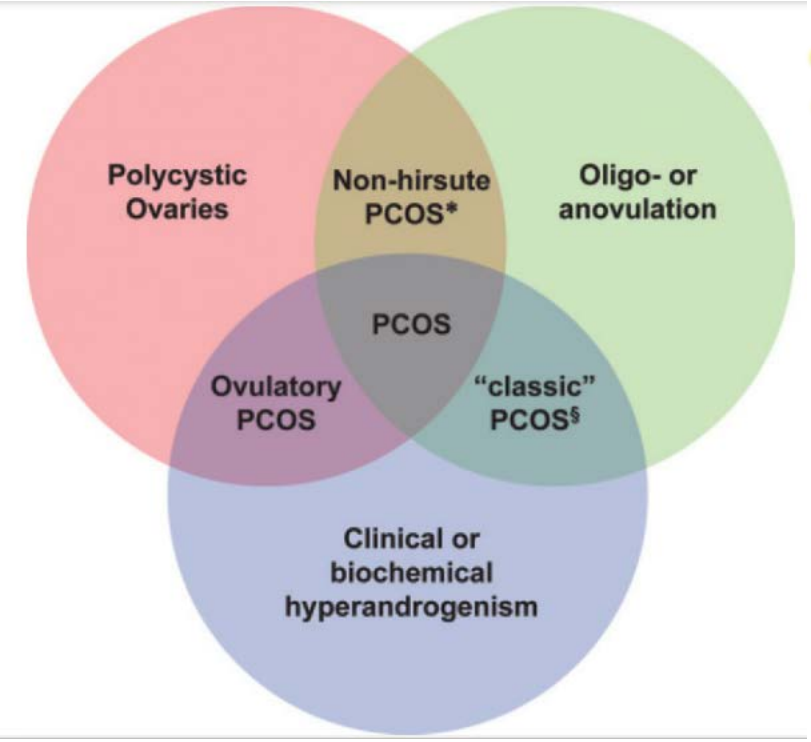
Menopausa

Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

PCOS
(Polycystic Ovary Syndrome)

La sindrome dell'ovaio policistico (PCOS) è considerata il disturbo endocrino più comune nelle donne in età riproduttiva, con una prevalenza stimata che va dal **6 al 15**%



Diagnosi

Presenza di almeno due dei tre seguenti elementi:

1. Oligomenorrea o amenorrea.
2. Segni clinici e/o biochimici di iperandrogenismo (irsutismo, acne, secrezione sebacea, alopecia…).
3. Presenza di ovaie policistiche all'esame ecografico pelvico.

Esclusione di altre cause (Tumori androgeno-secernenti, Sindrome di Cushing…)

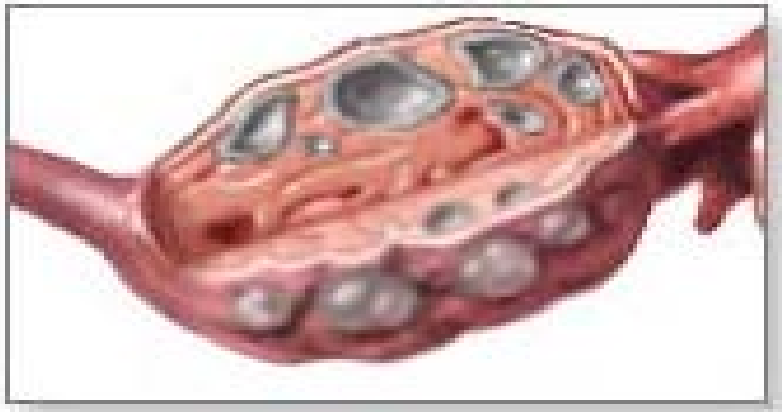
CRITERI DI ROTTERDAM

PCOS: Phenotypes

1990 US NIH criteria
2006 AE-PCOS criteria
2003 Rotterdam criteria

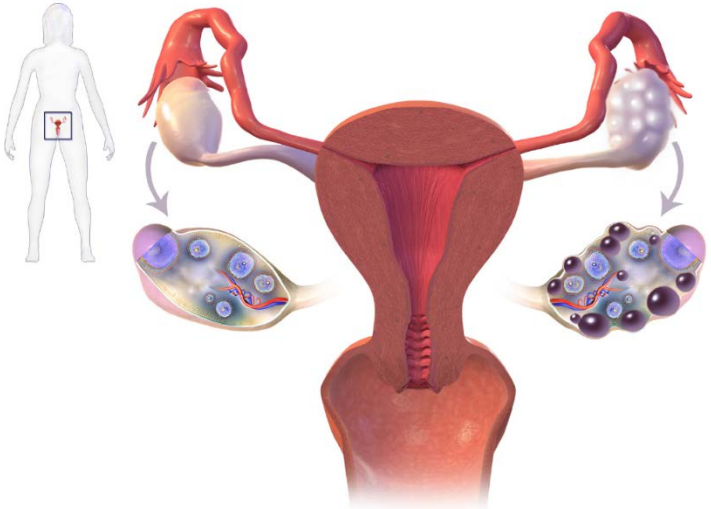
	Phenotype A	Phenotype B	Phenotype C	Phenotype D
Hyperandrogenism and hirsutism	**Present**	**Present**	**Present**	Absent
Ovulatory dysfunction	**Present**	**Present**	Absent	**Present**
Polycystic ovarian morphology	**Present**	Absent	**Present**	**Present**

Nature Reviews | Disease Primers



PCOS: Quartetto Clinico

Acanthosis Nigricans

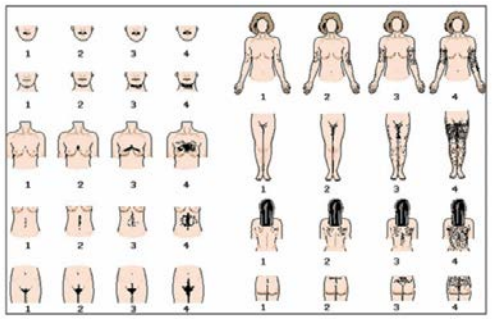


Polycystic Ovary Syndrome

Alopecia Androgenica

Acne

Irsutismo



Miglior marcatore clinico di iperandrogenismo

Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

Metabolico

Riproduttivo

Iperandrogenismo 70% (irsutismo, acne, alopecia androgenetica)

Acanthosis Nigricans

Anovulatorietà con infertilità e poliabortività

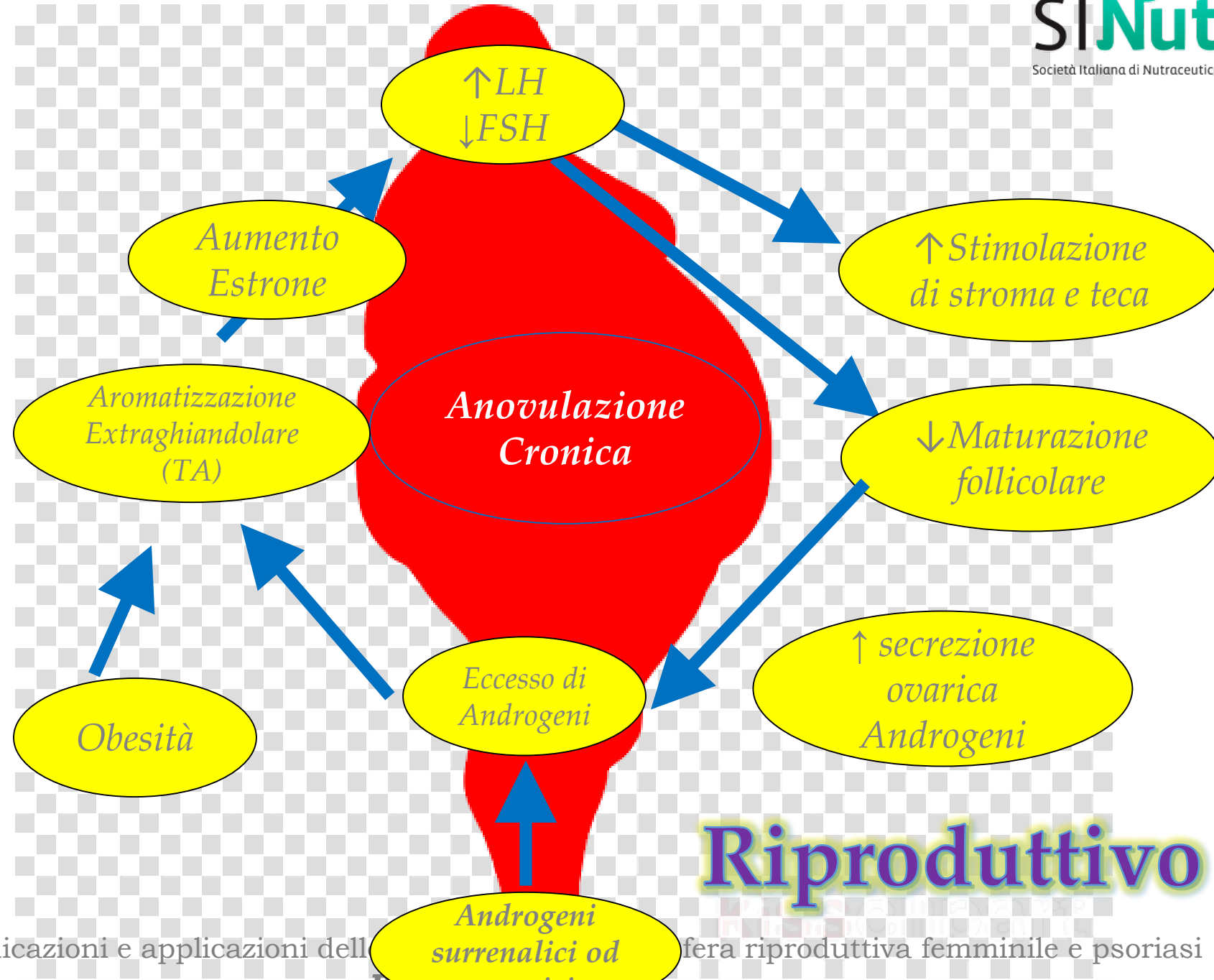
Alterazioni mestruali (amenorrea 50%, oligomenorrea, metrorragie 20%)

Intolleranza ai glucidi

Sindrome Metabolica

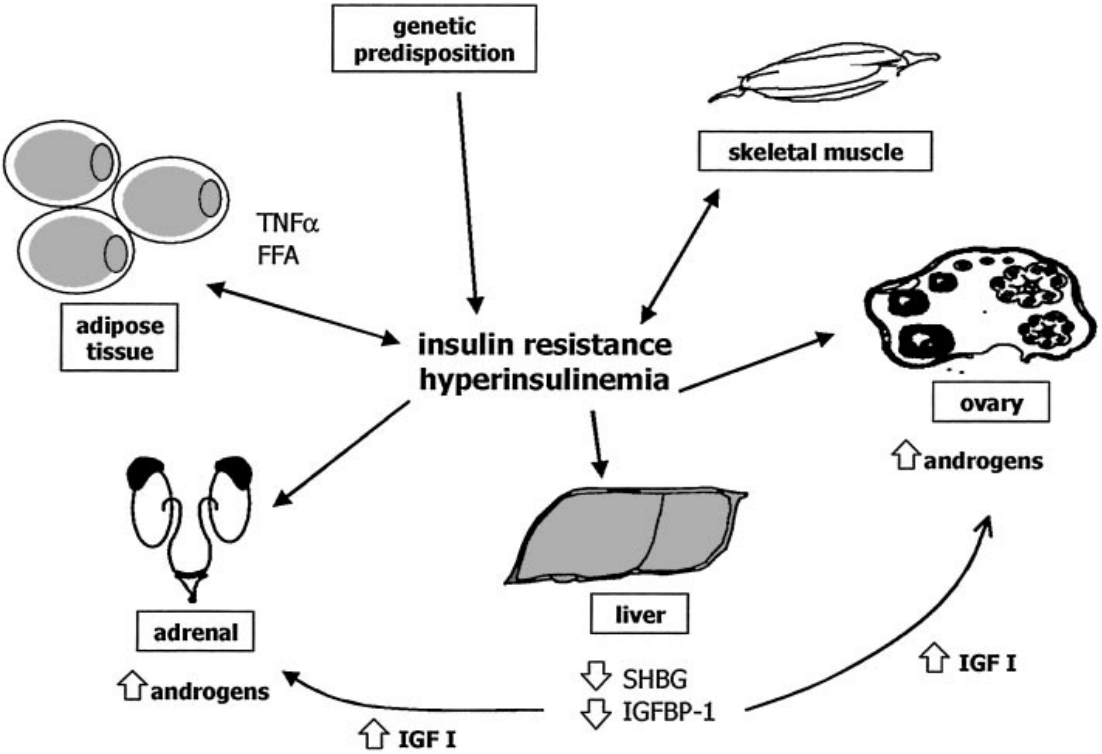
Ovaie ingrandite e micropolicistiche

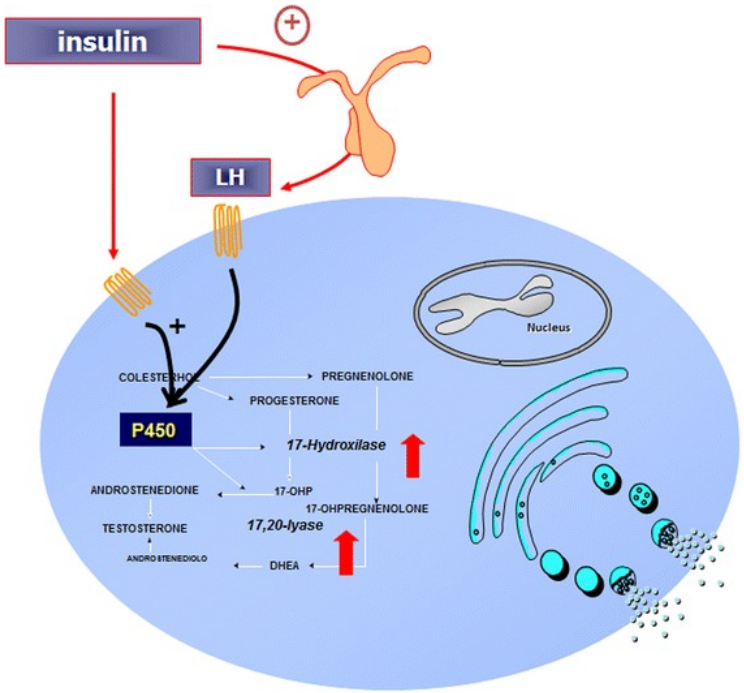
OBESITÀ (50% DEI CASI; DISTRIBUZIONE CENTRALE)



Riproduttivo

L'iperinsulinemia nella PCOS contribuire all'iperandrogenismo direttamente, attraverso la stimolazione della produzione ovarica di androgeni e inibizione della sintesi epatica di SHGB, aumentando così la disponibilità di testosterone. L'insulina aumenta anche la produzione di androgeni surrenali mediati dall' ACTH e accentua la steroidogenesi ovarica stimolata da LH.

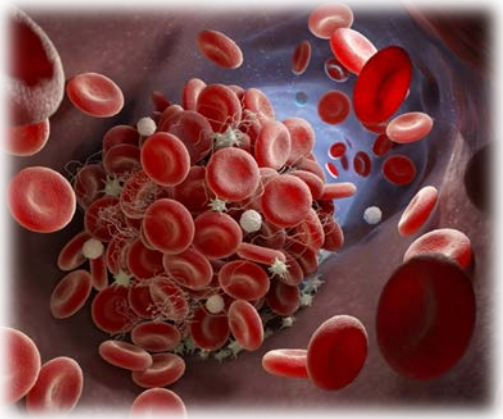




Metabolico

PCOS e Terapia

I contraccettivi orali sono il trattamento medico più comune nelle donne con PCOS. Tuttavia, molti pazienti con PCOS presentano alcune controindicazioni relative all'uso di contraccettivi orali.



Review > Metabolism. 2017 Aug;73:22-35. doi: 10.1016/j.metabol.2017.05.001.
Epub 2017 May 10.

Effects of oral contraceptives on metabolic profile in women with polycystic ovary syndrome: A meta-analysis comparing products containing cyproterone acetate with third generation progestins

Attualmente non esiste uno specifico trattamento medico per pazienti con PCOS, perciò lo sviluppo di nuove strategie di trattamento, è un problema urgente nei pazienti con PCOS.

PCOS e Terapia

La perdita di peso rappresenta il fattore più importante per migliorare il fenotipo iperandrogenico della PCOS.

Una perdita di peso del 5-10% migliora la funzione ovulatoria e i tassi di gravidanza, con riduzione dei livelli di insulina e testosterone libero.

La modifica dello stile di vita basata sulla restrizione calorica e la modulazione dei macronutrienti della dieta rappresentano il primo approccio terapeutico

Review > Diabetes Metab Syndr. 2017 Nov;11 Suppl 1:S429-S432. doi: 10.1016/j.dsx.2017.03.030. Epub 2017 Apr 5.

Nutritional management in women with polycystic ovary syndrome: A review study

Zeinab Faghfoori [1], Siavash Fazelian [2], Mahdi Shadnoush [3], Reza Goodarzi [4]

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 11S (2017) S429–S432

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

Nutritional management in women with polycystic ovary syndrome: A review study

Contents

1. Introduction . . . . . .
2. Obesity and weight loss in polycystic ovary syndrome
3. The macronutrient composition of weight-loss diets .
4. Glycemic index and polycystic ovary syndrome . . . . . .
5. Fatty acids and polycystic ovary syndrome . . . . . .
6. Vitamin D deficiency and polycystic ovary syndrome .
7. Minerals and polycystic ovary syndrome . . . . . .
8. Caffeine and polycystic ovary syndrome . . . . . .
9. Conclusion . . . . . .
References . . . . . .

Source and amount of carbohydrate in the diet and inflammation in women with polycystic ovary syndrome

Nutr Res Rev. 2018

Luigi Barrea[1]*, Paolo Marzullo[2], Giovanna Muscogiuri[1], Carolina Di Somma[3], Massimo Scacchi[4], Francesco Orio[5], Gianluca Aimaretti[6], Annamaria Colao[1] and Silvia Savastano[1]

[1]*Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy*

Nutrition Research Reviews

Abstract

High carbohydrate intake and low-grade inflammation cooperate with insulin resistance and hyperandrogenism to constitute an interactive continuum acting on the pathophysiology of polycystic ovary syndrome (PCOS), the most common endocrine disorder in women of reproductive age characterised by oligo-anovulatory infertility and cardiometabolic disorders. The role of insulin in PCOS is pivotal both in regulating the activity of ovarian and liver enzymes, respectively involved in androgen production and in triggering low-grade inflammation usually reported to be associated with an insulin resistance, dyslipidaemia and cardiometabolic diseases. Although an acute hyperglycaemia induced by oral glucose loading may increase inflammation and oxidative stress by generating reactive oxygen species through different mechanisms, the postprandial glucose increment, commonly associated with the Western diet, represents the major contributor of chronic sustained hyperglycaemia and pro-inflammatory state. Together with hyperinsulinaemia, hyperandrogenism and low-grade inflammation, unhealthy diet should be viewed as a key component of the 'deadly quartet' of metabolic risk factors associated with PCOS pathophysiology. The identification of a tight diet–inflammation–health association makes the adoption of healthy nutritional approaches a primary preventive and therapeutic tool in women with PCOS, weakening insulin resistance and eventually promoting improvements of reproductive life and endocrine outcomes. The intriguing nutritional–endocrine connections operating in PCOS underline the role of expert nutritionists in the management of this syndrome. The aim of the present review is to provide an at-a-glance overview of the possible bi-directional mechanisms linking inflammation, androgen excess and carbohydrate intake in women with PCOS.

Key words: **Carbohydrates: Polycystic ovary syndrome: Low-grade inflammation: Hyperandrogenism**

nutrients

MDPI

Article

Adherence to the Mediterranean Diet, Dietary Patterns and Body Composition in Women with Polycystic Ovary Syndrome (PCOS)

IMPACT FACTOR 5.717

Luigi Barrea [1,*,†], Angela Arnone [1,†], Giuseppe Annunziata [2,†], Giovanna Muscogiuri [1], Daniela Laudisio [1], Ciro Salzano [1], Gabriella Pugliese [1], Annamaria Colao [1] and Silvia Savastano [1]

Questions PREDIMED Questionnaire	PCOS Patients $n = 112$		Control Group $n = 112$		χ^2	p Values
	n	%	n	%		
Use of extra-virgin olive oil as main culinary lipid	88	78.6	108	96.4	14.74	**<0.001**
Extra virgin olive oil >4 tablespoons	64	57.1	55	49.1	1.15	0.284
Vegetables ≥2 servings/day	54	48.2	62	55.4	0.87	0.349
Fruits ≥3 servings/day	67	59.8	66	58.9	0.01	1.000
Red/processed meats <1/day	62	55.4	57	50.9	0.28	0.592
Butter, cream, margarine <1/day	47	42.0	55	49.1	0.88	0.348
Soda drinks <1/day	53	47.3	58	51.8	0.28	0.593
Wine glasses ≥ 7/week	30	26.8	35	31.3	0.35	0.555
Legumes ≥ 3/week	60	53.6	81	72.3	7.66	**0.006**
Fish/seafood ≥ 3/week	35	31.3	76	67.9	28.57	**<0.001**
Commercial sweets and confectionery ≤ 2/week	59	52.7	56	50.0	0.07	0.789
Tree nuts ≥ 3/week	31	27.7	76	67.6	34.64	**<0.001**
Poultry more than red meats	63	56.3	51	45.5	2.16	0.142
Use of sofrito sauce ≥ 2/week	68	60.7	73	65.2	0.31	0.580

nutrients

MDPI

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Parameters	PCOS Patients $n = 112$	Control Group $n = 112$	p-Value
Dietary Intake			
Total energy (kcal)	2245.31 ± 290.75	2254.84 ± 272.37	0.711
Protein (g of total kcal)	86.98 ± 10.15	88.43 ± 9.96	0.261
Carbohydrate (g of total kcal)	307.98 ± 42.03	310.47 ± 37.42	0.518
Complex (g of total kcal)	174.21 ± 25.43	191.48 ± 23.60	**<0.001**
Simple (g of total kcal)	133.77 ± 34.01	118.99 ± 33.62	**<0.001**
Fiber (g/day)	15.43 ± 3.66	17.22 ± 4.19	**<0.001**
Fat (g of total kcal)	73.94 ± 13.59	70.07 ± 10.73	**<0.001**
SFA (g of total kcal)	24.55 ± 7.51	17.39 ± 10.71	**<0.001**
Unsaturated fat (g of total kcal)	49.38 ± 8.63	52.67 ± 8.12	**0.002**
MUFA (g of total kcal)	38.21 ± 4.56	43.68 ± 5.86	**<0.001**
PUFA (g of total kcal)	11.16 ± 6.88	8.99 ± 4.69	**0.005**
n-6 PUFA (g/day)	7.82 ± 6.83	4.67 ± 3.87	**<0.001**
n-3 PUFA (g/day)	3.34 ± 2.24	4.32 ± 3.29	**<0.001**

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Parameters	Testosterone (ng/dL)		
	< 22.27 ng/dL *n* = 56	> 22.27 ng/dL *n* = 56	*p*-Value
Dietary Intake			
Total energy (kcal)	2141.83 ± 230.24	2348.78 ± 309.52	**<0.001**
Protein (g of total kcal)	88.01 ± 10.69	85.96 ± 9.55	0.287
Carbohydrate (g of total kcal)	292.29 ± 31.87	323.67 ± 45.26	**<0.001**
Complex (g of total kcal)	173.01 ± 20.24	175.41 ± 29.88	0.619
Simple (g of total kcal)	119.28 ± 26.68	148.25 ± 34.58	**<0.001**
Fiber (g/day)	17.08 ± 3.48	13.79 ± 3.04	**<0.001**
Fat (g of total kcal)	68.96 ± 10.70	78.92 ± 14.42	**<0.001**
SFA (g of total kcal)	20.51 ± 6.14	28.60 ± 6.54	**<0.001**
Unsaturated fat (g of total kcal)	48.45 ± 6.73	50.32 ± 10.16	0.254
MUFA (g of total kcal)	39.49 ± 3.45	36.94 ± 5.18	**0.003**
PUFA (g of total kcal)	8.96 ± 5.10	13.38 ± 7.71	**0.001**
n-6 PUFA (g/day)	5.51 ± 4.92	10.14 ± 7.69	**<0.001**
n-3 PUFA (g/day)	3.44 ± 2.28	3.23 ± 2.21	0.631

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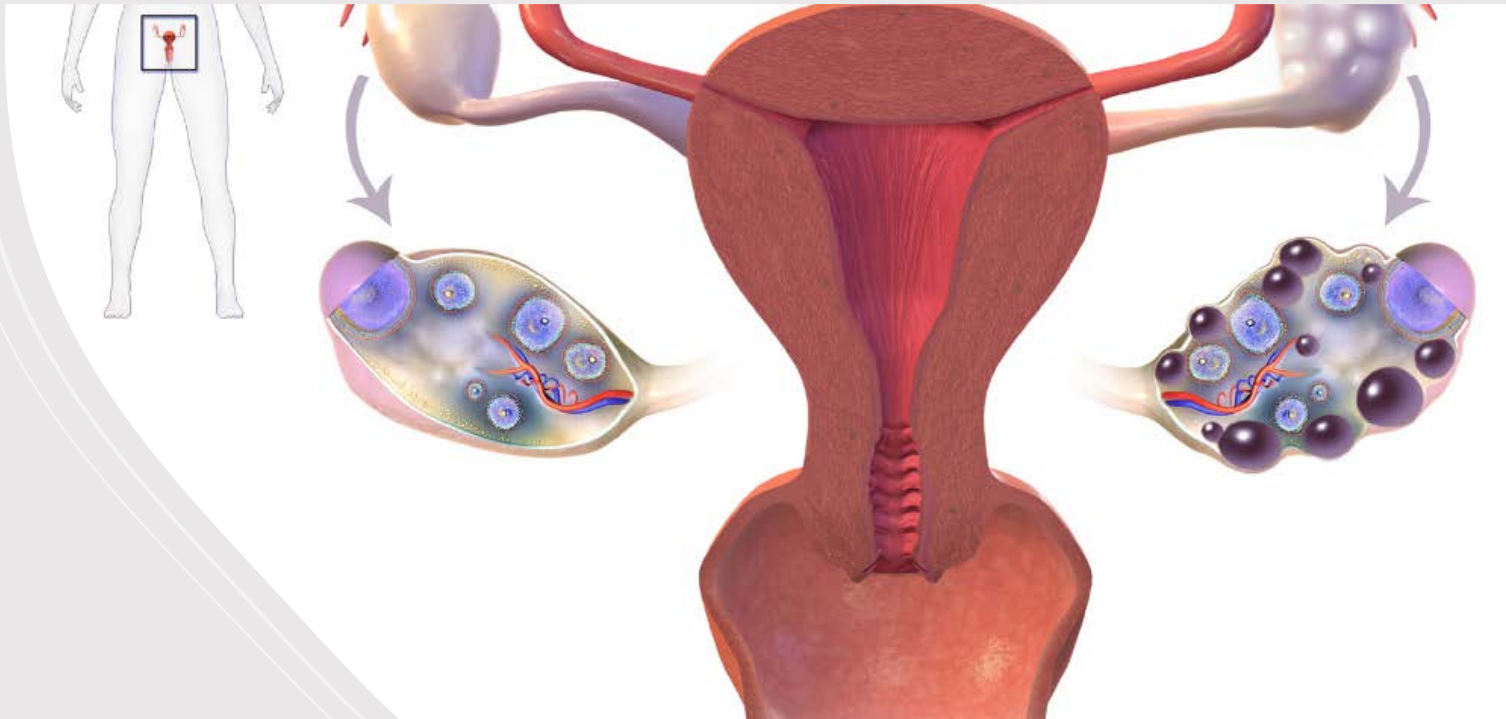
Table 6. Multiple regression analysis model (stepwise method) with the Testosterone as dependent variable to estimate the predictive value of food items of WC, PREDIMED score, CRP levels, HoMA-IR and nutrients intake (protein, complex carbohydrate, simple carbohydrate, SFA, MUFA, PUFA, n-6 PUFA, n-3 PUFA, fiber).

Parameters	Multiple Regression Analysis			
Model 1	**R^2**	**β**	**t**	***p* Value**
CRP levels	0.704	−0.841	16.28	**<0.001**
PREDIMED SCORE	0.724	−0.212	−2.96	**<0.001**
MUFA (g of total kcal)	0.738	−0.133	−2.61	**0.001**
Variable excluded: WC, HoMA-IR, protein, complex carbohydrate, simple carbohydrate, SFA, PUFA, n-6 PUFA, n-3 PUFA, fiber.				

Between adherence to the MD and dietary nutrients intake, testosterone levels were well predicted by PREDIMED score and MUFA intake. A *p* value in bold type denotes a significant difference ($p < 0.05$). CRP, C-reactive Protein; PREDIMED, PREvención con DIetaMEDiterránea; MUFA, MonoUnsaturated Fatty Acids; WC, Waist Circumference; HoMA-IR, Homeostasis model assessment insulin resistance; SFA, Saturated Fatty Acids; PolyUnsaturated Fatty Acids.

PCOS E KD



PCOS E KD

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ketogenic diet and Polycystic ovary syndrome

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The effects of a low-carbohydrate, ketogenic d
pilot study.

Mavropoulos JC, et al. Nutr Metab (Lond). 2005. PMID: 1635

Ketogenic diet in women with polycystic ovary
obese: A randomized, open-label, parallel-grou

Li J, et al. J Obstet Gynaecol Res. 2021. PMID: 33462940 Clini

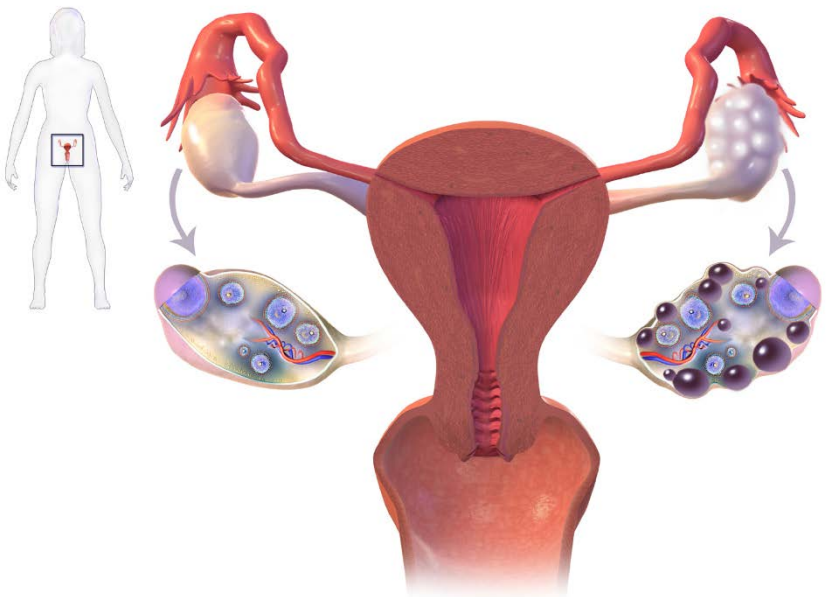
PCOS e KD: Studi Clinici

Nella PCOS, le prove degli effetti della KD sono scarse

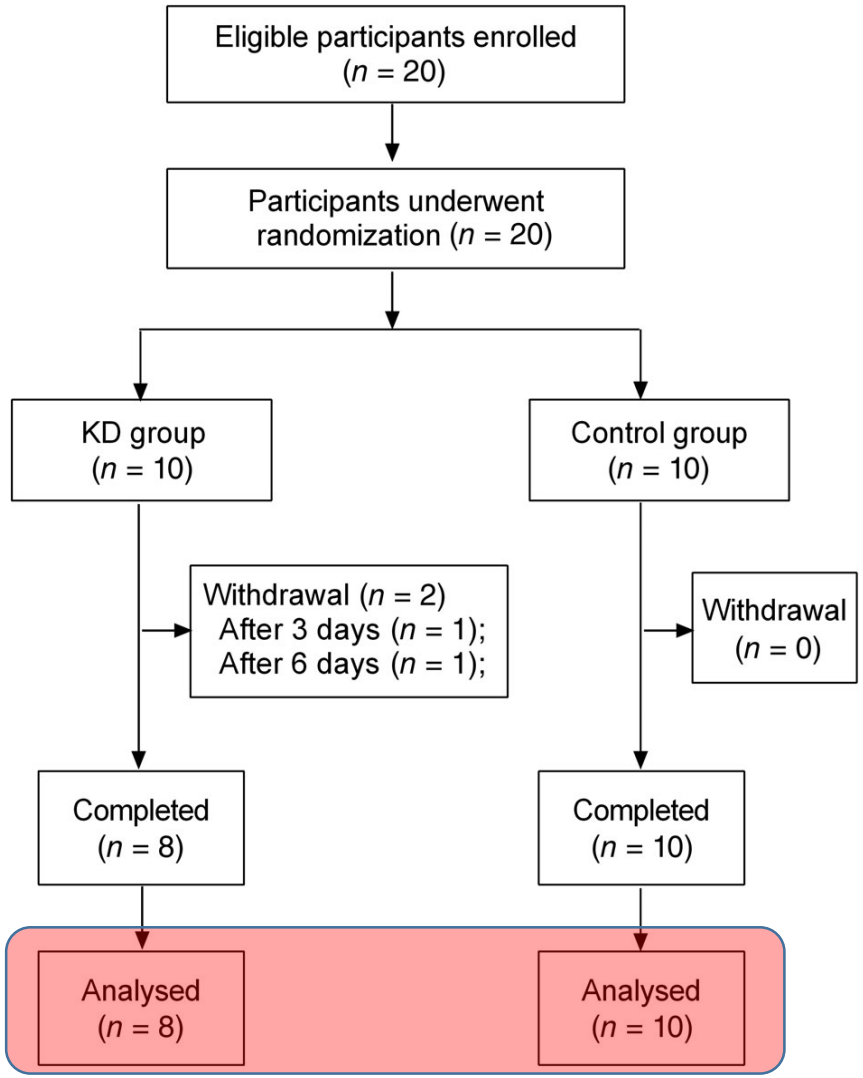
J Obstet Gynaecol Res. 2021 Mar;47(3):1145-1152. doi: 10.1111/jog.14650. Epub 2021 Jan 18.

Ketogenic diet in women with polycystic ovary syndrome and liver dysfunction who are obese: A randomized, open-label, parallel-group, controlled pilot trial

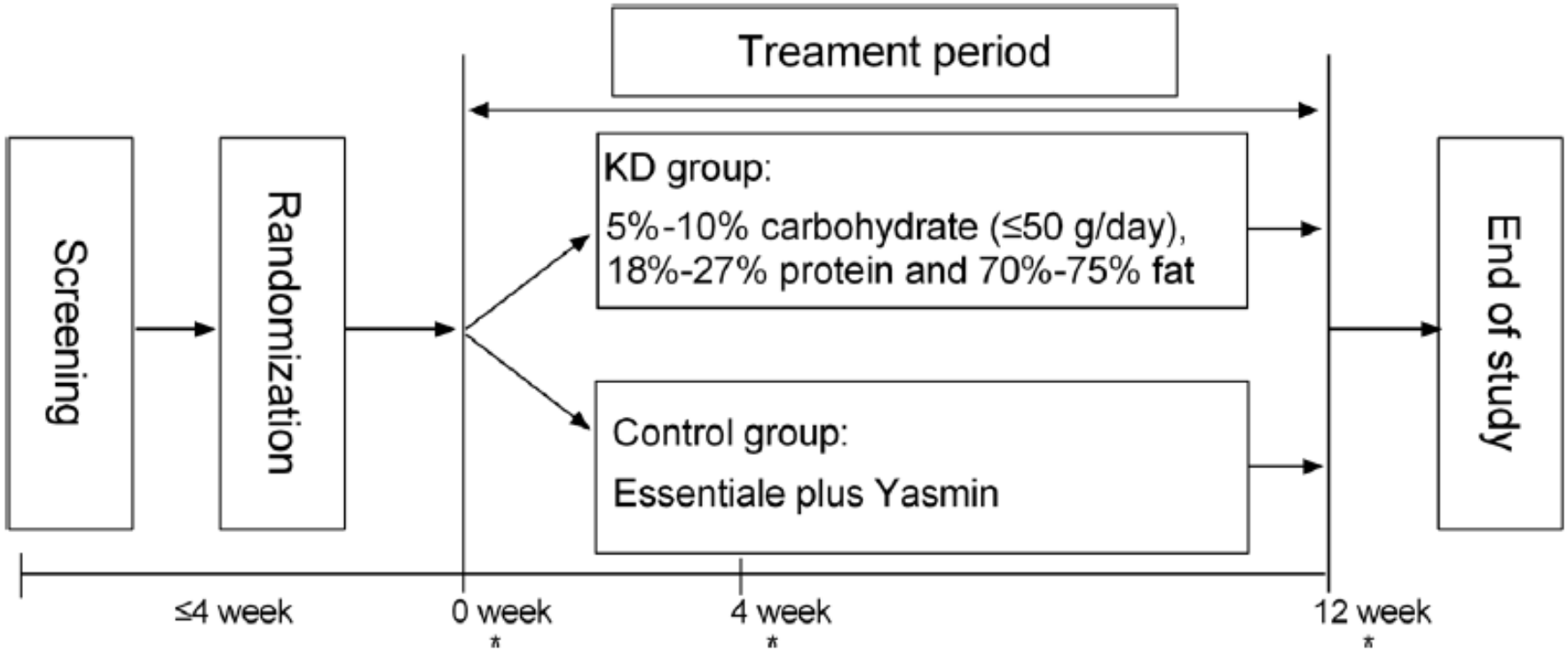
Jian Li [1], Wen-Pei Bai [1], Bo Jiang [2], Le-Ran Bai [3], Bei Gu [1], Shu-Xiang Yan [1], Fu-Ying Li [1], Bin Huang [1]



Polycystic Ovary Syndrome



PCOS e KD: Studi Clinici



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Essentiale plus – Fosfadidilcolina
Yasmin - Drospirenone + Etinilestradiolo

Protocollo chetogenico

Le calorie giornaliere sono state calcolate sulla base della valutazione della composizione corporea (1300-1500 kcal/die).

Il fabbisogno calorico quotidiano è stato diviso in tre pasti menu e prevedeva alimenti appropriato per la KD olio, carne, uova, pesce e verdure a ridotto contenuto in zuccheri.

Durante le 12 settimane di intervento, i soggetti sono stati contattati telefonicamente per garantire l'aderenza alla dieta.

Il rispetto del regime chetogenico è stato monitorato effettuando misurazioni giornaliere del livello urinario di chetoni.

PCOS e KD: Studi Clinici

Jian Li J. Obstet. Gynaecol. Res. 2021

TABLE 1 Baseline characteristics of the participants

Characteristic	Control group (n = 10)	KD group (n = 8)	p-value
Age (year, mean ± SD)	28.90 ± 4.93	31.13 ± 3.64	0.304
Weight (Kg, mean ± SD)	74.62 ± 8.23	87.19 ± 11.14	0.014
Height (cm, mean ± SD)	158.00 ± 6.39	163.00 ± 4.31	0.159
BMI (kg/m^2, mean ± SD)	32.81 ± 3.75	29.82 ± 2.36	0.056
Menstrual cycle (day, mean ± SD)	63.00 ± 19.75	72.50 ± 33.17	0.757

Abbreviations: BMI, body mass index; KD, ketogenic diet; SD, standard deviations.

NON VI ERANO DIFFERENZE STATISTICAMENTE SIGNIFICATIVE TRA I DUE GRUPPI

PCOS e KD: Studi Clinici

Changes in anthropometric characteristics and body composition variables after 12 weeks of intervention

BFP, body fat percentage;
VFA, visceral fat area;

	Control group		
	Baseline	Week 4	Week 12
Anthropometric characteristics			
BMI (kg/m^2)	29.82 ± 2.36	29.64 ± 2.65[a]	29.20 ± 2.24[a]
Weight (kg)	74.62 ± 8.23	74.12 ± 8.97[a]	73.14 ± 8.52[a]
Body composition			
BF (kg)	25.58 ± 4.02	25.28 ± 4.18[a]	24.85 ± 3.93[a]
BFP (%)	34.28 ± 3.83	33.92 ± 3.93[a]	33.85 ± 4.17[a]
VFA (cm^2)	96.01 ± 10.70	96.09 ± 12.75[a]	94.98 ± 10.75[a]
WHR (%)	0.87 ± 0.03	0.87 ± 0.02[a]	0.87 ± 0.02[a]

	KD group		
	Baseline	Week 4	Week 12
Anthropometric characteristics			
BMI (kg/m^2)	32.81 ± 3.75[b]	30.77 ± 3.62[b, c]	28.33 ± 2.62[b, c]
Weight (kg)	87.19 ± 11.14[d]	81.84 ± 10.99[b, c]	75.41 ± 8.01[b, c]
Body composition			
BF (kg)	35.38 ± 7.97[d]	31.51 ± 7.78[d, c]	28.57 ± 7.28[b, c]
BFP (%)	40.34 ± 5.37[d]	37.51 ± 4.65[b, c]	34.04 ± 3.74[b, c]
VFA (cm^2)	128.91 ± 34.93[d]	113.13 ± 31.32[b, c]	97.78 ± 26.43[b, c]
WHR (%)	0.93 ± 0.05[d]	0.90 ± 0.04[b, c]	0.88 ± 0.04[b, c]

$p > 0.05$
A vs baseline,
b vs control group;
c vs baseline,
D vs control group

Jian Li J. Obstet. Gynaecol. Res. 2021

PCOS e KD: Studi Clinici

Jian Li J. Obstet. Gynaecol. Res. 2021

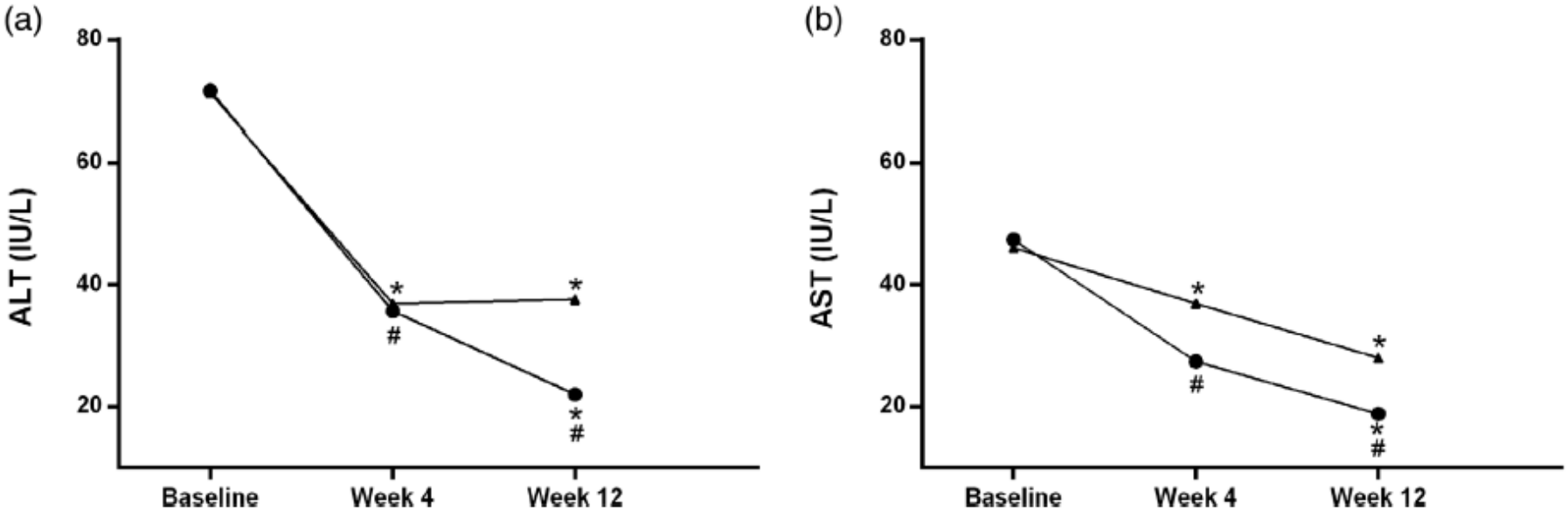
Differenze nei parametric ormonali e metabolici nei due gruppi ma non tra I gruppi

TABLE 3 Changes in endocrine and metabolic biomarkers after 12 weeks of intervention

	Control group			KD group		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Menstrual cycle (day)	63.00 ± 19.75	54.00 ± 14.68[a]	33.00 ± 6.32[b]	72.50 ± 33.17[c]	46.50 ± 20.09[b,c]	32.50 ± 2.67[b,c]
Hormonal levels						
FSH (IU/L)	5.67 ± 2.27	5.83 ± 1.70[a]	6.63 ± 2.07[a]	6.46 ± 1.65[c]	5.28 ± 1.10[a,c]	6.90 ± 2.55[a,c]
LH (IU/L)	8.92 ± 5.18	6.04 ± 2.28[a]	8.26 ± 6.64[a]	11.13 ± 9.02[c]	6.28 ± 1.94[a,c]	10.37 ± 14.27[a,c]
E (pmol/L)	76.29 ± 78.47	42.80 ± 17.56[a]	38.70 ± 20.25[a]	84.13 ± 101.93[c]	72.13 ± 61.74[a,c]	68.25 ± 65.08[a,c]
P (pmol/L)	3.63 ± 6.89	0.64 ± 0.42[a]	0.47 ± 0.25[a]	0.81 ± 0.90[c]	1.03 ± 1.72[a,c]	0.50 ± 0.34[a,c]
T (nmol/L)	0.73 ± 0.13	0.61 ± 0.16[a]	0.58 ± 0.26[a]	0.67 ± 0.16[c]	0.52 ± 0.16[a,c]	0.46 ± 0.21[a,c]
PRL (ng/mL)	9.02 ± 2.13	9.67 ± 4.60[a]	10.10 ± 5.49[a]	13.18 ± 7.92[c]	10.04 ± 3.34[a,c]	11.59 ± 8.05[a,c]
LH/FSH	1.61 ± 0.58	1.04 ± 0.26[a]	1.29 ± 0.92[a]	1.58 ± 0.76[c]	1.20 ± 0.33[a,c]	0.86 ± 0.32[a,c]
Metabolic biomarkers						
T-CHOL (mmol/L)	4.99 ± 0.74	5.02 ± 0.62[a]	4.83 ± 0.60[a]	5.28 ± 0.99[c]	4.46 ± 1.14[a,c]	4.77 ± 1.22[a,c]
TRIG (mmol/L)	2.74 ± 1.25	2.99 ± 1.58[a]	3.14 ± 2.42[a]	2.44 ± 1.66[c]	1.59 ± 0.85[a,d]	1.66 ± 0.80[a,c]
HDL (mmol/L)	1.23 ± 0.36	1.56 ± 0.57[a]	1.25 ± 0.41[a]	1.03 ± 0.10[c]	0.97 ± 0.10[a,d]	1.04 ± 0.10[a,c]
LDL (mmol/L)	2.74 ± 0.86	2.43 ± 1.04[a]	2.52 ± 0.84[a]	3.41 ± 0.74[c]	2.69 ± 1.00[a,c]	2.83 ± 0.99[a, b]
GLU (mmol/L)	5.28 ± 0.49	5.17 ± 0.82[a]	5.12 ± 0.58[a]	5.92 ± 0.85[c]	5.22 ± 0.67[b,c]	5.11 ± 0.46[b,c]

Abbreviations: E, estradiol; FSH, follicle-stimulating hormone; GLU, blood glucose; HDL, high density lipoprotein; LDL, low density lipoprotein; LH, luteinizing hormone; P, progesterone; PRL, prolactin; T, testosterone; T-CHOL, total cholesterol; TRIG, triglyceride; KD, ketogenic diet; [a]Versus baseline, $p > 0.05$; [b]Versus baseline, $p < 0.05$; [c]Versus control group, $p > 0.05$ and [d]Versus control group, $p < 0.05$.

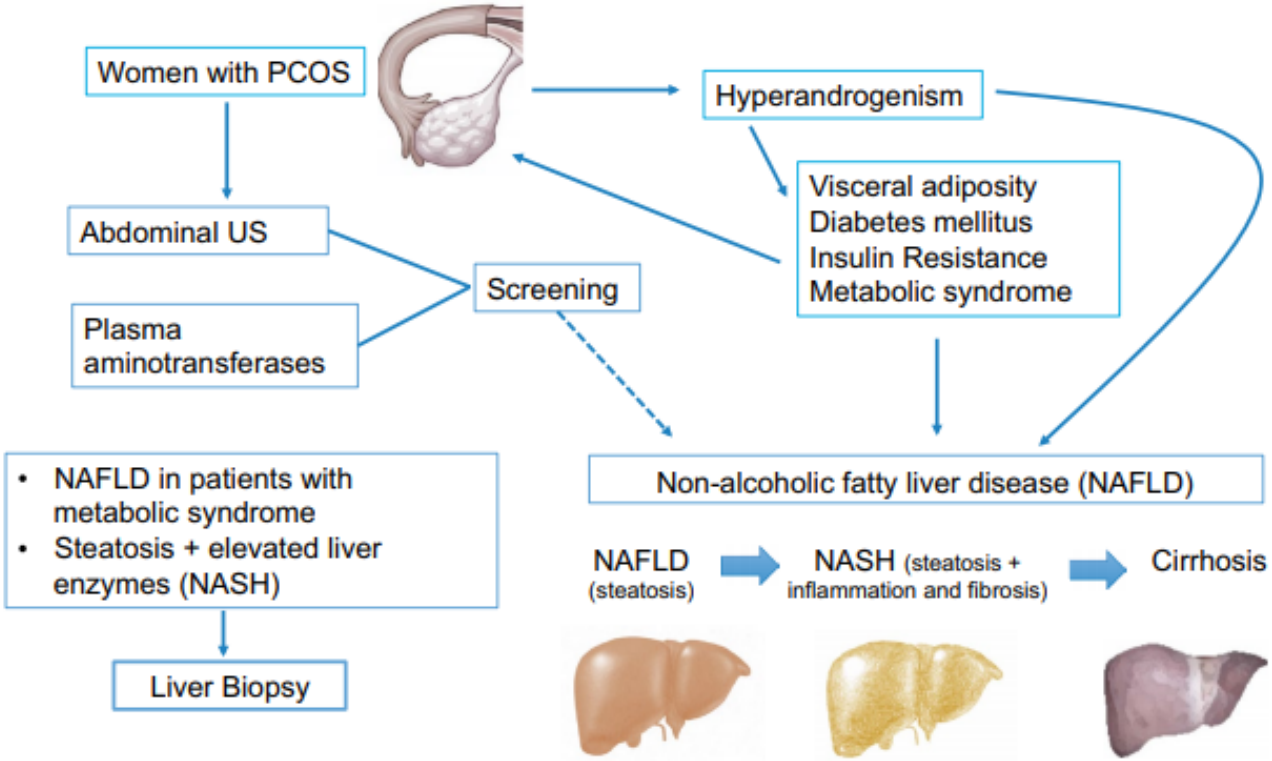
PCOS e KD: Studi Clinici
Liver function markers



Moreover, the plasma ALT and AST of KD group at 12 weeks was significantly lower than that in control group ($p<0.05$), suggesting the superiority of KD than conventional treatment in improving liver function.

Jian Li J. Obstet. Gynaecol. Res. 2021

PCOS e KD



Review > Endocrine. 2020 Jan;67(1):1-8. doi: 10.1007/s12020-019-02085-7. Epub 2019 Sep 19.

Nonalcoholic fatty liver disease in women with polycystic ovary syndrome

Stavroula A Paschou [1], Stergios A Polyzos [2], Panagiotis Anagnostis [3], Dimitrios G Goulis [3], Christina Kanaka-Gantenbein [4], Irene Lambrinoudaki [5], Neoklis A Georgopoulos [6], Andromachi Vryonidou [7]

I dati provenienti da studi clinici e meta-analisi indicano una maggiore prevalenza di NAFLD nelle donne con PCOS che va dal 34% al 70% rispetto al 14% al 34% nelle donne sane.

La resistenza all'insulina e l'iperandrogenismo sono i due principali legami fisiopatologici tra queste due entità.

Godoy-Matos et al. Diabetol Metab Syndr (2020) 12:60
https://doi.org/10.1186/s13098-020-00570-y

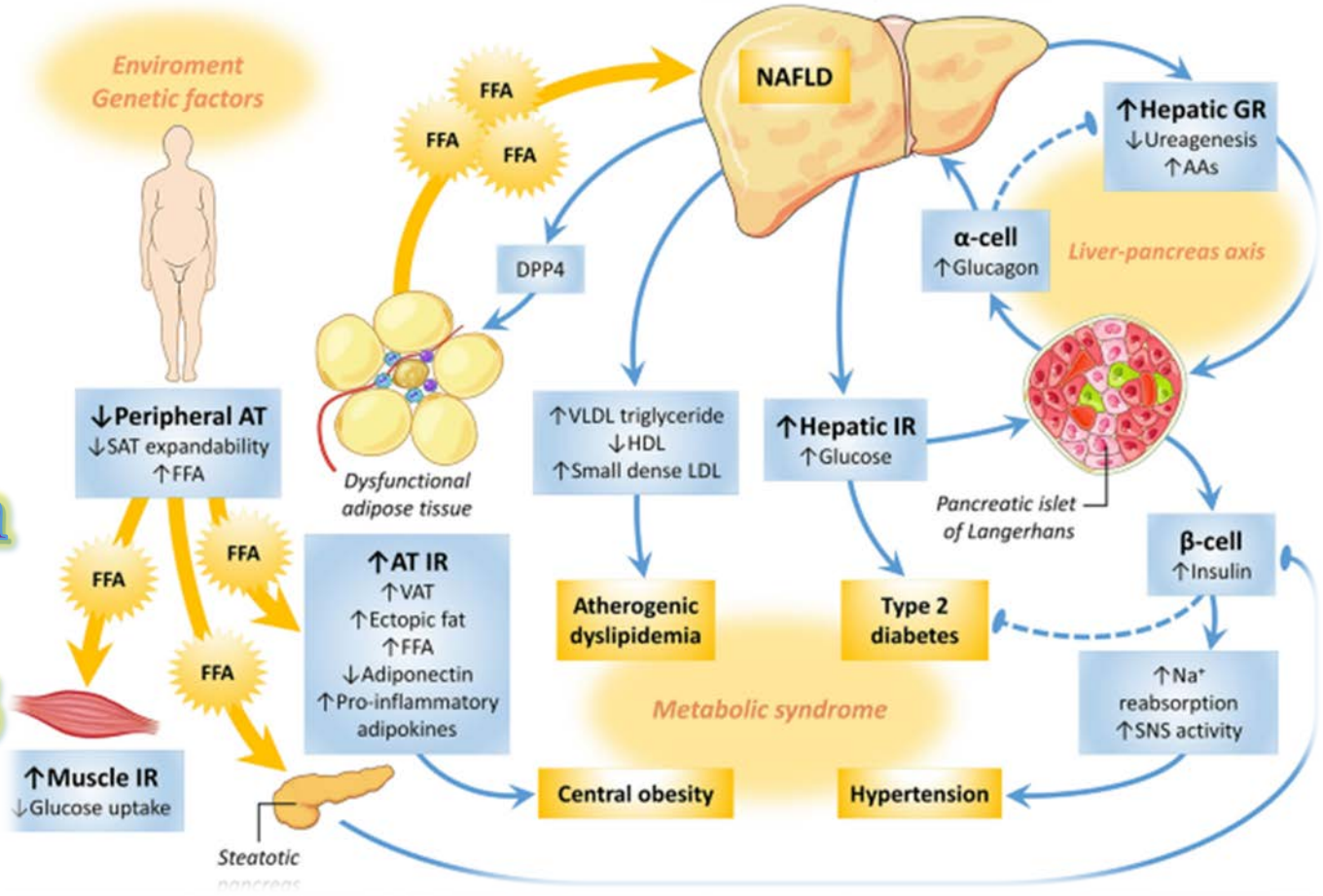
Diabetology & Metabolic Syndrome

REVIEW Open Access

NAFLD as a continuum: from obesity to metabolic syndrome and diabetes

Amélio F. Godoy-Matos[1*], Wellington S. Silva Júnior[2] and Cynthia M. Valerio[1]

NAFLD: hepatic manifestation of obesity and the MetS



Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

NAFLD, MetS, and PCOS

Contraccettivi orali sono controindicati nelle donne con funzionalità epatica alterata

World Journal of Gastroenterology

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DOI: 10.3748/wjg.v20.i26.8351

World J Gastroenterol 2014 July 14; 20(26): 8351-8363
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
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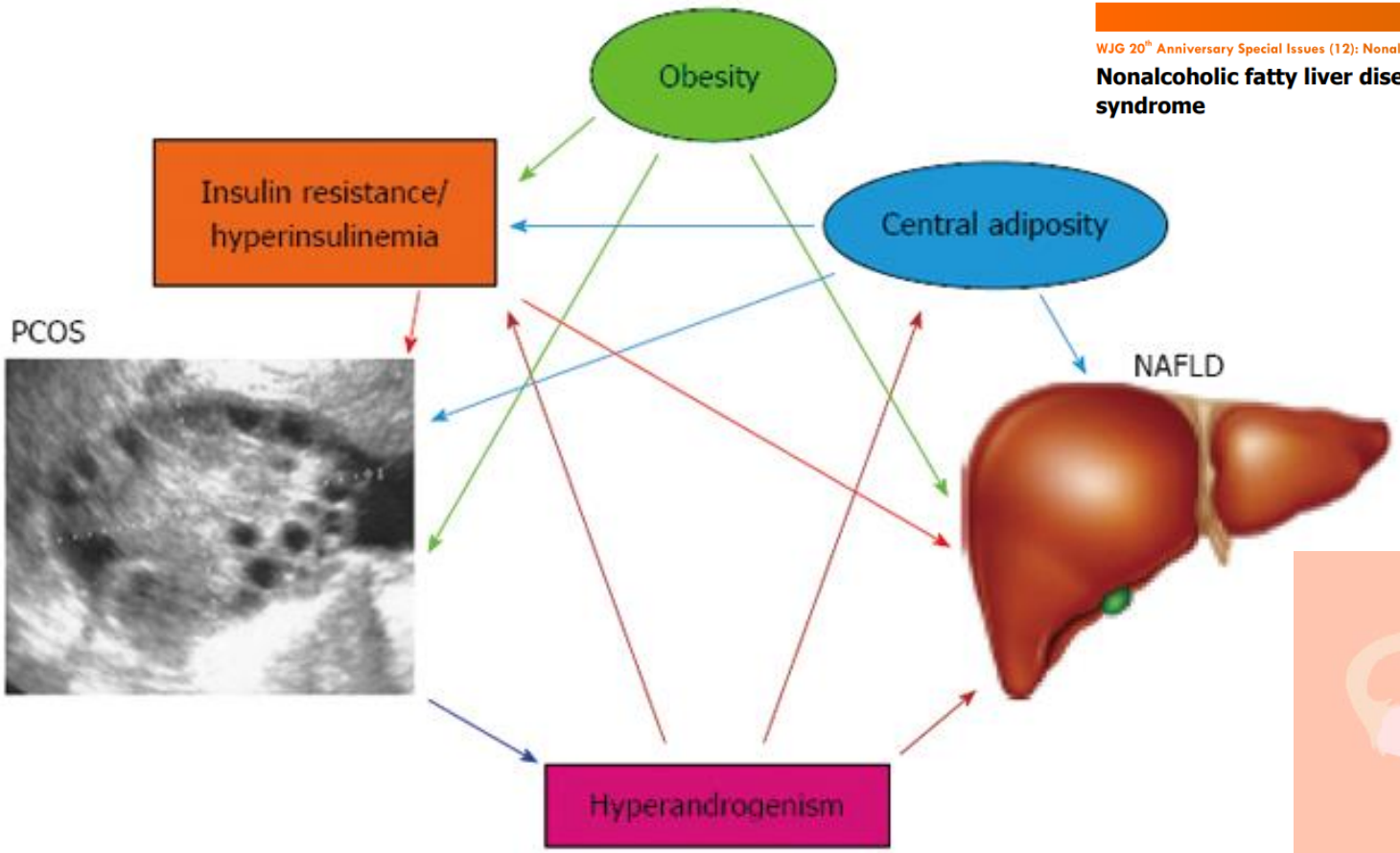
TOPIC HIGHLIGHT

WJG 20th Anniversary Special Issues (12): Nonalcoholic fatty liver disease

Nonalcoholic fatty liver disease and polycystic ovary syndrome



PCOS E KD

.gov

ketogenic diet and Polycystic ovary syndrome

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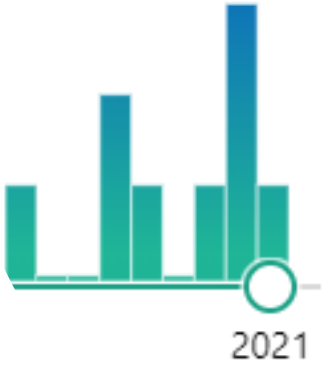


Effects of a ketogenic diet in overweight wome

Paoli A, et al. J Transl Med. 2020. PMID: 32103756 Free PMC

The effects of a low-carbohydrate, ketogenic d
pilot study.

Mavropoulos JC, et al. Nutr Metab (Lond). 2005. PMID: 1635

Ketogenic diet in women with polycystic ovary
obese: A randomized, open-label, parallel-grou

Li J, et al. J Obstet Gynaecol Res. 2021. PMID: 33462940 Clini

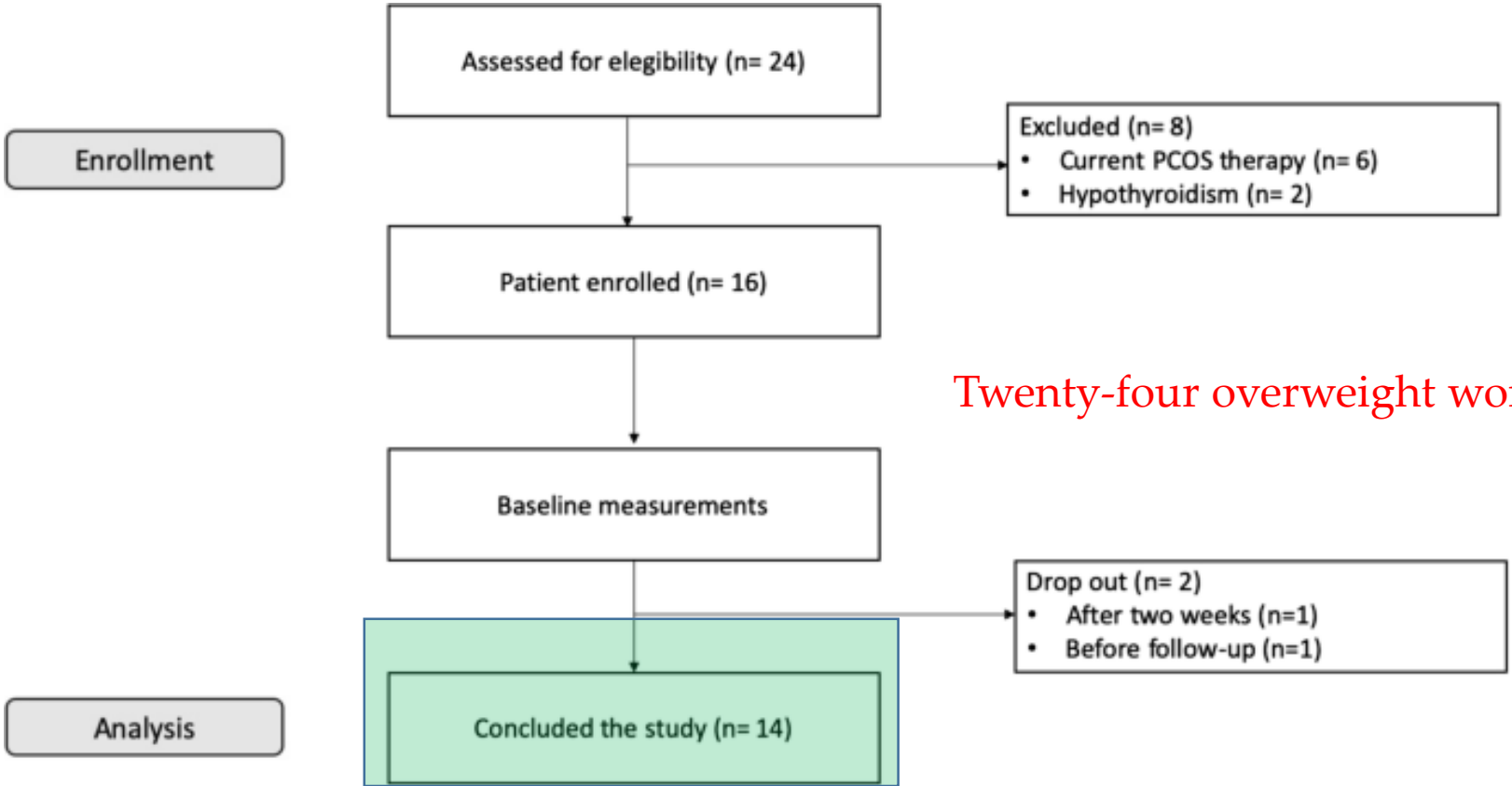
Paoli *et al. J Transl Med* (2020) 18:104
https://doi.org/10.1186/s12967-020-02277-0

Journal of
Translational Medicine

RESEARCH Open Access

Effects of a ketogenic diet in overweight women with polycystic ovary syndrome

Antonio Paoli[1,2*], Laura Mancin[1,3], Maria Cristina Giacona[4], Antonino Bianco[5] and Massimiliano Caprio[6,7]



Twenty-four overweight women

Protocollo dietetico

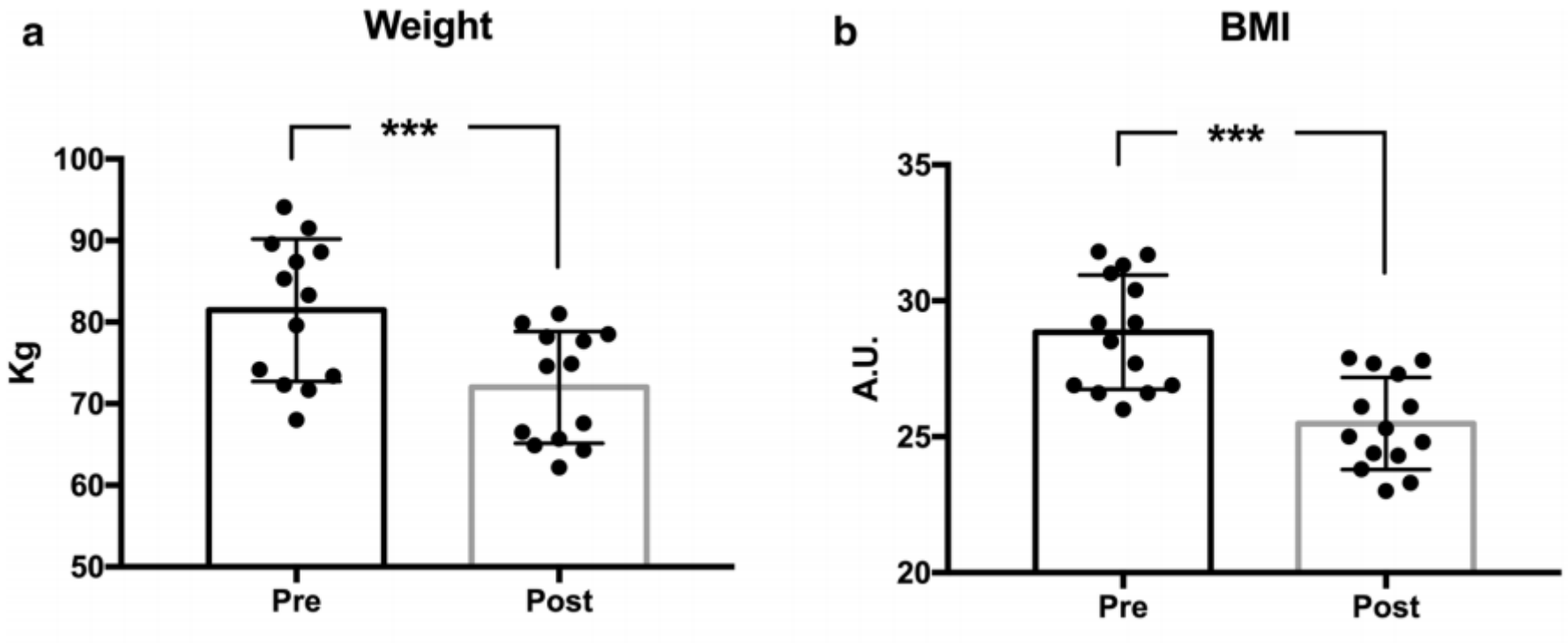
Protocollo chetogenico eucalorico mediterraneo (circa 1600 kcal/giorno) con l'utilizzo di alcuni fitoestratti. I soggetti potevano mangiare *ad libitum* verdure a foglia verde, crocifere, zucchine, cetrioli e melanzane. La quantità di carne, uova e pesce erano limitati (120 g di carne o 20 g di pesce o 2 uova). Inoltre, i soggetti consumati giornalmente quattro integratori alimentari ed estratti vegetali liquidi.

Table 1 KEMEPHY diet composition

	g	% Total E	Kcal
Daily total energy			1672 ± 90
Carbohydrate	20.3 ± 5.2	4.8 ± 1.2	81.5 ± 18.9
Fat	132.4 ± 11.7	71.1 ± 9.3	1188.2 ± 100.2
Protein	100.8 ± 8.6	24.1 ± 5.6	403.4 ± 45.3
Fats distribution		% total fats	
Saturated		38.8 ± 6.9	
Monounsaturated		50.9 ± 6.5	
Polyunsaturated		9.7 ± 5.6	
Protein (g/Kg body weight)	1.23 ± 0.8		

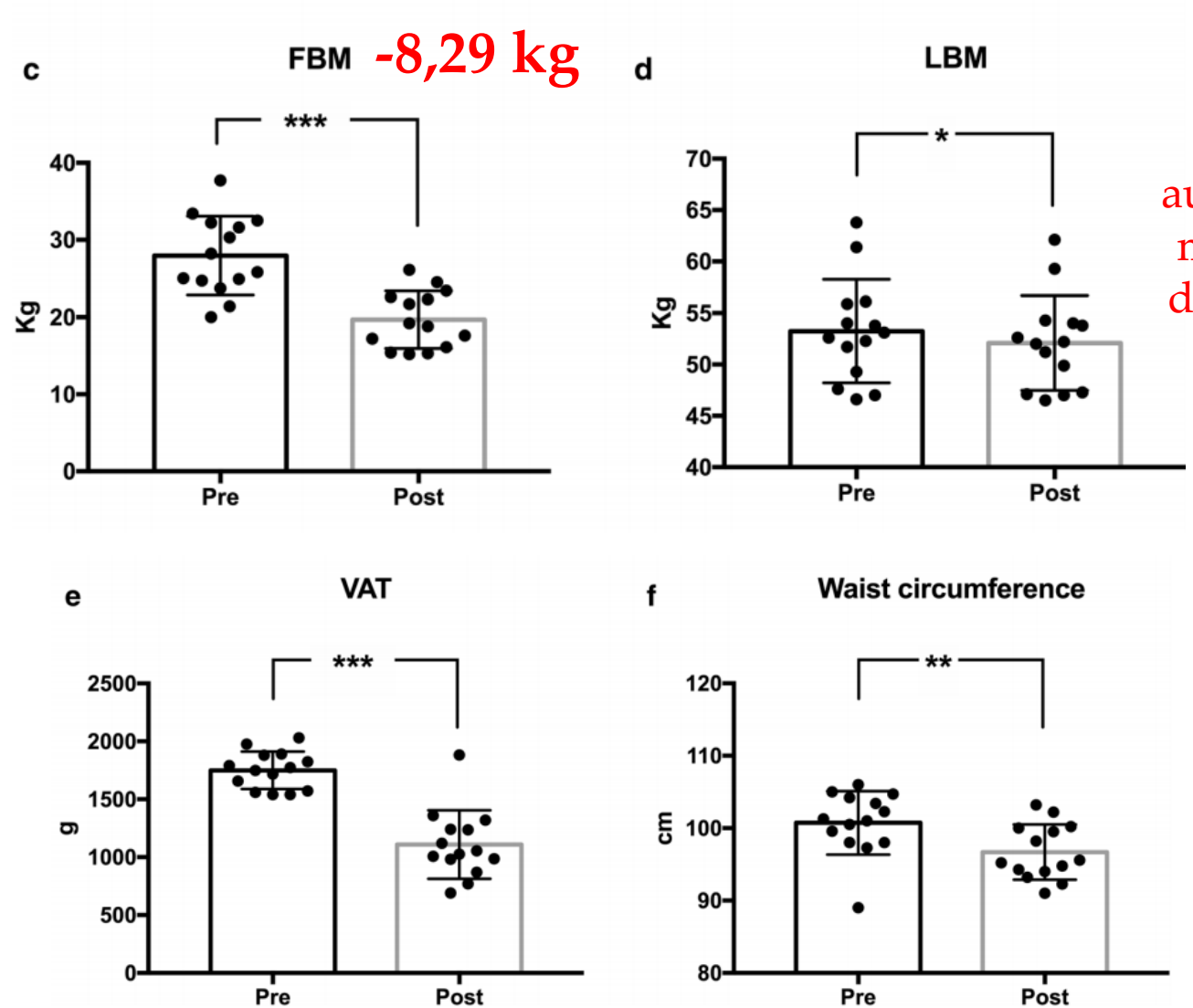
-9,43 kg

-3,35



Changes in anthropometric variables after 12 weeks of KD

*Changes in anthropometric variables after 12 weeks of KD. BMI body mass index, FBM fat body mass, LBM mean body mass. Standard deviation is represented in the figure. ***p<0.0001; **p=0.0015; *p=0.0205*



Il valore assoluto era leggermente ridotto ma il valore percentuale era aumentato (p<0,0001), con un miglioramento complessivo della composizione corporea

*Changes in anthropometric variables after 12 weeks of KD. BMI body mass index, FBM fat body mass, LBM mean body mass. Standard deviation is represented in the figure. ***p<0.0001; **p=0.0015; *p=0.0205*

Changes in anthropometric variables after 12 weeks of KD

Paoli et al. J Transl Med (2020) 18:104
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Journal of Translational Medicine

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Antonio Paoli[1,2*], Laura Mancin[1,3], Maria Cristina Giacona[4], Antonino Bianco[5] and Massimiliano Caprio[6,7]

Table 3 Metabolic biomarkers before and after 12 weeks of KD

	Pre	Post	P value
Glucose (mmol/L)	5.10 ± 0.25	4.64 ± 0.24	< 0.0001
Insulin (μU/mL)	12.62 ± 0.48	11.31 ± 0.60	< 0.0001
HOMA-IR	2.85 ± 0.15	2.32 ± 0.13	< 0.0001
Triglycerides (mmol/L)	2.31 ± 0.40	1.87 ± 0.27	< 0.0008
Total cholesterol (mmol/L)	5.36 ± 0.36	4.72 ± 0.33	< 0.0001
LDL (mmol/L)	3.11 ± 0.60	2.33 ± 0.17	< 0.0001
HDL (mmol/L)	1.79 ± 0.41	2.02 ± 0.43	= 0.0146

Paoli et al. J Transl Med (2020) 18:104
https://doi.org/10.1186/s12967-020-02277-0

Journal of Translational Medicine

KDA Ketogenic Diet ACADEMY

SINut Società Italiana di Nutraceutica

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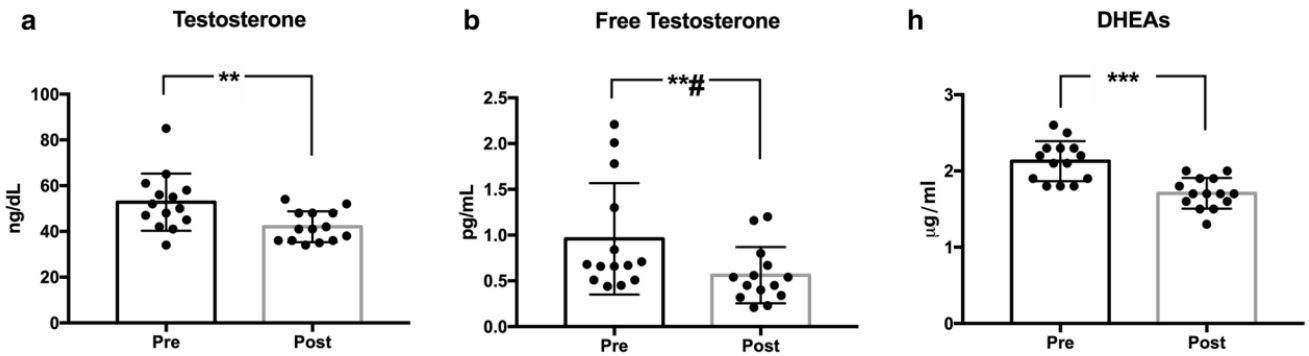
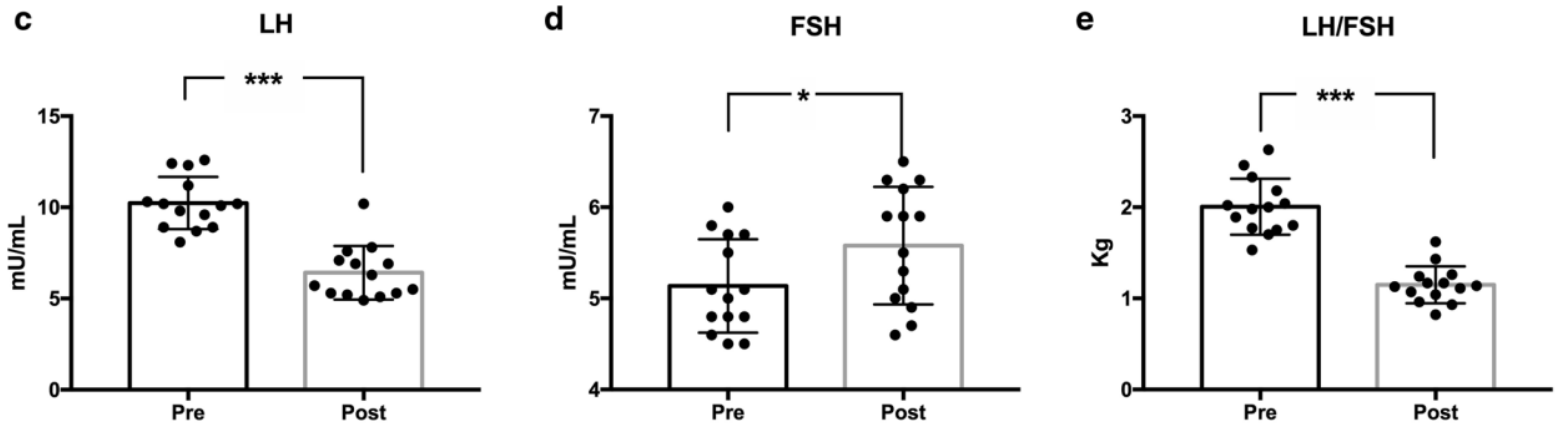
Effects of a ketogenic diet in overweight women with polycystic ovary syndrome

Antonio Paoli[1,2*], Laura Mancin[1,3], Maria Cristina Giacona[4], Antonino Bianco[5] and Massimiliano Caprio[6,7]



L'inversione caratteristica del rapporto LH/FSH era presente all'inizio dello studio e scomparso dopo 12 settimane (pre 2,00±0,30 *vs* post 1,15±0,20; $p<0,0001$).



Paoli *et al. J Transl Med* (2020) 18:104
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Journal of
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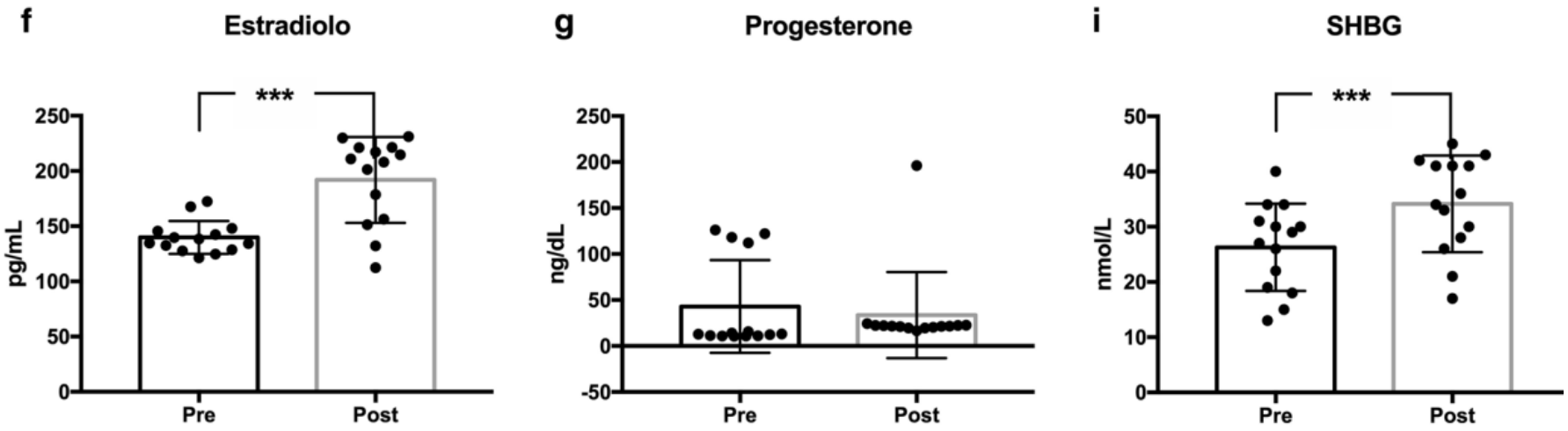


Conclusions: Our results suggest that a KD may be considered as a valuable non pharmacological treatment for PCOS. Longer treatment periods should be tested to verify the effect of a KD on the dermatological aspects of PCOS. Trial registration Clinicaltrial.gov, NCT04163120, registrered 10 November 2019, retrospectively registered, https://clinicaltrials.gov.

KDA Ketogenic Diet ACADEMY

Journal of Endocrinological Investigation (2019) 42:1365–1386
https://doi.org/10.1007/s40618-019-01061-2

CONSENSUS STATEMENT

Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: systematic review and consensus statement from the Italian Society of Endocrinology (SIE)

M. Caprio[1,2] · M. Infante[3] · E. Moriconi[1,4] · A. Armani[1] · A. Fabbri[3] · G. Mantovani[5] · S. Mariani[4] · C. Lubrano[4] · E. Poggiogalle[4] · S. Migliaccio[6] · L. M. Donini[4] · S. Basciani[4] · A. Cignarelli[7] · E. Conte[7] · G. Ceccarini[8] · F. Bogazzi[9] · L. Cimino[10] · R. A. Condorelli[10] · S. La Vignera[10] · A. E. Calogero[10] · A. Gambineri[11] · L. Vignozzi[12] · F. Prodam[13] · G. Aimaretti[13] · G. Linsalata[14] · S. Buralli[14] · F. Monzani[14] · A. Aversa[15] · R. Vettor[16] · F. Santini[8] · P. Vitti[9] · L. Gnessi[4] · U. Pagotto[11] · F. Giorgino[7] · A. Colao[17] · A. Lenzi[4] on behalf of the Cardiovascular Endocrinology Club of the Italian

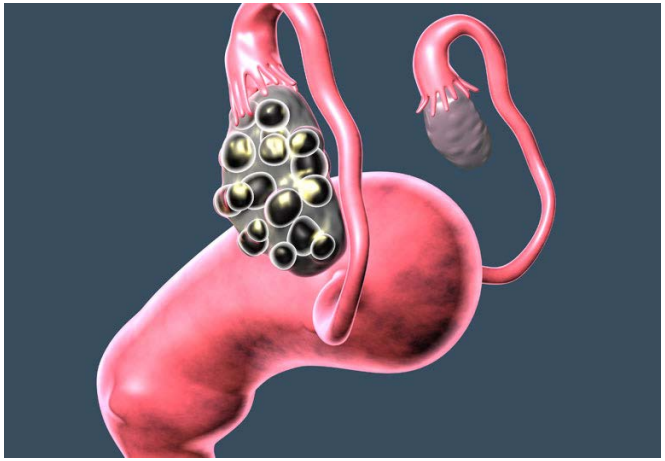
SINut Società Italiana di Nutraceutica

VLCKD and polycystic ovary syndrome in women

Società Italiana Endocrinologia

Recommendations

- We suggest a weight-loss program with VLCKD for overweight/obese patients with polycystic ovary syndrome (PCOS) not responsive to multicomponent standardized diet to improve insulin resistance (2 ØOOO).
- We suggest a weight-loss program with VLCKD for overweight/obese patients with PCOS not responsive to multicomponent standardized diet to improve ovulatory dysfunctions and hyperandrogenemia (2 ØOOO).



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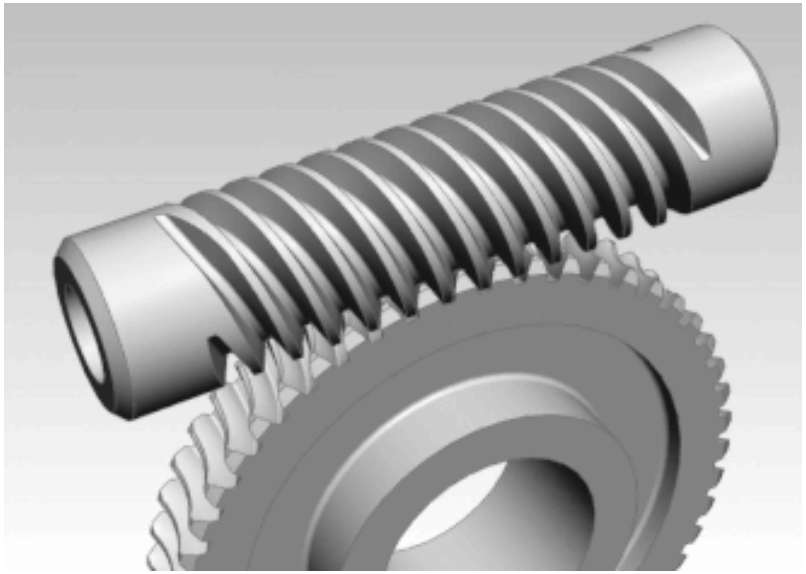
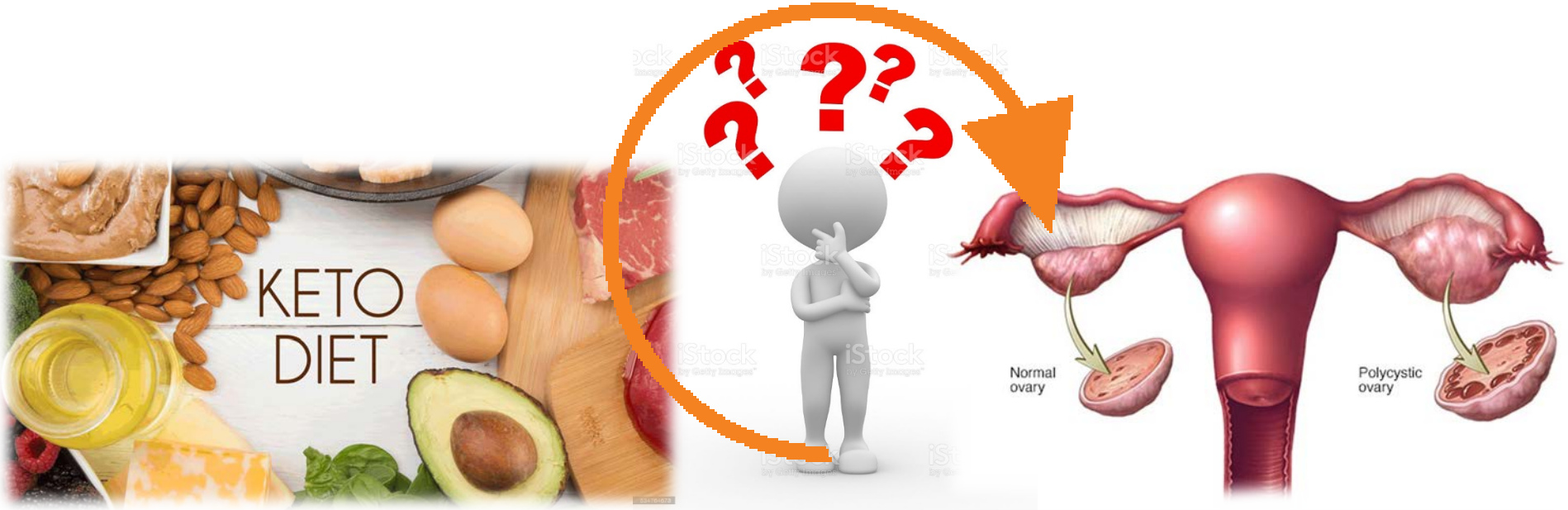




Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

La KD attiva AMPK e SIRT-1, anche in assenza di deprivazione calorica, portando effetti benefici sull'omeostasi del glucosio e migliorano la sensibilità all'insulina

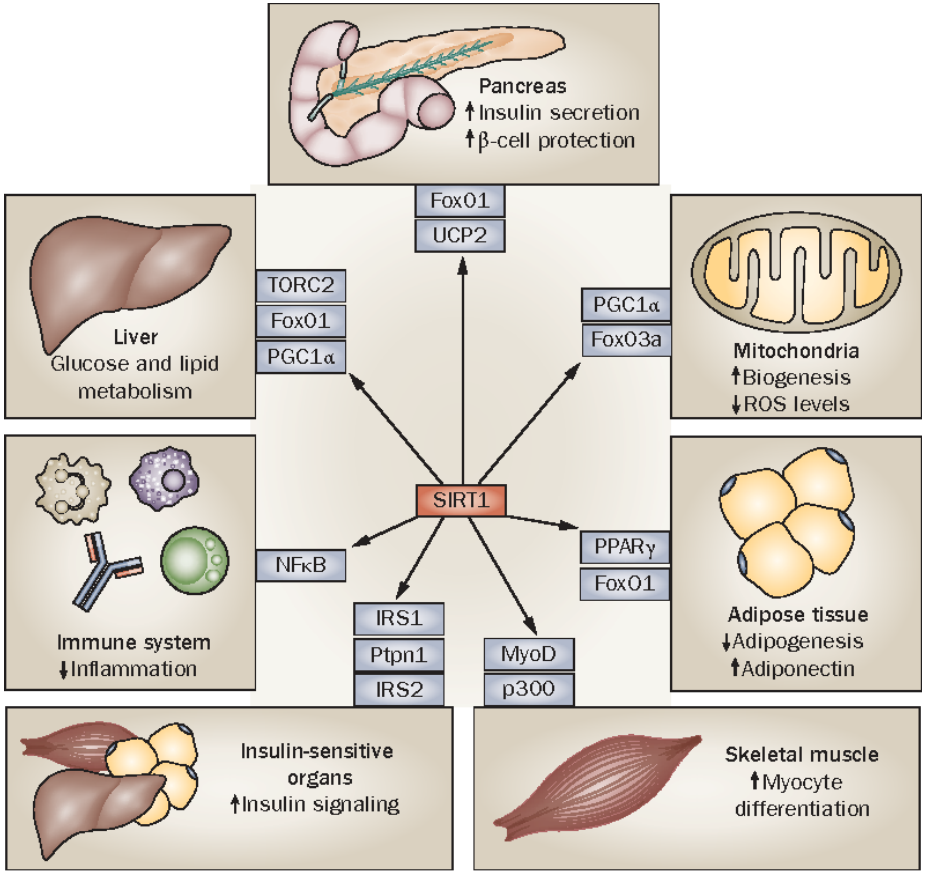
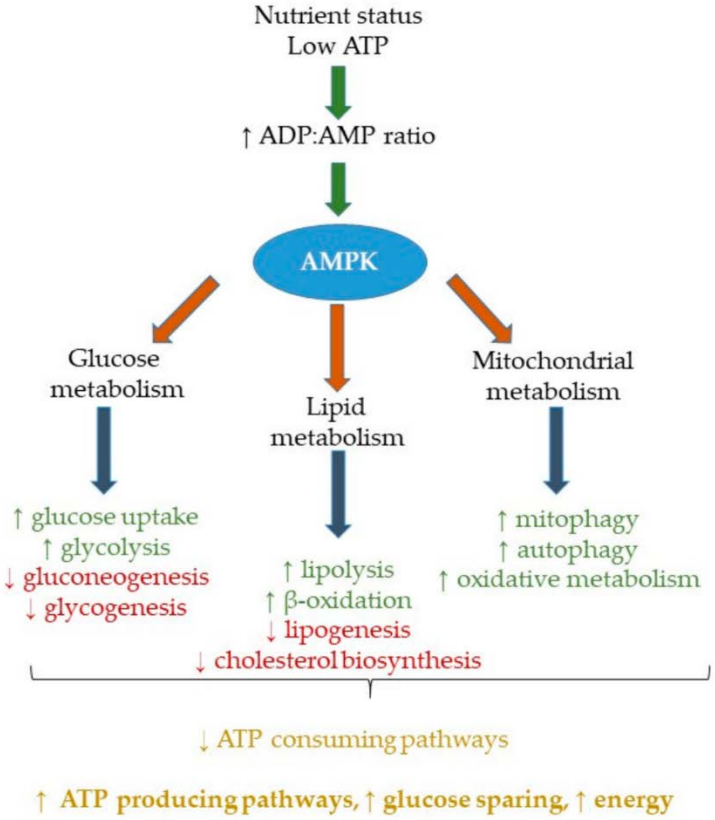
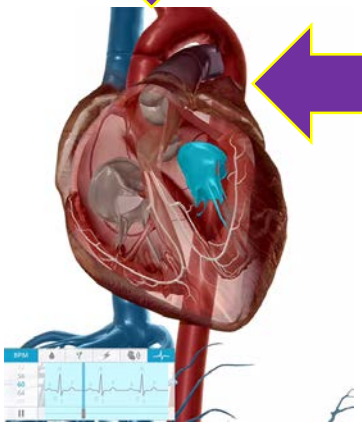
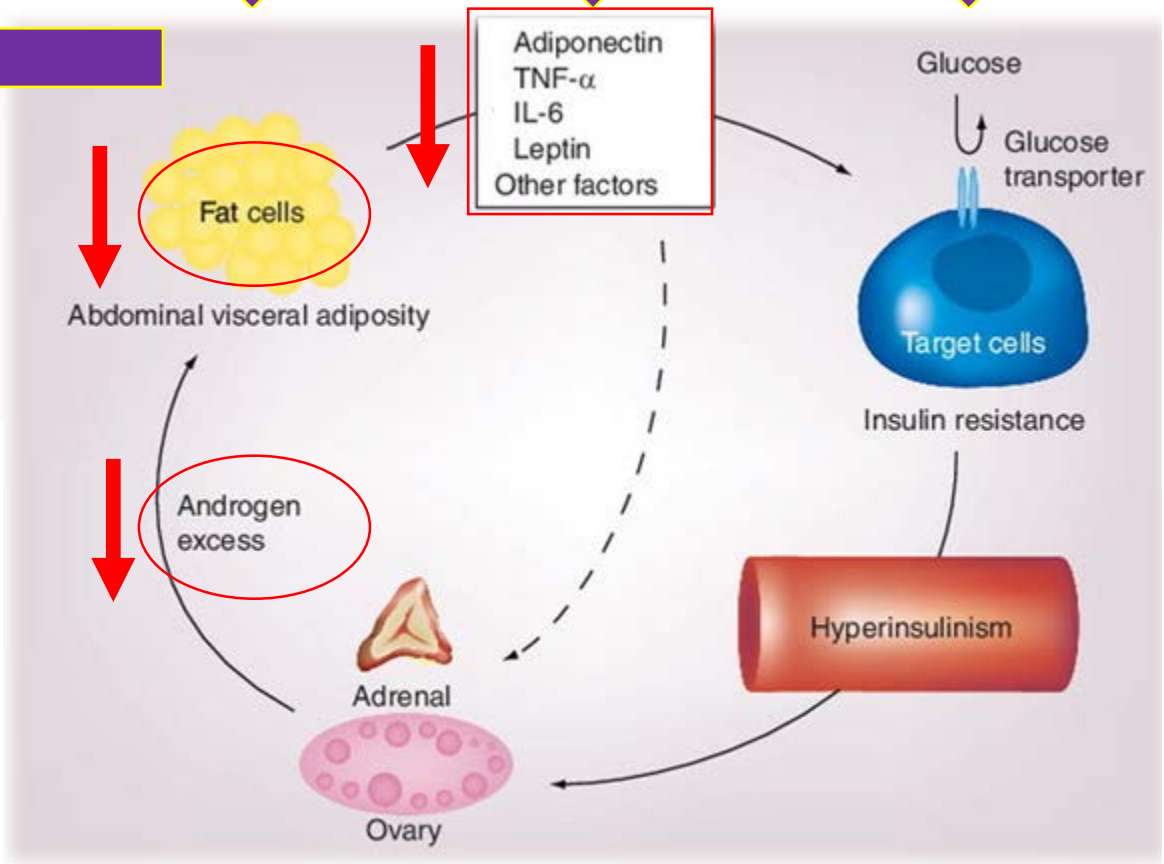


Figure 3 | Proposed roles and targets of SIRT1 in insulin resistance. By its



Ketogenic Diet and PCOS





La riduzione dei lipidi circolanti, l'infiammazione di basso grado e lo stress ossidativo aiuta anche a prevenire le complicanze cardiovascolari

La chetosi fisiologica indotta da un basso apporto di CHO riduce i livelli di insulina e di conseguenza anche quelli di IGF-1, sopprimendo così lo stimolo sulla produzione di androgeni, sia ovariche che surrenali.

Take home messages Ketogenic Diet in PCOS

1. Le pazienti con PCOS hanno un aumentato rischio cardiovascolare e la terapia con contraccettivi orali potrebbe avere effetti negativi;
2. L'uso dei contraccettivi orali non "guariscono" dalla PCOS e dopo la sospensione in queste donne si ripresentano spesso anovulazione e dismenorrea;
3. In questo la dieta chetogenica potrebbe rappresentare una valida alternativa non farmacologica nella gestione della PCOS, come da indicazioni delle stesse linee guida nazionali ed internazionali.

LA DIETA CHETOGENICA È UN POSSIBILE AUSILIO TERAPEUTICO NELLA PCOS

KDA Ketogenic Diet ACADEMY

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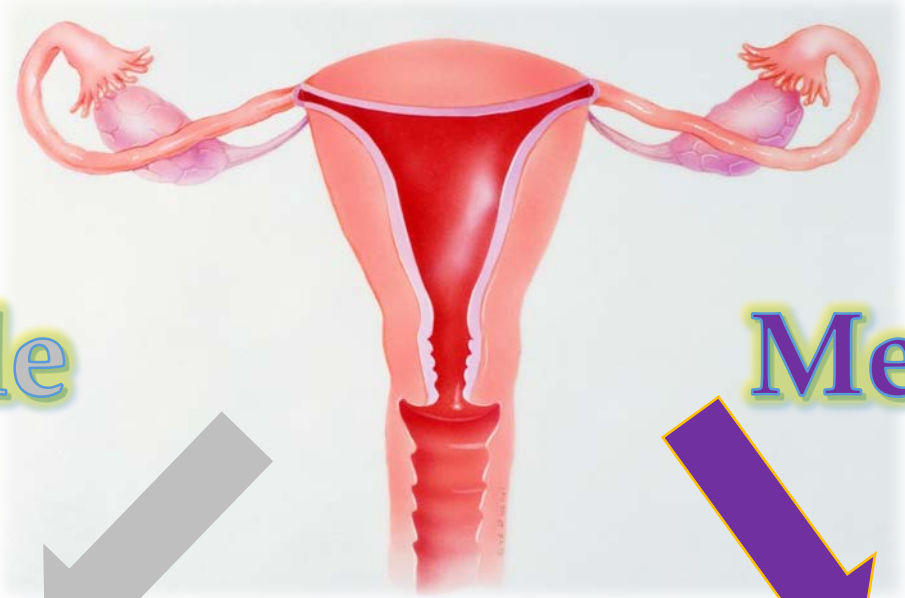
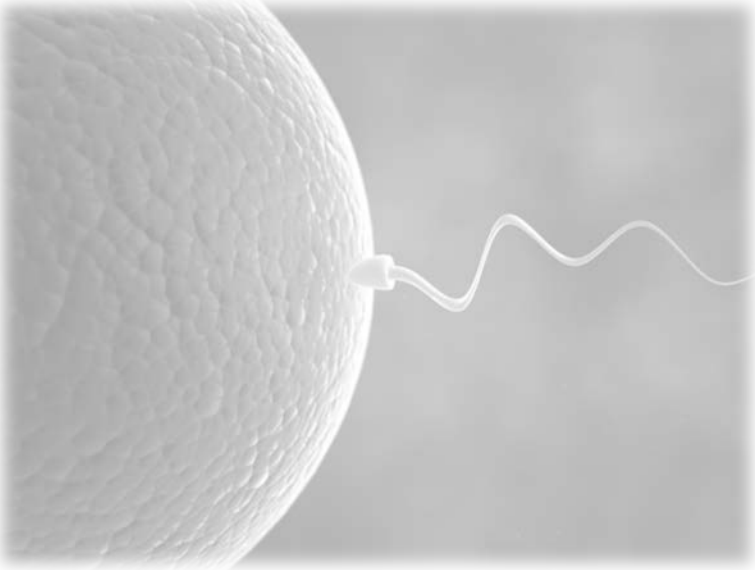


Età fertile

Menopausa



MENOPAUSE

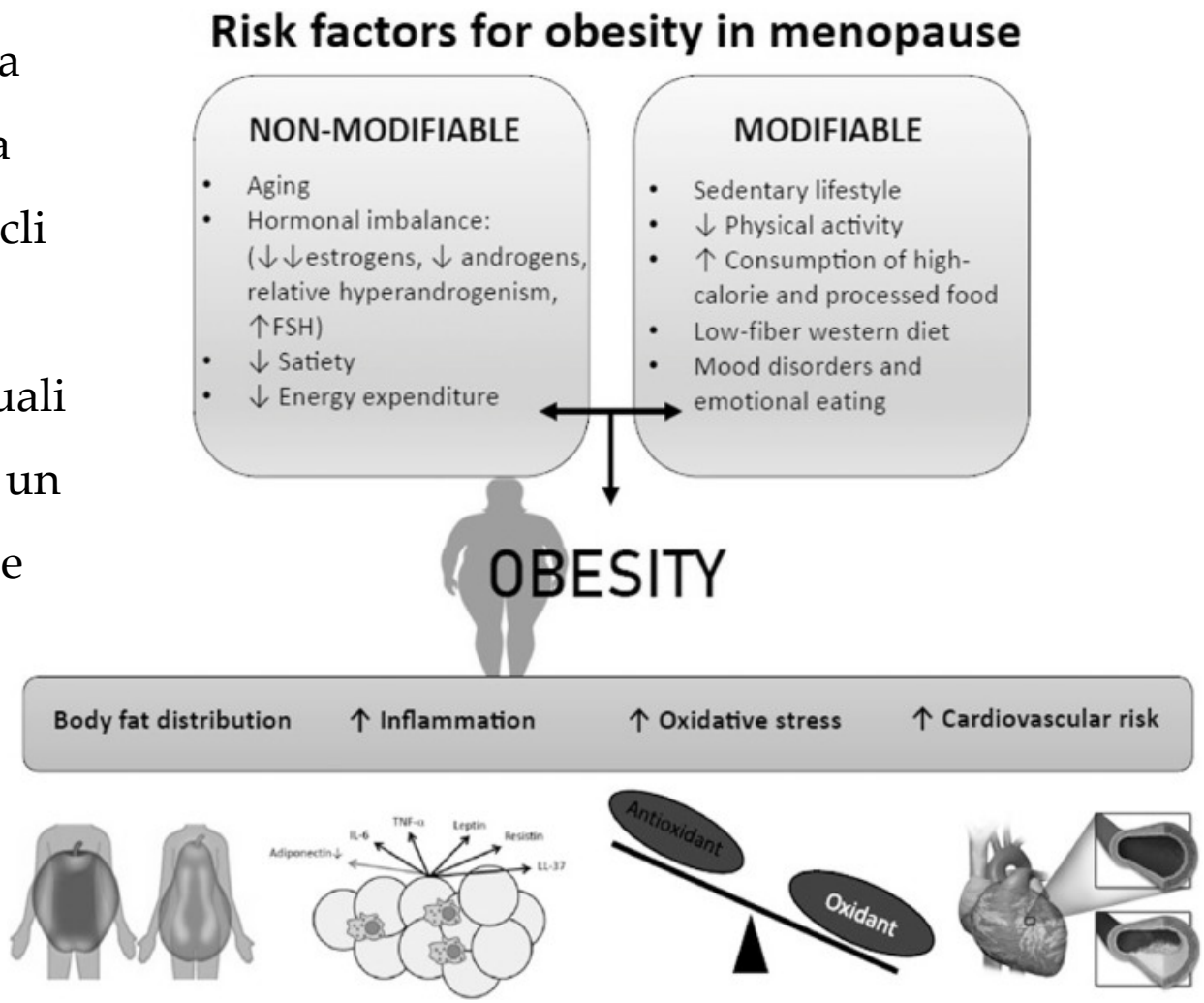
Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

Mediterranean diet as tool to manage obesity in menopause: A narrative review

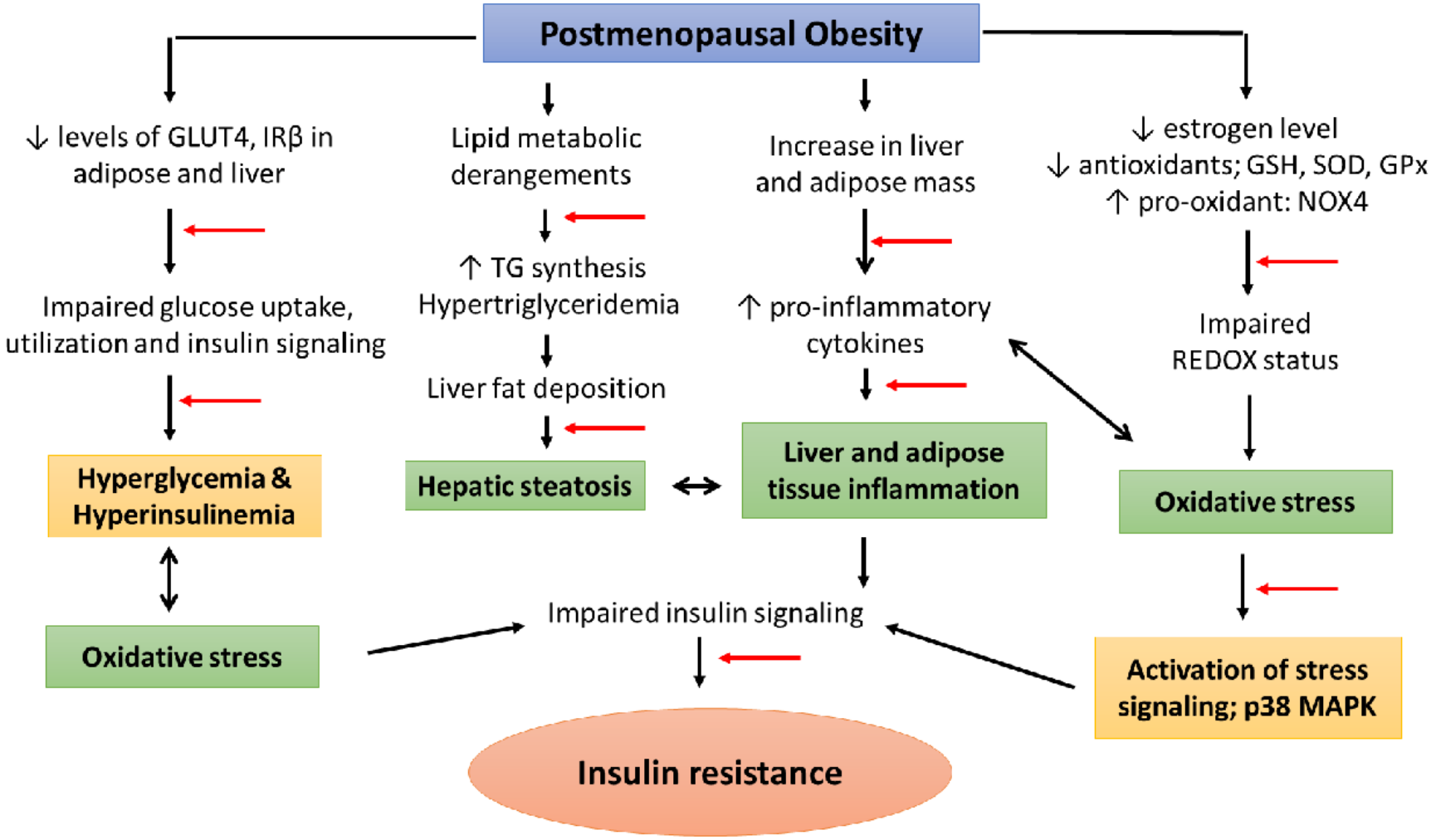
Barrea L and Pugliese G, et al. 2020

La menopausa è un evento fisiologico nella vita di una donna caratterizzato dalla cessazione spontanea dei cicli mestruali causata da una riduzione degli ormoni sessuali (estrogeni e progesterone) e un conseguente aumento delle gonadotropine.



L'aumento di peso è un fenomeno comune in menopausa

Menopause


Postmenopausal Obesity
↓ levels of GLUT4, IRβ in adipose and liver
Impaired glucose uptake, utilization and insulin signaling
Hyperglycemia & Hyperinsulinemia
Oxidative stress
Lipid metabolic derangements
↑ TG synthesis
Hypertriglyceridemia
Liver fat deposition
Hepatic steatosis
Increase in liver and adipose mass
↑ pro-inflammatory cytokines
Liver and adipose tissue inflammation
↓ estrogen level
↓ antioxidants; GSH, SOD, GPx
↑ pro-oxidant: NOX4
Impaired REDOX status
Oxidative stress
Activation of stress signaling; p38 MAPK
Impaired insulin signaling
Insulin resistance

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
2021, VOL. 61, NO. 7, 1201–1211
https://doi.org/10.1080/10408398.2020.1755220

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Citation metrics

- 11.176 (2020) Impact Factor

REVIEW

Check for updates

Mediterranean diet as medical prescription in menopausal women with obesity: a practical guide for nutritionists

Luigi Barrea[a,b]*, Gabriella Pugliese[a,b]*, Daniela Laudisio[a,b], Annamaria Colao[a,b,c], Silvia Savastano[a,b], and Giovanna Muscogiuri[a,b]

ABSTRACT

Menopausal transition is associated with weight gain and increased visceral fat distribution, which acts as an endocrine organ secreting the pro-inflammatory adipocytokines, which leads to metabolic disorders typical of menopause, including type 2 diabetes and cardiovascular diseases. Given the increasing number of aging population, the nutritional strategies to prevent obesity and obesity-related diseases in menopausal women is becoming a growing need and it should be one of the main objective for Nutritionists. The Mediterranean diet is characterized from foods with anti-inflammatory and antioxidant actions, such as extra-virgin olive oil, vegetables, fruits, legumes, nuts, red wine, and whole-grain cereals. Several evidences showed that the Mediterranean diet acts on both weight control and menopause, in addition to the known effects of the Mediterranean diet on cardiovascular and metabolic diseases. The Mediterranean diet is comparable with pharmacological interventions in terms of reducing the risk of obesity and cardiovascular and metabolic events. Considering that there are no specific dietary guidelines to manage weight in menopause, the aim of this review is to provide a nutritional guideline for the management of weight in menopause, particularly focusing on the Mediterranean diet.

KD

Menopause

Neuroscience and Biobehavioral Reviews 94 (2018) 11–16

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Menopause and Mood

Ketogenic diet as a metabolic therapy for mood disorders: Evidence and developments

Elisa Brietzke[a,b,*], Rodrigo B. Mansur[a], Mehala Subramaniapillai[a], Vicent Balanzá-Martínez[c], Maj Vinberg[d], Ana González-Pinto[e], Joshua D. Rosenblat[a], Roger Ho[f,g], Roger S. McIntyre[a,h]

Neuroscience and Biobehavioral R

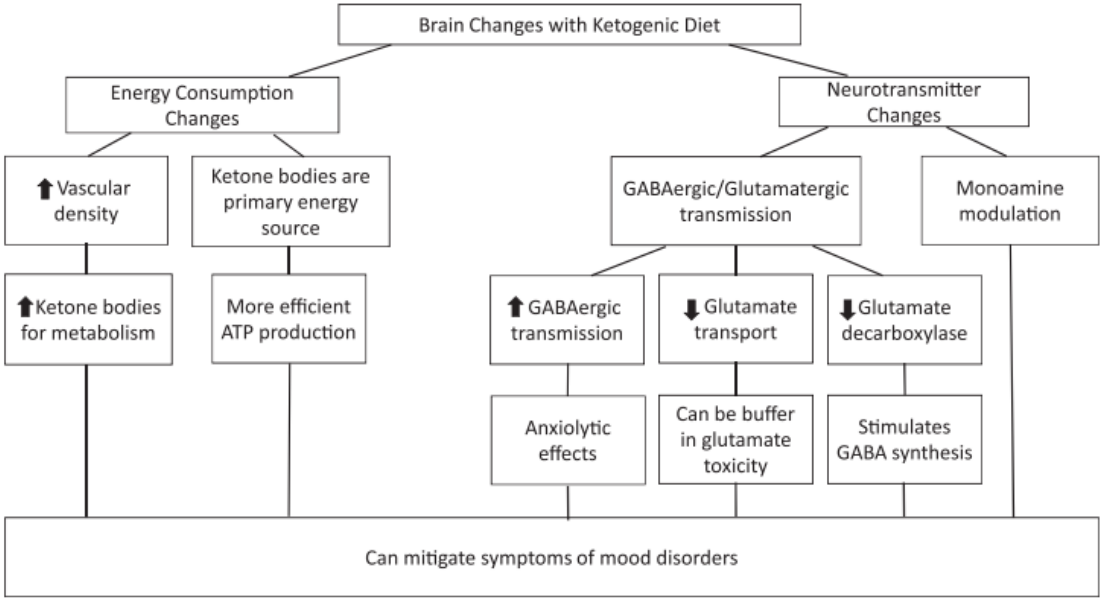


Fig. 1. Putative actions of ketogenic diet in mood disorders.

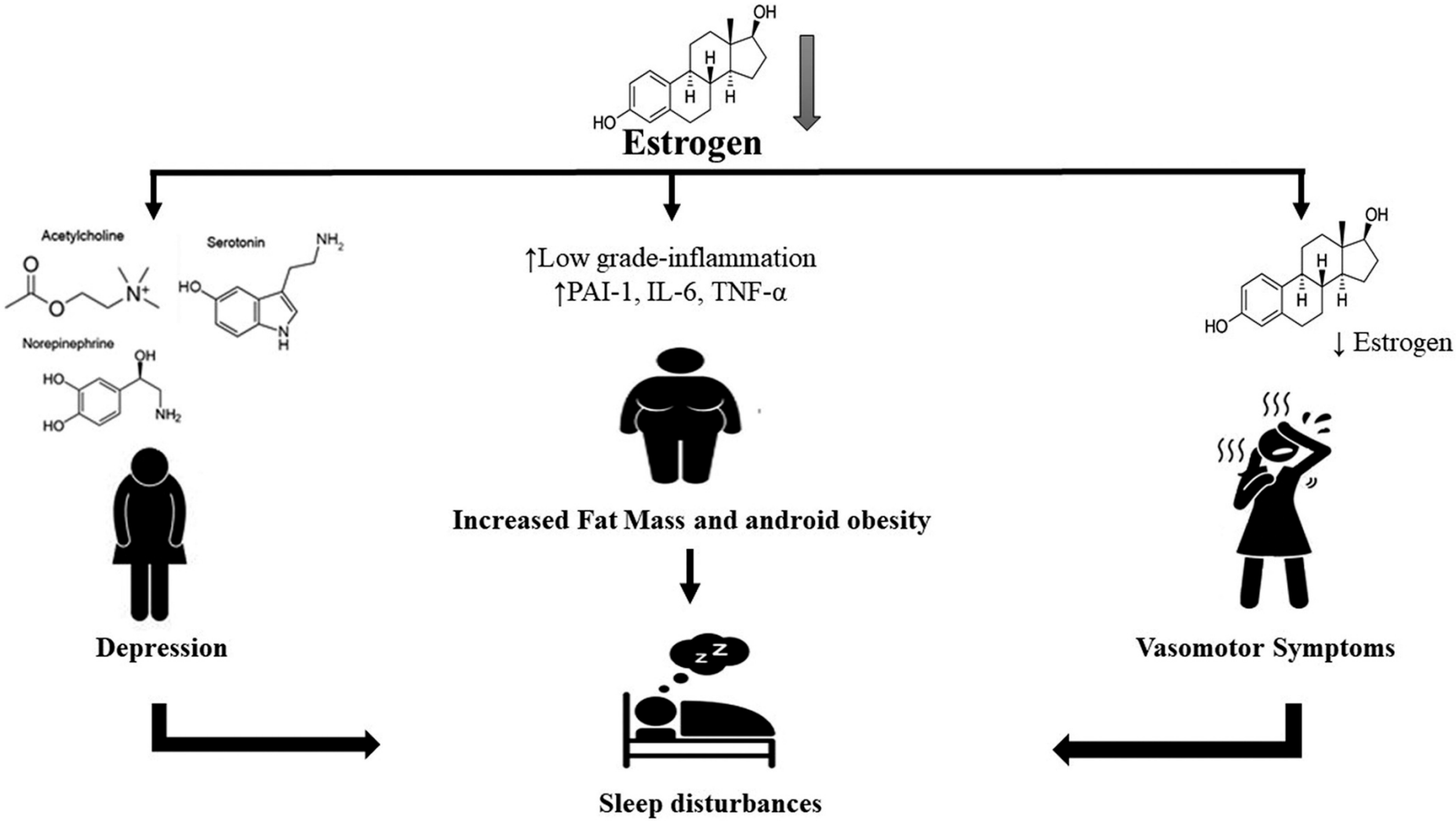
La menopausa è associata a cambiamenti nell'umore dovuto al calo estrogenico. Anche i disturbi del sonno associati alla menopausa e iperidrosi notturna, portano a sbalzi d'umore

Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

A practical nutritional guide for the management of sleep disturbances in menopause

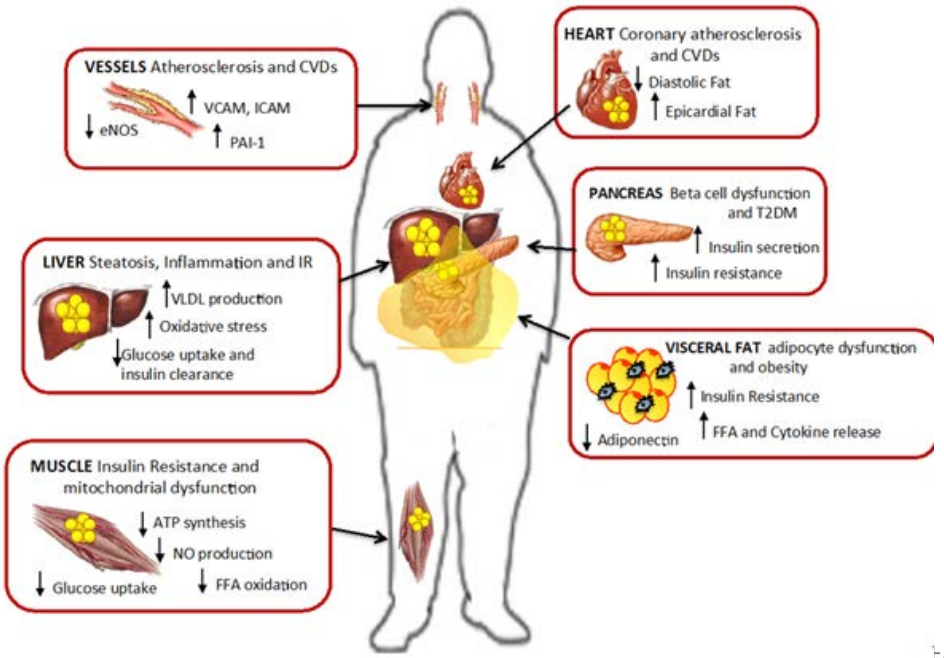
Daniela Laudisio [a,b], Luigi Barrea [a,b], Gabriella Pugliese [a,b], Sara Aprano [a,b], Bianca Castellucci [a,b], Silvia Savastano [a,b], Annamaria Colao [a,b,c], and Giovanna Muscogiuri [a]



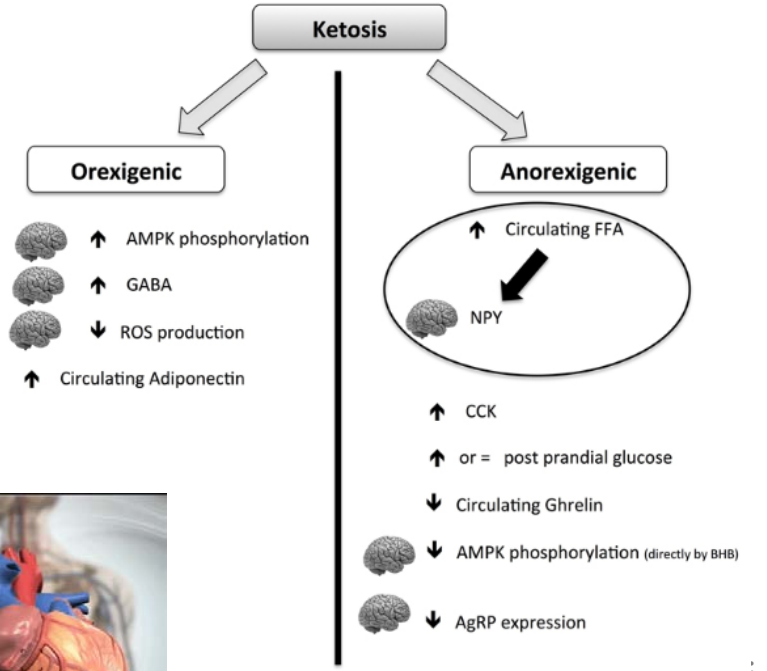
VLCKD in Menopause: Obesity and hunger satiety circuit

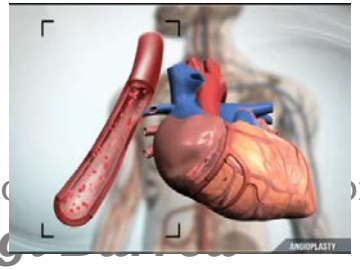
La VLCKD rappresenta una strategia dietetica ideale per un calo ponderale sicuro, rapido ed efficace nel paziente con obesità. In particolare, questa terapia deve essere considerata come strumento utilissimo nei pazienti con elevato grado di insulino-resistenza, per cui il calo ponderale risulta difficile. ***Raynor HA, Champagne CM. J Acad Nutr Diet 2016***

Grasso Ectopico



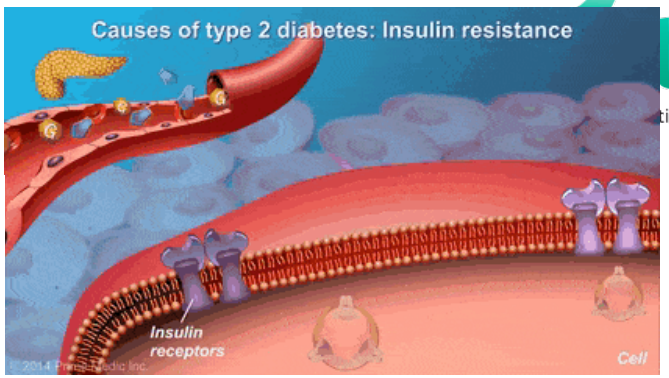
Circuito fame/sazietà





VLCKD and Type 2 Diabetes

Reviews in Endocrine and Metabolic Disorders (2020) 21:381–397
https://doi.org/10.1007/s11154-020-09580-7



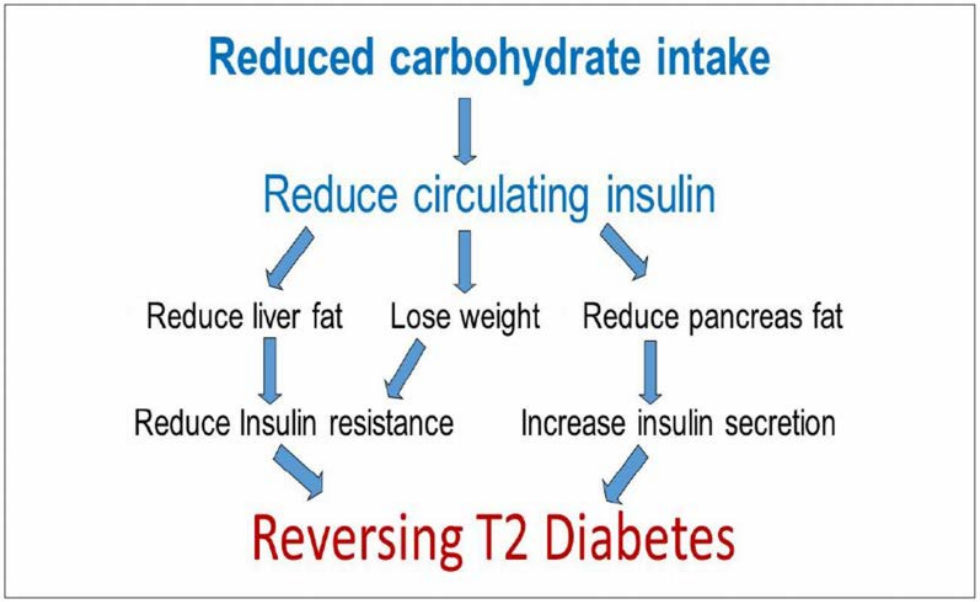
Ketogenic diets as treatment of obesity and type 2 diabetes mellitus

Check for updates

Felipe F. Casanueva[1,2] · Marco Castellana[3] · Diego Bellido[4] · Pierpaolo Trimboli[5] · Ana I. Castro[1,2] · Ignacio Sajoux[6] · Gemma Rodriguez-Carnero[1] · Diego Gomez-Arbelaez[7] · Ana B. Crujeiras[1,2,8] · Miguel A. Martinez-Olmos[1,2]

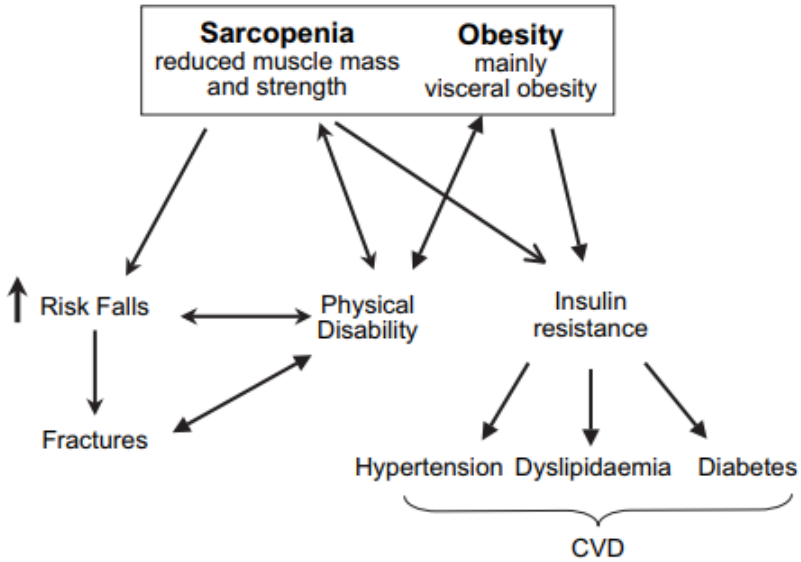
(Table 3) [84]. This means that one should distinguish pathological ketosis, as the one observed in patients with diabetes ketoacidosis, from physiological ketosis, that is no detrimental since was able to maintain humans and animals alive along evolution.

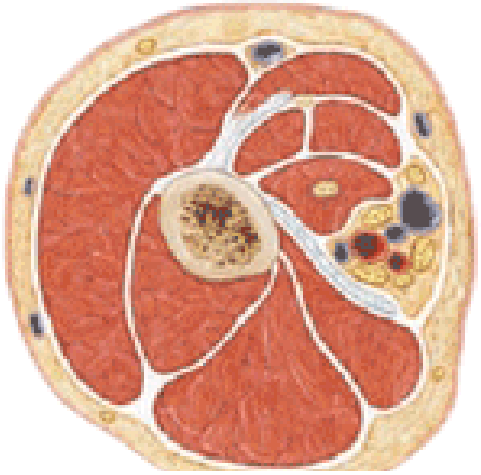
Concerning type 2 diabetes, in the same meta-analysis VLCKDs were associated with a reduction in HbA1c of −0.7%. Two issues should be discussed in regard to this



Diabetes & Menopause

Sarcopenic Obesity





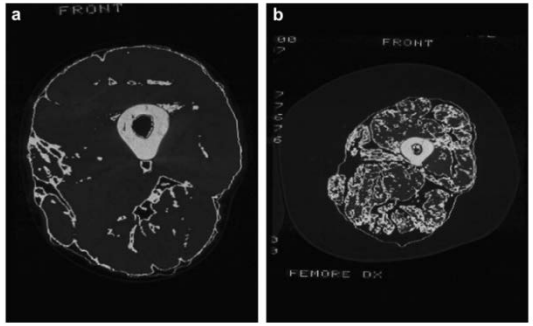
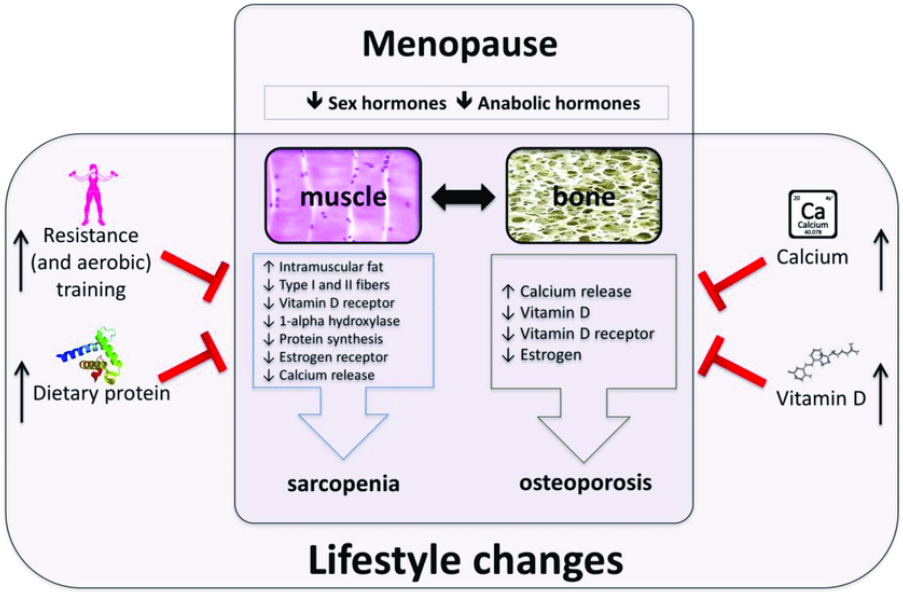


Figure 1 Muscle lipidic infiltration measured by mid-thigh CT scan in a subject of normal weight (a) and in a sarcopenic obese subject (b).



Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

VLCKD and Sarcopenic Obesity: Clinical Trials

European Review for Medical and Pharmacological Sciences 2017; 21: 2274-2289

Efficacy and safety of very-low-calorie ketogenic diet: a double blind randomized crossover study

C. COLICA[1], G. MERRA[2], A. GASBARRINI[3], A. DE LORENZO[4], G. CIOCCOLONI[5], P. GUALTIERI[5], M.A. PERRONE[6,7], S. BERNARDINI[6], V. BERNARDO[8], L. DI RENZO[4], M. MARCHETTI[9,10]

21-days VLCKDs not impair nutritional state; **NOT CAUSE NEGATIVE CHANGES IN GLOBAL MEASUREMENTS OF NUTRITIONAL STATE INCLUDING SARCOPENIA**, bone mineral content, hepatic, renal and lipid profile.

This is the first study that analyzes comprehensively body composition, metabolic profile, and inflammation and oxidative stress genes expression after VLCKD. Our results show the **EFFICACY OF VLCKD WITH SYNTHETIC AMINOACIDIC PROTEIN REPLACEMENT, FOR THE REDUCTION OF CARDIOVASCULAR RISK, WITHOUT THE DEVELOPMENT OF SARCOPENIA AND ACTIVATION OF INFLAMMATORY AND OXIDATIVE PROCESSES**.

Our pilot study showed that a **VLCKD WAS HIGHLY EFFECTIVE IN TERMS OF BODY WEIGHT REDUCTION WITHOUT TO INDUCE LEAN BODY MASS LOSS, PREVENTING THE RISK OF SARCOPENIA**. Further clinical trials are needed on a larger population and long-term body weight maintenance and risk factors management effects of VLCKD.

European Review for Medical and Pharmacological Sciences 2017; 21: 329-345

Effects of very-low-calorie diet on body composition, metabolic state, and genes expression: a randomized double-blind placebo-controlled trial

G. MERRA[1], S. GRATTERI[2], A. DE LORENZO[3], S. BARRUCCO[4], M.A. PERRONE[5,6], E. AVOLIO[7], S. BERNARDINI[5], M. MARCHETTI[8], L. DI RENZO[4]

European Review for Medical and Pharmacological Sciences 2016; 20: 2613-2621

Very-low-calorie ketogenic diet with aminoacid supplement versus very low restricted-calorie diet for preserving muscle mass during weight loss: a pilot double-blind study

G. MERRA[1], R. MIRANDA[2,3], S. BARRUCCO[2], P. GUALTIERI[2], M. MAZZA[2], E. MORICONI[2,4], M. MARCHETTI[5], T.F.M. CHANG[6], A. DE LORENZO[2,4], L. DI RENZO

KDA Ketogenic Diet ACADEMY

Citation Impact
5.531 - 2-year Impact Factor
5.760 - 5-year Impact Factor

SINut Società Italiana di Nutraceutica

KETOGENIC DIET: CLINICAL MONITORING

REVIEW Open Access

The management of very low-calorie ketogenic diet in obesity outpatient clinic: a practical guide

Giovanna Muscogiuri[†], Luigi Barrea[*†], Daniela Laudisio, Gabriella Pugliese, Ciro Salzano, Silvia Savastano and Annamaria Colao

Table 2 Anthropometric measurements and laboratory assessment to be monitored during the VLCKD

	Parameters	Baseline	During active stages	At the end of VLCKD
Anthropometric assessment	Weight, height, BMI	✓	✓	✓
	Body composition and hydration status (by bioelectrical impedance analysis)	✓	✓	✓
Laboratory assessment	Complete blood count with platelets	✓	✓	✓
	Sodium, potassium, magnesium, and inorganic phosphate	✓	✓	✓
	Serum liver and kidney tests (including albumin, AST, ALT, blood urea nitrogen, creatinine, γ-GT, total and direct bilirubin)	✓	✓	✓
	Fasting lipid profile	✓		✓
	25(OH)D, calcium	✓		✓
	Glucose, Insulin	✓		✓
	β-Hydroxybutyrate (capillary blood or urine)		✓	
	TSH, FT4	✓		
	Complete urinalysis and microalbuminuria (urine)	✓	✓	✓

Take Home message

La dieta chetogenica può fornire una possibilità terapeutica nella donna con PCOS e in menopausa:

- ✓ Migliora il controllo glicometabolico, l'IR e il DM2;
- ✓ Riduce il rischio cardiovascolare,
- ✓ Svolge un'azione anti-infiammatoria e antiossidante,
- ✓ Preserva la massa magra rivelandosi l'approccio nutrizionale ideale nell'obesità sarcopenica,
- ✓ Consente una personalizzazione del trattamento (combinazione con altre strategie nutrizionali/farmacologiche)

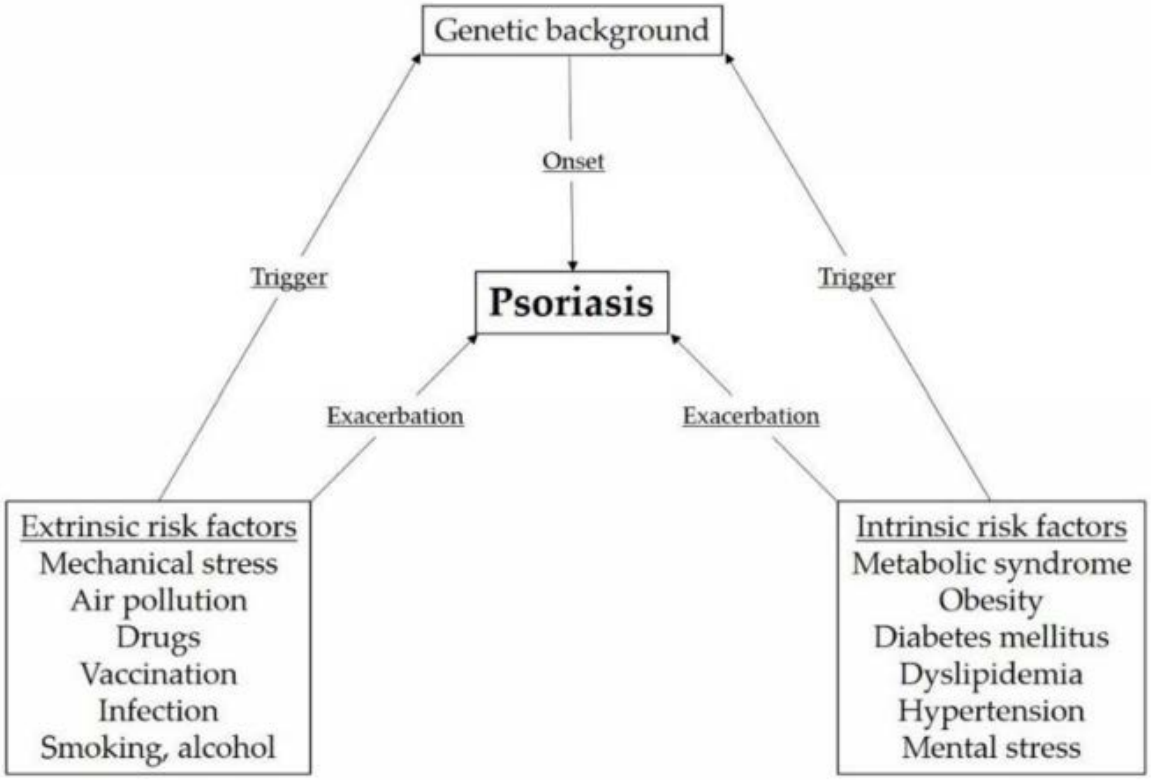
Va sottolineato al paziente il concetto di terapia metabolica, in cui l'autogestione è associata a carenze nutrizionali. Necessario uno stretto monitoraggio clinico e bioumorale, vanno anche ben chiarite le fonti "nascoste" di carboidrati.

Nuove indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

RISK FACTORS FOR THE ONSET AND EXACERBATION OF PSORIASIS



International Journal of *Environmental Research and Public Health*

MDPI

Review

Environmental Risk Factors in Psoriasis: The Point of View of the Nutritionist

Luigi Barrea [1,*], Francesca Nappi [1], Carolina Di Somma [2], Maria Cristina Savanelli [1], Andrea Falco [1], Anna Balato [3], Nicola Balato [3] and Silvia Savastano [4]

La psoriasi è definita come una malattia infiammatoria della pelle, non trasmissibile, ad andamento cronico-recidivante che nella sua forma più comune si manifesta con placche eritemato-squamose che possono interessare qualsiasi area del corpo

OBESITY AND PSORIASIS

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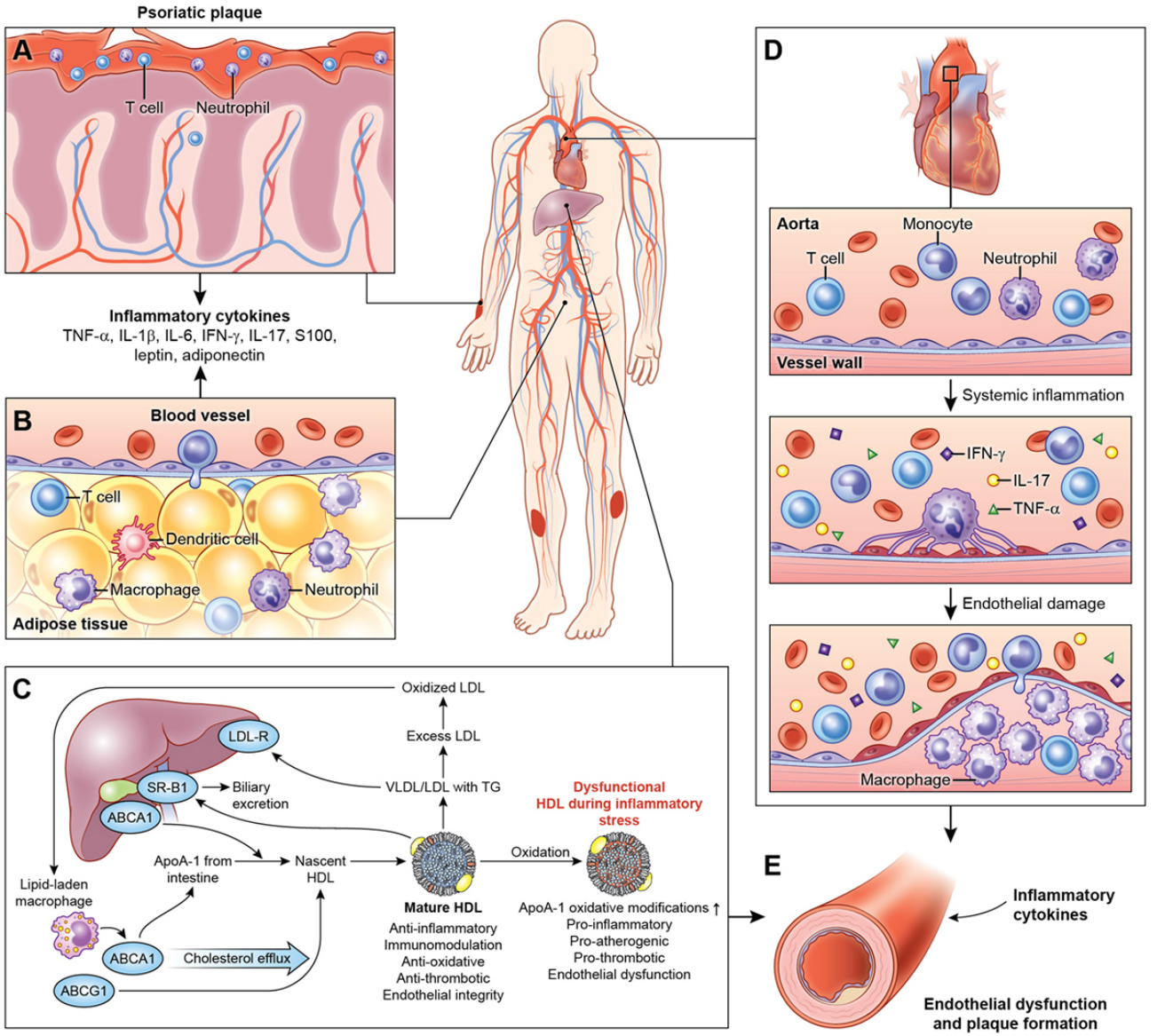
Società Italiana di Nutraceutica

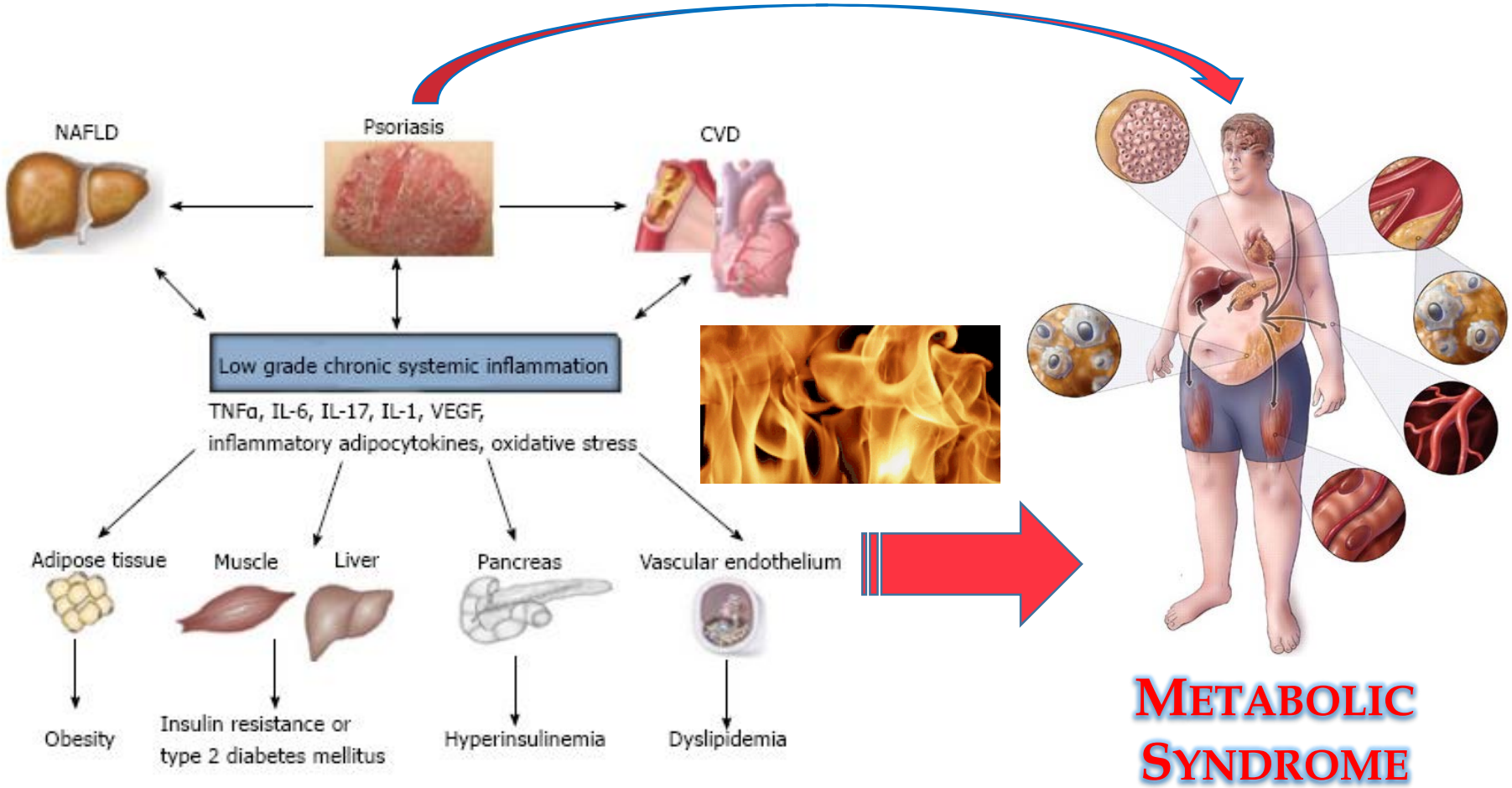
Aumento delle citochine infiammatorie

Aumento delle citochine infiammatorie



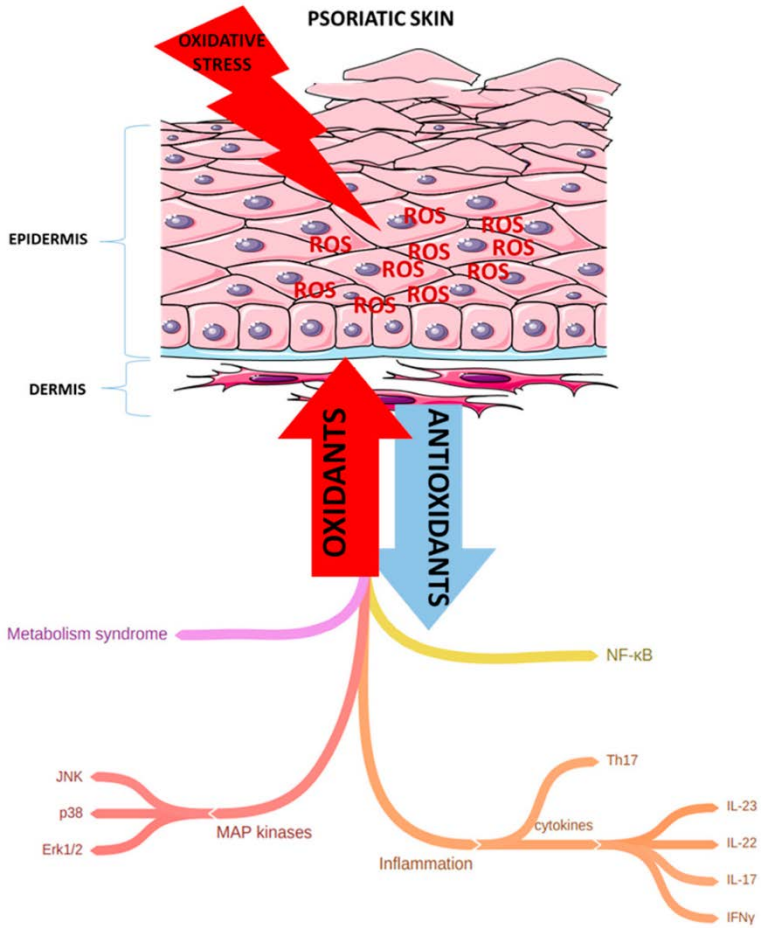
Sajja AP et al Front Immunol. 2018

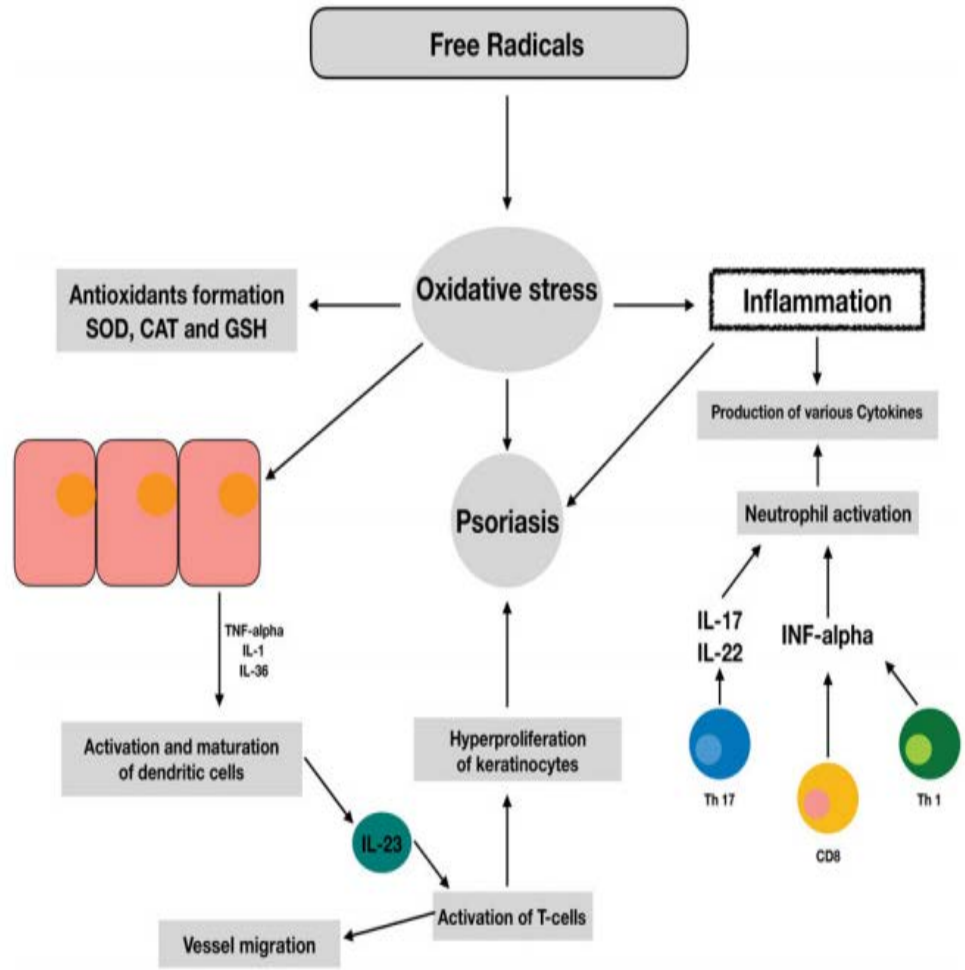
PSORIASIS: DIFFERENT DISEASES ON A UNIQUE BACKGROUND



Ganzetti G et al World J Cardiol. 2016

Oxidative Stress as an Important Contributor to the Pathogenesis of Psoriasis





Joanna Pleńkowska J et al. Int J Mol Sci 2020

Serafinella Patrizia Cannavò SP et al. Free Radic Res . 2019

Oxidative Stress and Metabolic Syndrome

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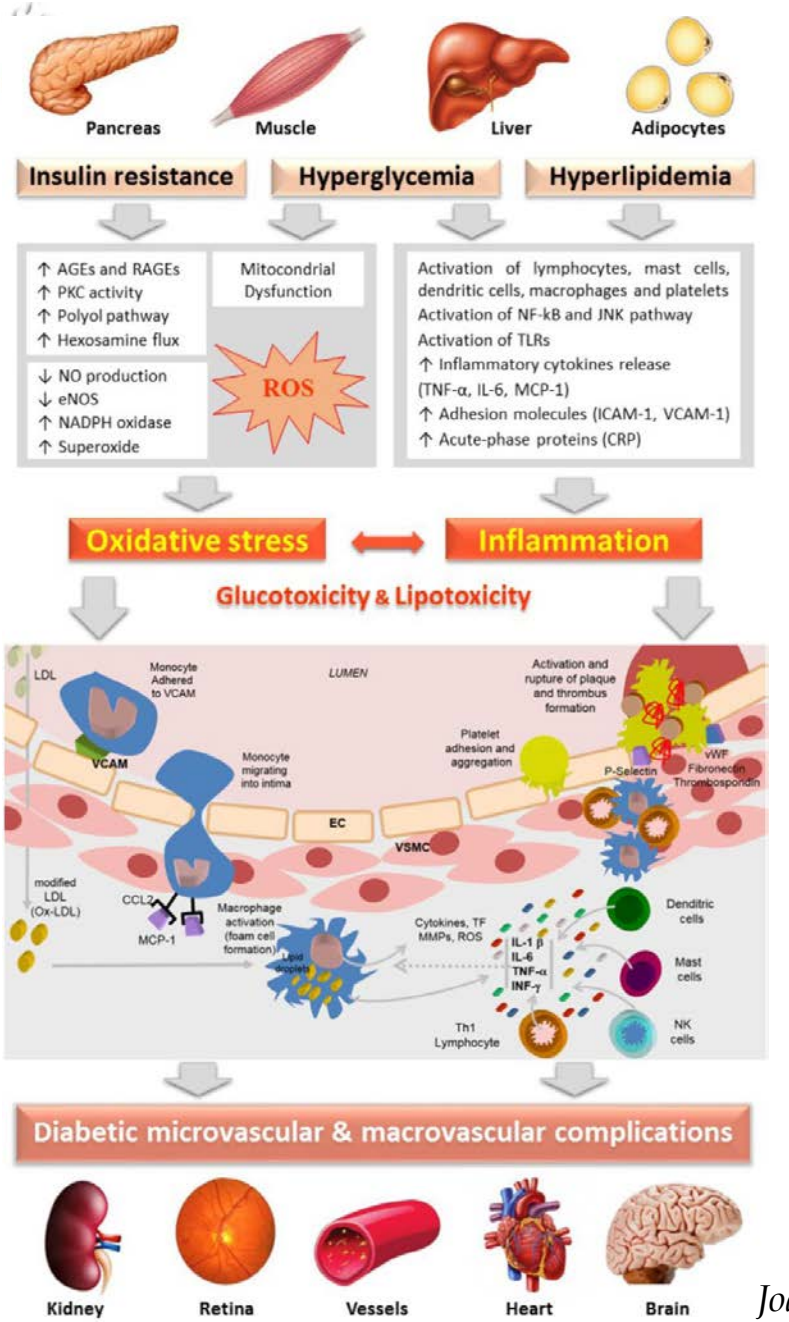
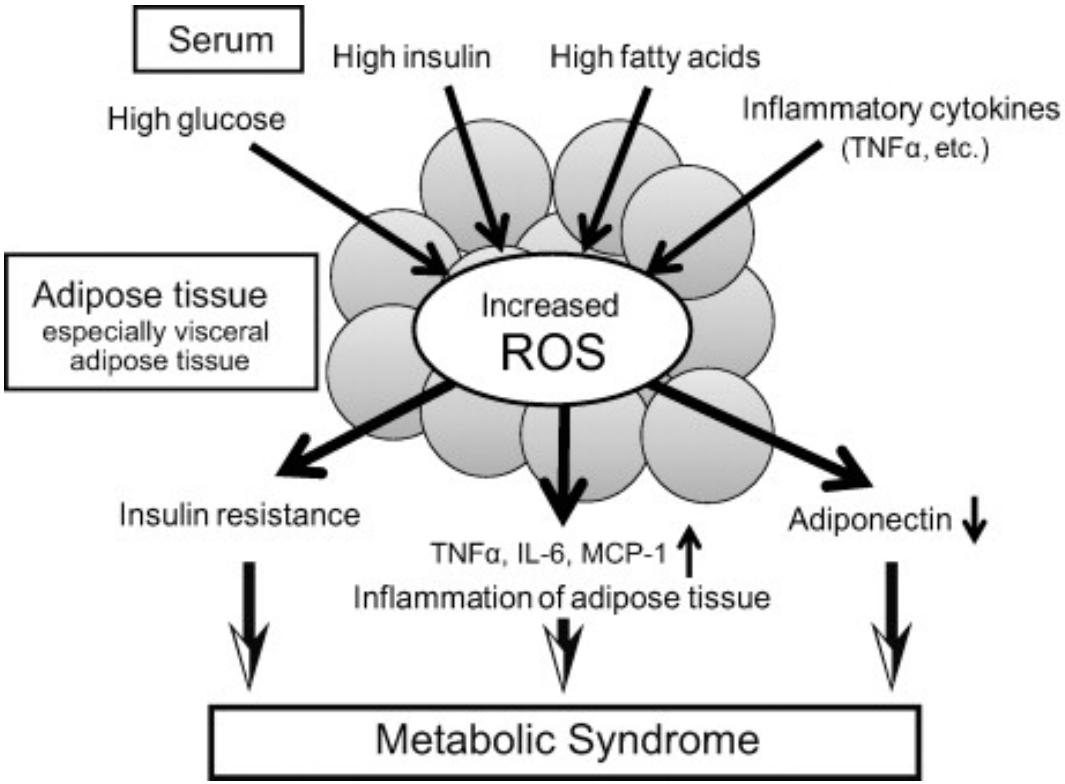


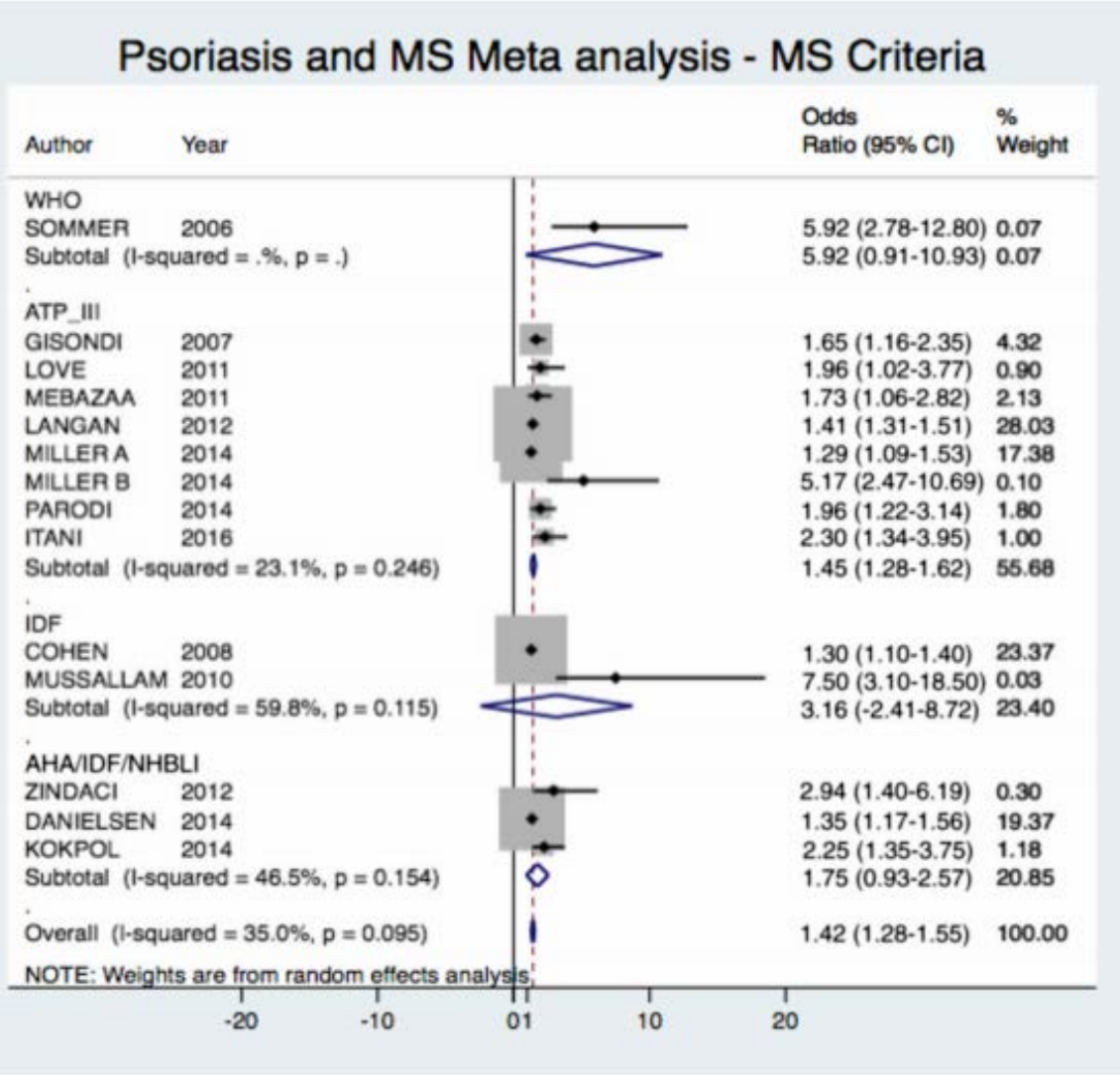
João S Teodoro JS et al. Front Physiol. 2019

Matsuda M et al. Obes Res Clin Pract 2013



Psoriasis and Metabolic Syndrome

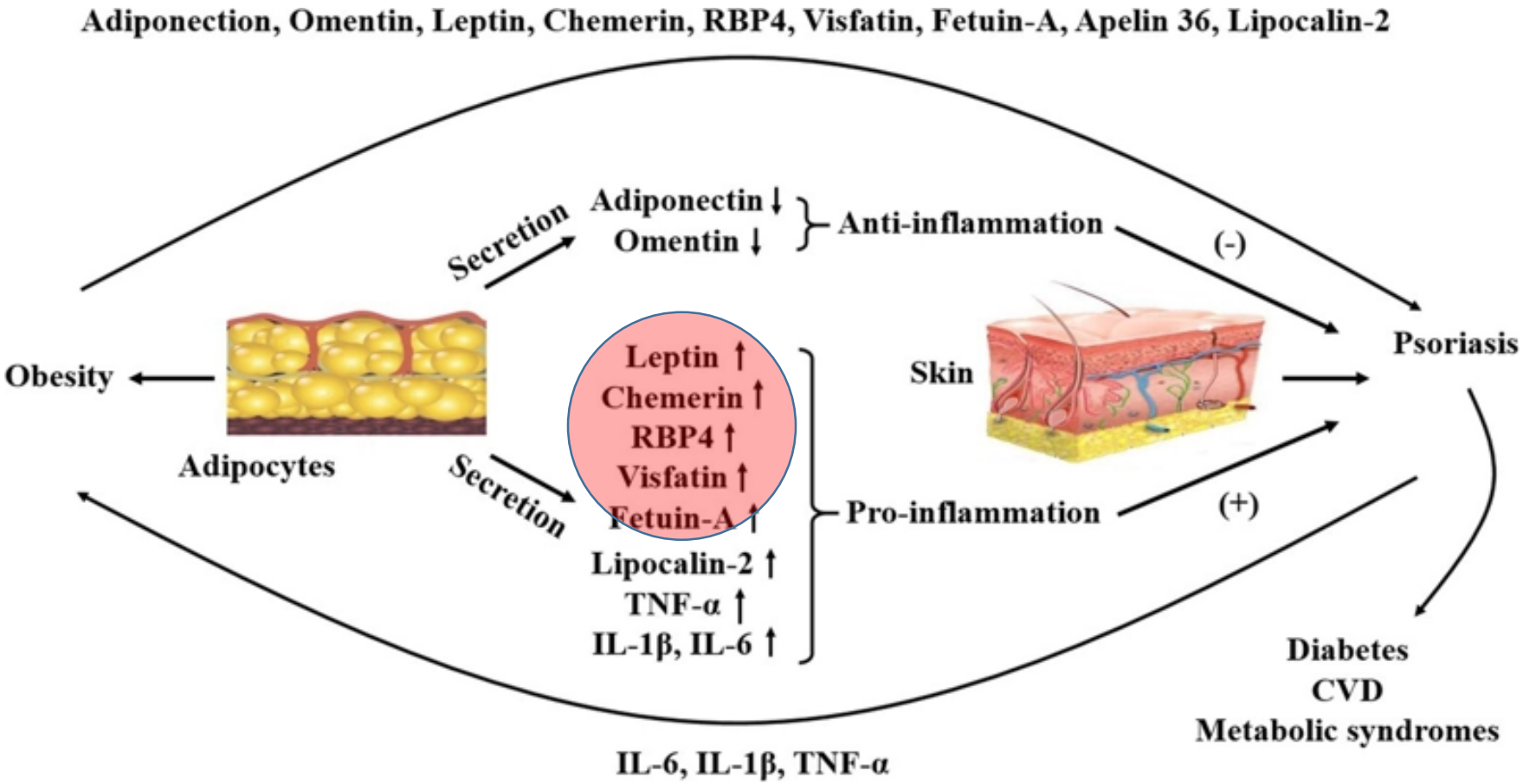
Systematic review and meta-analysis



Because of the increased risk for MS, clinicians should consider screening patients with psoriasis for metabolic risk factors

Rodríguez-Zúñiga MJM, J Am Acad Dermatol. 2017

Dati di letteratura dimostrano che i pazienti con psoriasi sono caratterizzati da aumentate concentrazioni di leptina e resistina e ridotti livelli di adiponectina, che influenzano la produzione di mediatori pro e antinfiammatori coinvolti nella patogenesi della psoriasi. Inoltre la resistina è stata proposta come potenziale biomarcatore dell'efficacia del trattamento (Kyriakou A. et al. Br J Dermatol. 2018)

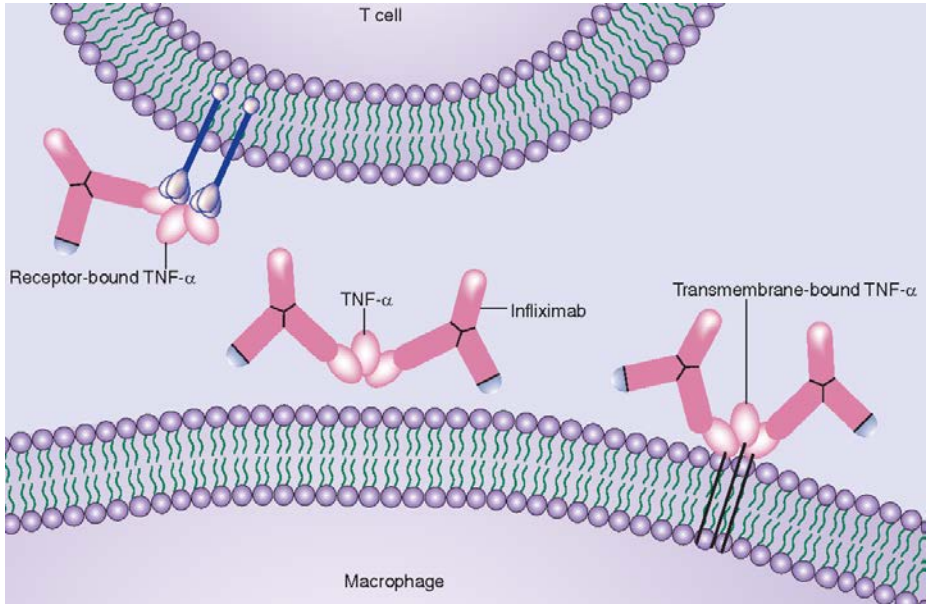


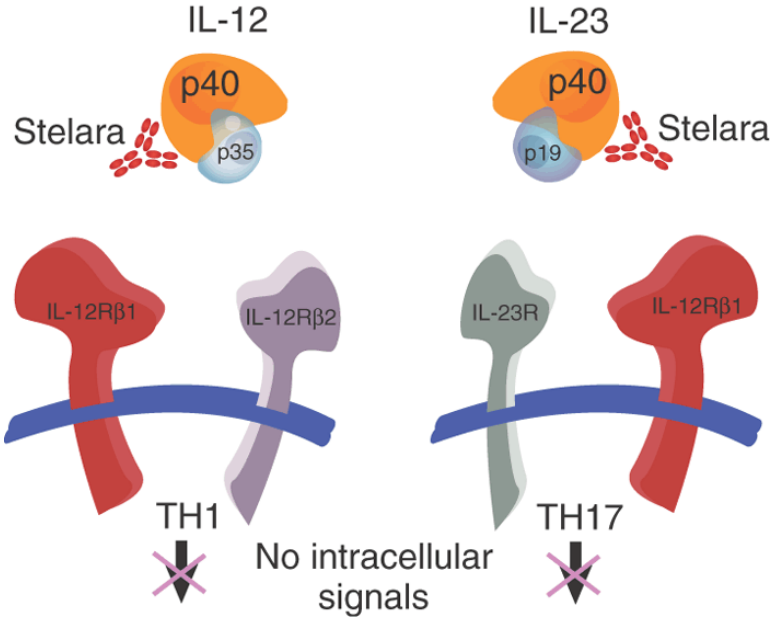
Psoriasi: Oltre la Terapia Farmacologica

Nell'ultimo decennio la psoriasi di grado moderata-grave viene trattata con successo con farmaci biologici che prendono di mira:

Fattore di necrosi tumorale-α (etanercept, adalimumab e infliximab)

La subunità p40 dell'IL-12 e IL-23 (ustekinumab) per bloccare la risposta immunitaria alla base della malattia.





Mahil SK, et al. Br J Dermatol. 2020

PSORIASI: OLTRE LA TERAPIA FARMACOLOGICA

Nonostante la loro efficacia, alcuni pazienti non riescono a ottenere una risposta adeguata e le linee guida suggeriscono

1. la titolazione a un dosaggio più elevato
2. il passaggio a un agente biologico di seconda linea
3. la combinazione della terapia biologica con altri farmaci immunosoppressivi sistemici
4. **La combinazione della terapia biologica con il miglioramento dello stile di vita**

Review > JAMA Dermatol. 2015 Apr;151(4):432-8. doi: 10.1001/jamadermatol.2014.3456.

Combining biologic therapies with other systemic treatments in psoriasis: evidence-based, best-practice recommendations from the Medical Board of the National Psoriasis Foundation

April W Armstrong [1], Jerry Bagel [2], Abby S Van Voorhees [3], Andrew D Robertson [4], Paul S Yamauchi [5]

PSORIASI: OLTRE LA TERAPIA FARMACOLOGICA

In particolare, gli studi hanno dimostrato che l'aderenza a regimi dietetici ipocalorici non solo può aumentare l'efficacia della terapia, ma anche migliorare la risposta ad essi al farmaco poiché la perdita di peso, riducendo il tessuto adiposo viscerale, riduce le citochine pro-infiammatorie, come il TNF-α.

International Journal of *Environmental Research and Public Health*

MDPI

Review

Environmental Risk Factors in Psoriasis: The Point of View of the Nutritionist

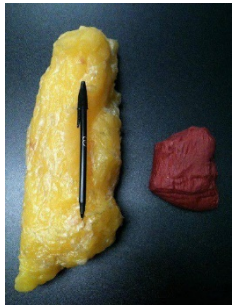
Luigi Barrea [1,*], Francesca Nappi [1], Carolina Di Somma [2], Maria Cristina Savanelli [1], Andrea Falco [1], Anna Balato [3], Nicola Balato [3] and Silvia Savastano [4]

Psoriasi: Oltre la Terapia Farmacologica

Nutrition: a key environmental dietary factor in clinical severity and cardio-metabolic risk in psoriatic male patients evaluated by 7-day food-frequency questionnaire.

Barrea L, Macchia PE, Tarantino G, Di Somma C, Pane E, Balato N, Napolitano M, Colao A, Savastano S.

J Transl Med. 2015 Sep 16;13:303. doi: 10.1186/s12967-015-0658-y.



Bioelectrical phase angle and **psoriasis**: a novel association with **psoriasis** severity, quality of life and metabolic syndrome.

Barrea L, Macchia PE, Di Somma C, Napolitano M, Balato A, Falco A, Savanelli MC, Balato N, Colao A, Savastano S.

J Transl Med. 2016 May 10;14(1):130. doi: 10.1186/s12967-016-0889-6.

Coffee consumption, metabolic syndrome and clinical severity of **psoriasis**: good or bad stuff?

Barrea L, Muscogiuri G, Di Somma C, Annunziata G, Megna M, Falco A, Balato A, Colao A, Savastano S.

Arch Toxicol. 2018 May;92(5):1831-1845. doi: 10.1007/s00204-018-2193-0. Epub 2018 Mar 28.

PMID: 29594327

Vitamin D and its role in **psoriasis**: An overview of the dermatologist and nutritionist.

Barrea L, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, Savastano S.

Rev Endocr Metab Disord. 2017 Jun;18(2):195-205. doi: 10.1007/s11154-017-9411-6.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2020.1818053

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REVIEW

Check for updates

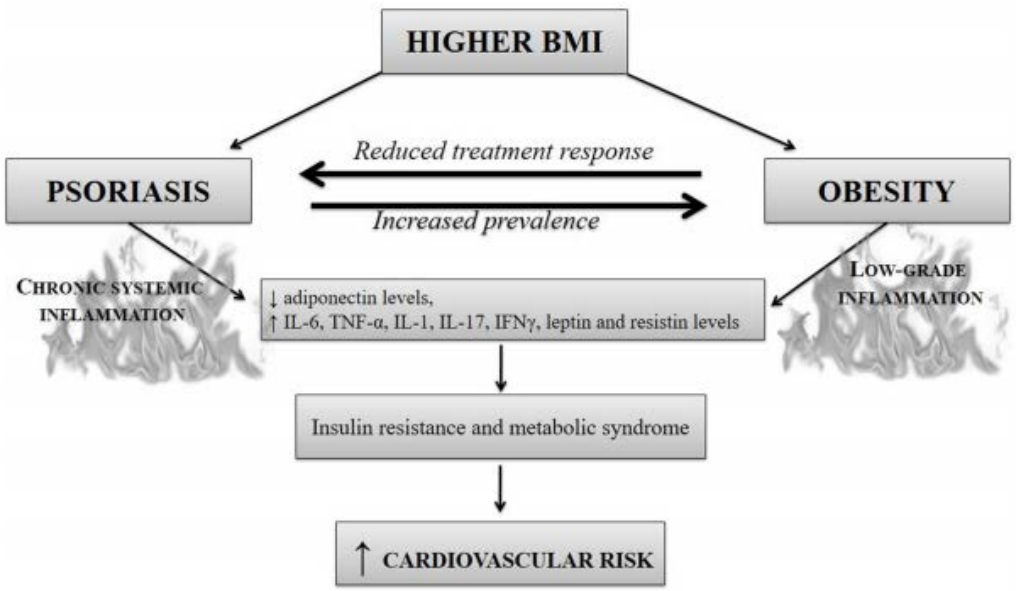
Very low-calorie ketogenic diet (VLCKD) in patients with psoriasis and obesity: an update for dermatologists and nutritionists

Luigi Barrea[a,b*], Matteo Megna[c*], Sara Cacciapuoti[c], Evelyn Frias-Toral[d,e], Gabriella Fabbrocini[c], Silvia Savastano[a,b], Annamaria Colao[a,b,f], and Giovanna Muscogiuri[a,b]

Citation metrics

- 11.176 (2020) Impact Factor

This review aims to summarize the current evidence regarding the efficacy of VLCKD as potential treatment of psoriasis, mostly in the context of obesity, highlighting antioxidant and anti-inflammatory properties of this dietary pattern.



VLCKD: Psoriasis and Obesity

Sono stati condotti solo pochi studi sull'efficacia di VLCKD in pazienti con psoriasi

Table 2. Studies on VLCKD and psoriasis.

Reference	Subjects	Diet	Treatment duration	Outcomes
Castaldo et al. 2015	1 (40 years old woman)	protein-based, ketogenic enteral nutrition liquid of ~300 kcal/day	24 h a day *per* 4 weeks	>80% PASI reduction 11 Kg weight reduction
Castaldo et al. 2020	37 (11 males, mean age= 43.1 years)	-first phase of 4-week of VLCKD (protein sparing) -second phase of a 6 week of hypocaloric Mediterranean-like diet at low glycemic index	10 week of 2-phase: -first phase of 4-week -second phase of a 6 week	Mean change of −10.6 in PASI score 64.9% of subjects reached PASI75 response or more Mean reduction in BSA of −17.4% Mean change in body weight of −12.0 %

BSA, Body Surface Area; PASI, Psoriasis Area Severity Index; PASI75, reduction of 75% of initial PASI value; VLCKD, Very Low-calorie Ketogenic Diet.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2020.1818053

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REVIEW

Very low-calorie ketogenic diet (VLCKD) in patients with psoriasis and obesity: an update for dermatologists and nutritionists

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Very low-calorie ketogenic diet may allow restoring response to systemic therapy in relapsing plaque psoriasis

Giuseppe Castaldo[a], Giovanna Galdo[b], Felice Rotondi Aufiero[b], Emanuele Cereda[c,*]

Una donna 40enne, affetta da psoriasi a placche ricorrenti e artrite psoriasica (entesite), obesità complicata da dislipidemia e sindrome metabolica.

E' stata trattata con successo con terapia biologica (adalimumab sottocutaneo, 80 mg per 1 settimana poi, 40 mg ogni 2 settimane) per 12 mesi.

All'inizio del trattamento con agenti biologici PASI score era di 37 e dopo 3 mesi di terapia il PASI score è sceso a 0. Dopo 6 mesi la paziente ha una recidiva e le lesioni cutanee erano localizzate principalmente al cuoio capelluto, agli arti e alle pieghe sottomammarie

KDA Ketogenic Diet ACADEMY

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Purtroppo non è stato possibile considerare l'associazione con altri farmaci sistemici perché, la paziente lamentava effetti collaterali al trattamento con ciclosporina (forti cefalee) e non aveva precedentemente risposto a metotrex

Di conseguenza, prima di considerare l'uso di dosi più elevate di terapia biologica, il paziente è stato trattato con nutrizione enterale chetogenica a base di proteine.

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Composizione della Dieta

Formula liquida, priva di carboidrati e povera di grassi, contenente una quantità fissa di aminoacidi a catena ramificata (10 g), glutammina (5 g) e proteine del latte al fine di raggiungere un contenuto proteico totale di 1,2 g per chilogrammo di peso corporeo ideale (contenuto calorico totale, ~300 kcal/giorno). Sono stati forniti anche un integratore multivitaminico-multiminerale completo e sostanze alcalinizzanti.

La somministrazione della formula è stata eseguita in continuo (24 h al giorno) per 4 settimane mediante sondino nasogastrico in poliuretano (8-francese) collegato ad una pompa di alimentazione peristaltica.

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PROTOCOLLO DI STUDIO

After VLC enteral nutrition [day 28]	After low-calorie oral diet [day 70]	After VLC enteral nutrition [day 98]
Primo ciclo di 4 settimane di nutrizione enterale chetogenica a base di proteine VLC	Dieta ipocalorica e normale con proteine (1200 kcal/giorno) per 6 settimane	Secondo ciclo di 4 settimane di nutrizione enterale chetogenica a base di proteine VLC

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Table 1 Clinical features of the patient during the follow-up.

	Before VLC enteral nutrition [day 0]	After VLC enteral nutrition [day 28]	After low-calorie oral diet [day 70]	After VLC enteral nutrition [day 98]
Body weight, kg	92	81	75.4	67.4
BMI, kg/m^2	35	31	29.1	26
Waist circumference, cm	111	104	96	86.5
Waist to hip ratio	0.97	0.96	0.92	0.91
Glucose, mg/dL	83	66	83	64
Insulin, μU/mL	13.8	5.8	13.6	2.7
C-peptide, ng/mL	2.35	1.34	2.16	0.98
HOMA-IR	2.83	0.94	2.79	0.43
AMFT, mm	19	12	9	7
Blood pressure, mmHg	135/80	120/80	110/80	110/70
Total cholesterol, mg/dL	160	102	135	152
HDL, mg/dL	41	38	43	47
Triglycerides, mg/dL	73	58	60	59
PASI, score	15	2.4	0.4	0.3
BSA, %	10	7	4	1
DLQI, score	12	3	0	0

↓~20% del peso

↓spessore del grasso viscerale aorto-mesenterico

↓98% PASI

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Prof. Luigi Barrea

VLCKD

Potrebbe consentire il ripristino di una rapida risposta alla terapia sistemica in pazienti con recidiva psoriasica.

Questo intervento dovrebbe essere considerato nei pazienti con sovrappeso/obesità prima di passare a una terapia sistemica.

Le VLCKD dovrebbero essere preferite alle diete ipocaloriche non chetogeniche per migliorare la risposta alla terapia sistemica almeno nei pazienti con psoriasi da moderata a grave.

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Applied nutritional investigation

Aggressive weight-loss program with a ketogenic induction phase for the treatment of chronic plaque psoriasis: A proof-of-concept, single-arm, open-label clinical trial

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Baseline characteristics of the study population

Characteristic	Descriptive statistics
Male sex, n (%)	11 (29.7)
Age (y), mean (SD)	43.1 (13.8)
Disease duration (y), mean (SD)	6.3 (5.9)
Body weight (kg), mean (SD)	86.3 (19.6)
Body mass index (kg/m^2), mean (SD)	31.7 (6.7)
Aortomesenteric fat thickness* (mm), mean (SD)	17.3 (7.9)
PASI score, mean (SD) [range]	13.8 (6.9) [7–32]
BSA involvement (%), mean (SD) [range]	22.4 (15.8) [10–70]
Itch severity (VAS score), median (IQR)	35.0 (10.0–70.0)
DLQI score, mean (SD)	15.9 (11.8)

BSA, body surface area; DLQI, Dermatology Life Quality Index; IQR, interquartile range; PASI, Psoriasis Area and Severity Index; SD, standard deviation; VAS, visual analogue scale.

- 37 Pazienti adulti, sovrappeso/obesi,
- naïve ai farmaci,
- psoriasi cronica a placche (diagnosi confermata da 2 dermatologi) che interessa almeno il 10% della superficie corporea (BSA)

2 COMPOSIZIONE DELLA DIETA

I pazienti sono stati sottoposti a un programma WL in 2 fasi

1. **dieta chetogenica a bassissimo contenuto calorico (VLCKD) per 4 settimane**

Formula liquida orale a base di proteine del latte (<500 kcal/giorno), 1,2 g di proteine per kg di peso corporeo ideale (20% a colazione e 40% a pranzo e cena). CHO: 10 a 20 g (da verdure: 400-500 g/die) e da 20 a 30 g di olio d'oliva/die. Integrazione con sostanze alcalinizzanti e multivitaminico-multiminerale completo (100% delle dosi consigliate).

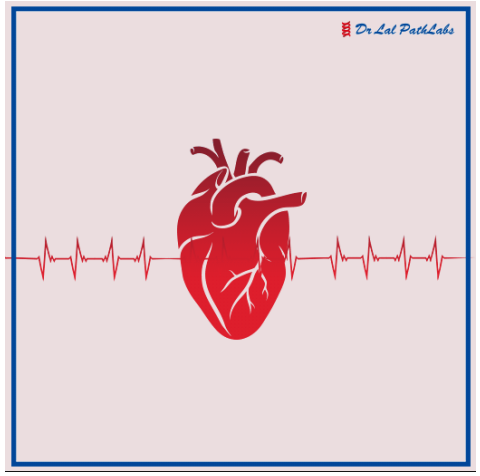
2 COMPOSIZIONE DELLA DIETA

2. Una successiva dieta ipocalorica, a basso indice glicemico, di tipo mediterraneo (ipo-MD) di 6 settimane

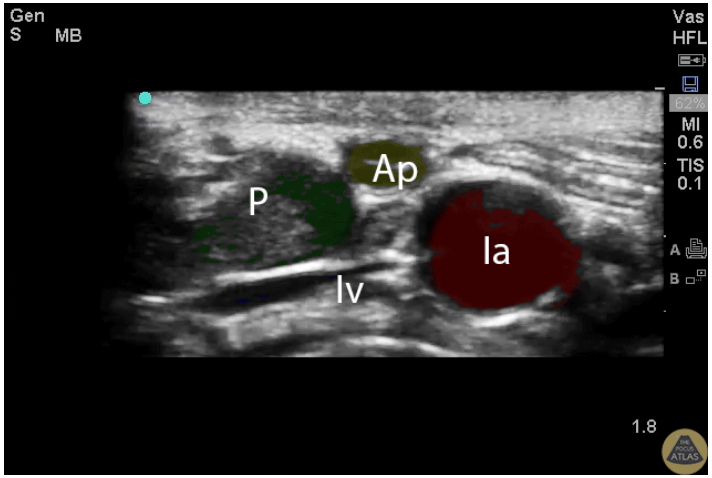
CHO 54%; proteine 18%; grassi 28% [acidi grassi saturi <7%]) che forniva da 25 a 30 kcal/kg di peso corporeo al giorno e si basava sull'uso di basso indice glicemico indici alimentari.

Durante lo studio non sono stati prescritti farmaci immunosoppressivi specifici per la malattia (né farmaci topici [cioè agenti steroidei] né farmaci sistemici).

2 OUTCOMES VALUTATI



- Antropometrici
- Spessore del grasso aorto-mesenterico
- Ematochimici e biochimici
- Pressione arteriosa
- Dermatologiche



Castaldo G. et al. Nutrition. 2020

RESULTS

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Frequency of adverse events

Adverse event	Ketogenic phase (n)	Hypocaloric phase (n)
Symptoms		
Asthenia	7	1
Headache	3	0
Dizziness	1	0
Nausea	3	0
Palpitations	1	0
Muscle cramps	4	1
Hunger	3	1
Bloating	5	0
Constipation	10	3
Biochemical parameters		
Increased aspartate amino-transferase (>39 UI/dL)	2	0
Increased alanine amino-transferase (>34 UI/dL)	4	0
Increased creatine phosphokinase (>190 UI/dL)	2	0
Increased lactate dehydrogenase (>600 UI/dL)	1	0
Reduced serum sodium (<135 mEq/L)	2	0
Increased serum urate (>7.0 mg/dL)	1	0
Increased blood urea nitrogen (>50 mg/dL)	1	0

Non si è verificato alcun evento avverso grave.

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Study endpoints on a continuous scale

Endpoint	End of ketogenic phase (wk 4)	*P*-value*	End of hypocaloric phase (wk 10)	*P*-value*
Change in PASI, mean (95% CI)	−7.2 (−8.7 to −5.6)	< 0.001	−10.6 (−12.8 to −8.4)†	< 0.001
Reduction in BSA involvement (%), mean (95% CI)	−10.1 (−13.1 to −7.1)	< 0.001	−17.4 (−22.4 to −12.3)	< 0.001
Change in itch severity (VAS score), mean (95% CI)	−27.2 (−37.7 to −16.6)	< 0.001	−33.2 (−44.1 to −22.4)	< 0.001
Change in DLQI score, mean (95% CI)	−9.7 (−12.6 to −6.8)	< 0.001	−13.4 (−17.0 to −9.7)	< 0.001
Change in body weight (%), mean (95% CI)	−9.5 (−10.5 to −8.4)	< 0.001	−12.0 (−13.7 to −10.4)	< 0.001
Change in AMFT (mm), mean (95% CI)	−4.0 (−5.2 to −2.7)	< 0.001	−5.9 (−7.8 to −4.0)	< 0.001

AMFT, aorto-mesenteric fat thickness; CI, confidence interval; PASI, Psoriasis Area and Severity Index; BSA, body surface area; DLQI, Dermatology Life Quality Index; VAS, visual analogue scale.

weight reduction of 12.0% (-10.6 kg)

Alla fine della fase VLCKD, la riduzione media del punteggio PASI era già >50% (–7,2; p<0,001),

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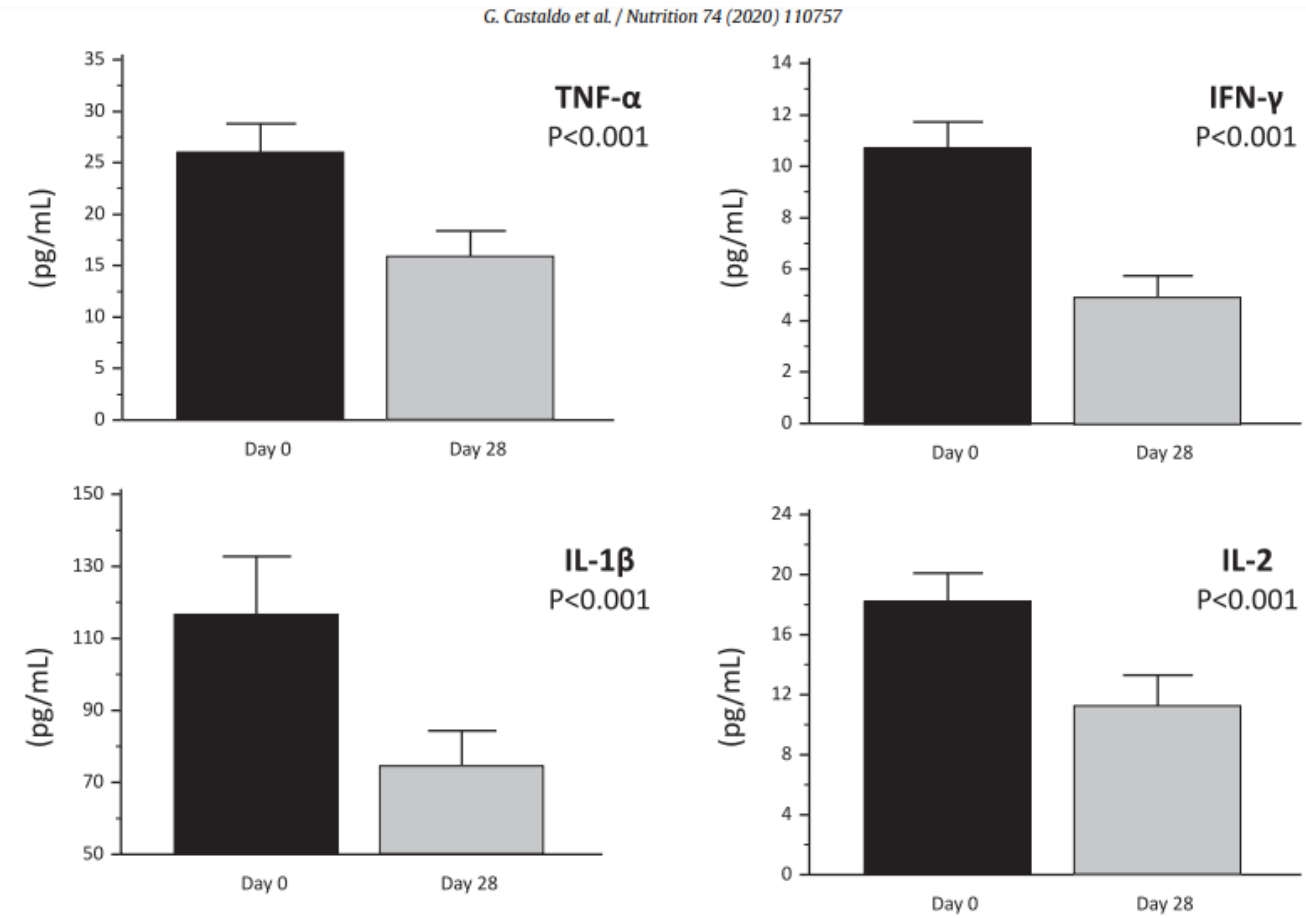
RESULTS



Change in plasma cytokines at the end of the very low-calorie ketogenic diet phase (wk 4)

Castaldo G. et al. Nutrition. 2020

DISCUSSION

Questo è il primo studio che ha affrontato l'efficacia di un programma VLCKD come strategia terapeutica di prima linea per i pazienti con psoriasi.

L'efficacia della VLCKD dipende dalla sostanziale riduzione del grasso viscerale e dalla relativa interruzione del background infiammatorio, che si è verificata principalmente durante le prime 4 settimane dell'intervento.

Il grasso viscerale è un'importante fonte di mediatori dell'infiammazione (ad es. TNF-α e IFN-γ) che svolgono un ruolo importante nella fisiopatologia della psoriasi

Castaldo G. et al. Nutrition. 2020

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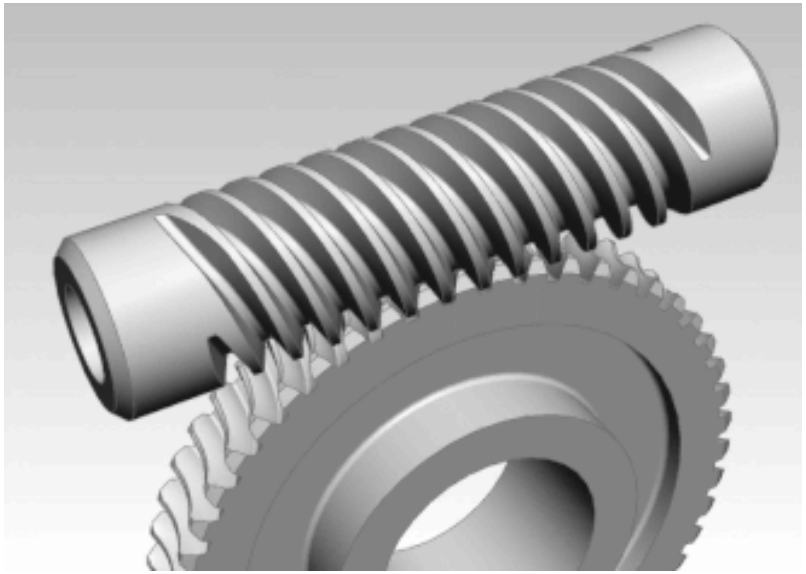
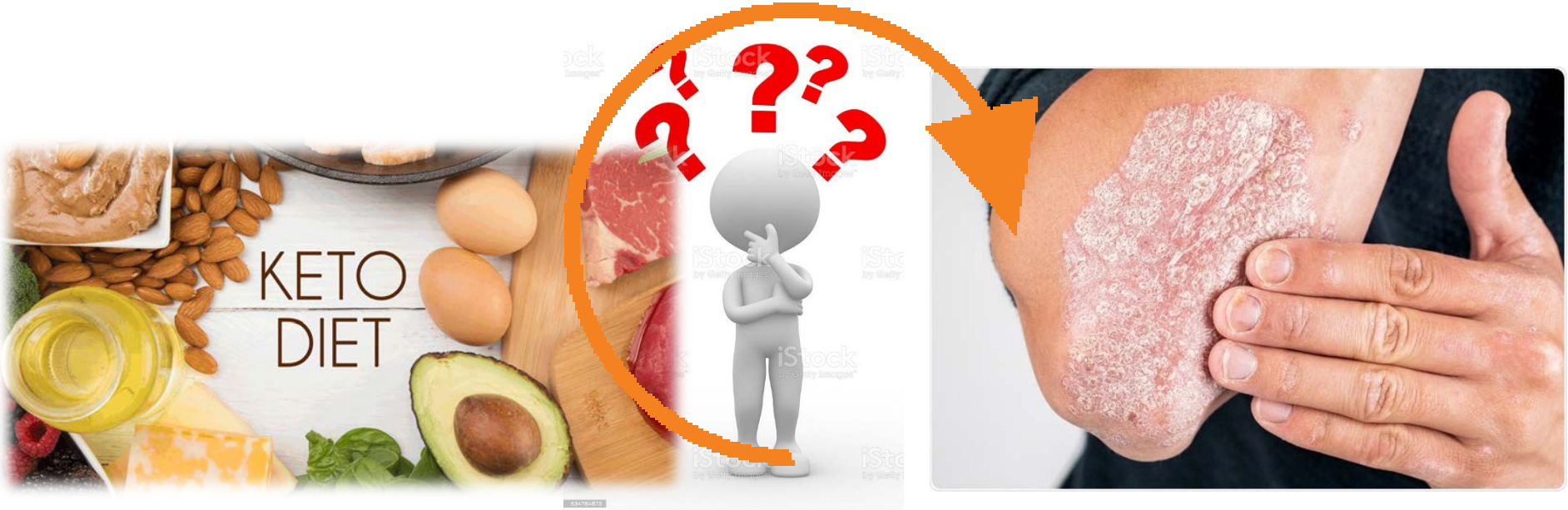




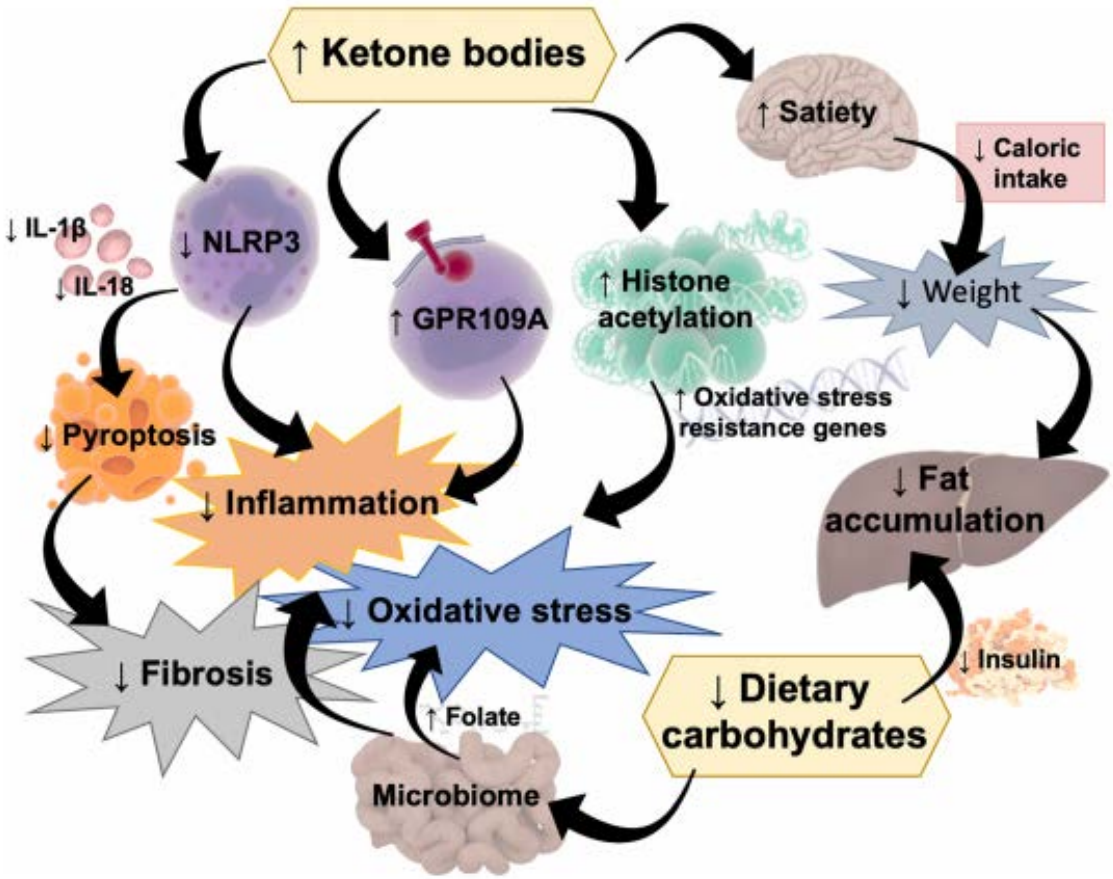
Nuove Indicazioni e applicazioni delle diete chetogeniche: sfera riproduttiva femminile e psoriasi

Prof. Luigi Barrea

Ketogenic Diet: Inflammation and Oxidation

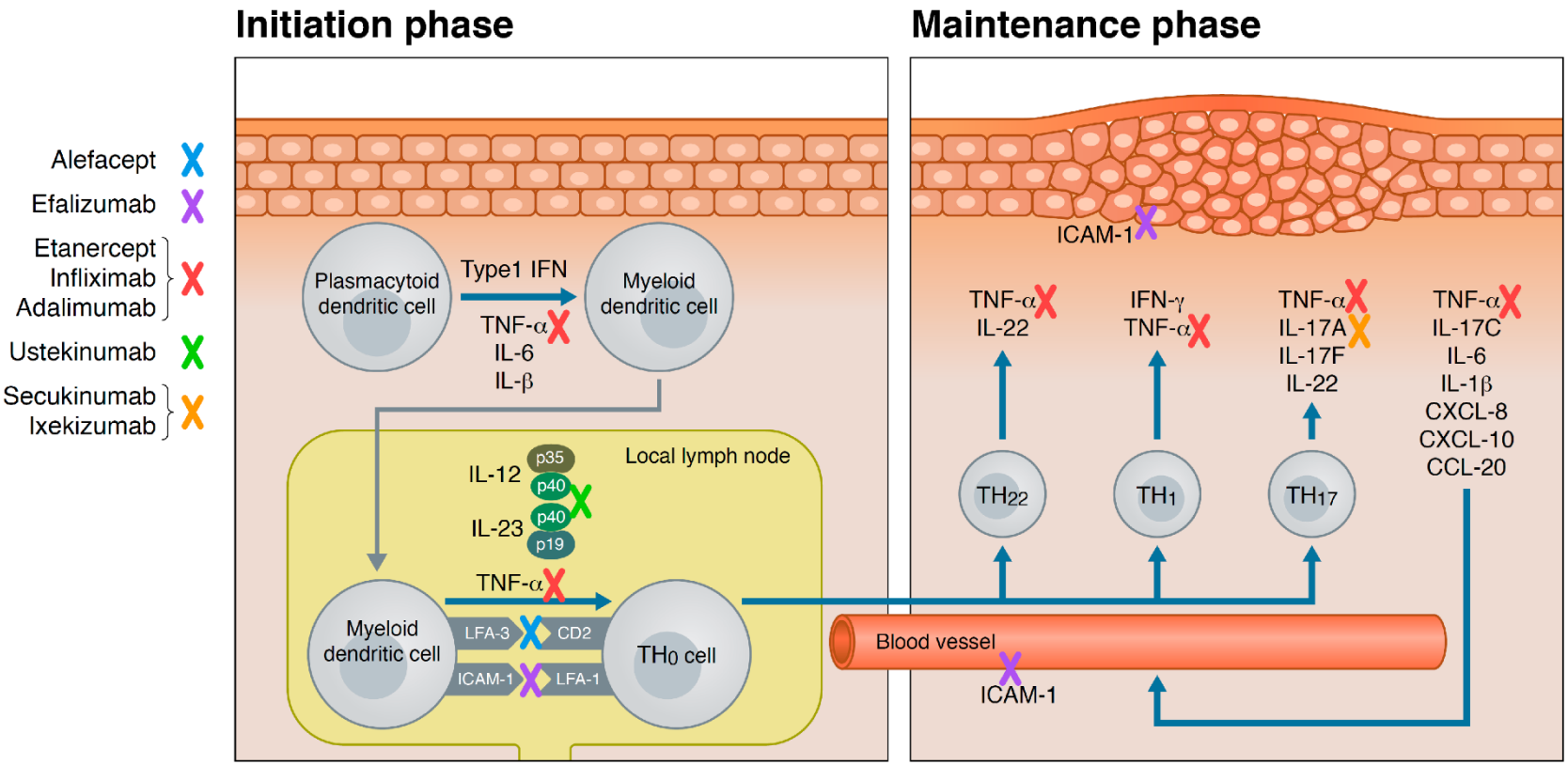
Il β-idrossibutirrato inibisce l'inflammasoma NLRP3 nei monociti umani stimolati da lipopolisaccaridi (LPS) con conseguente riduzione di IL-1β e IL-18 in modo dose-dipendente

Yun-Hee Y et al. Nat Med. 2015



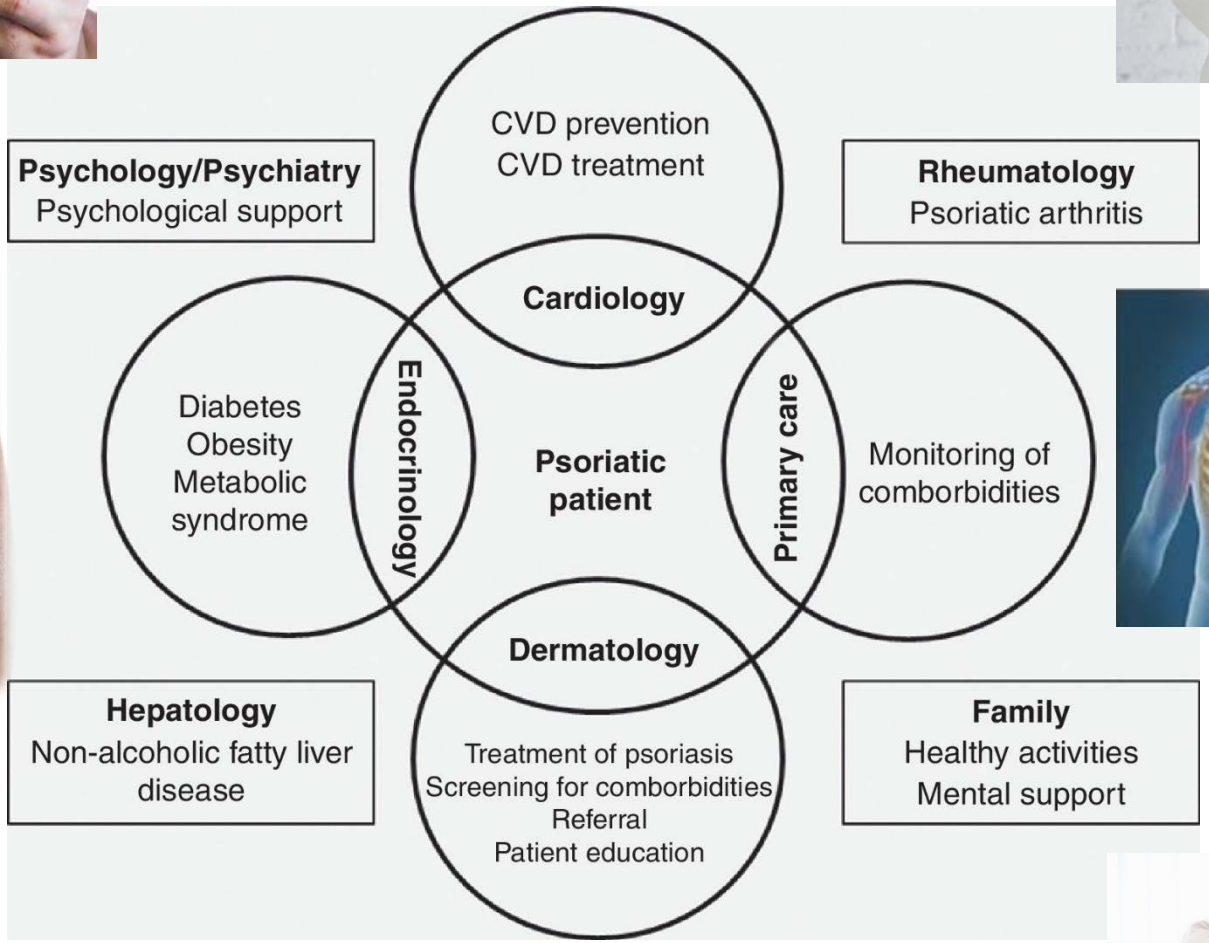
Watanabe M. et al Obes Rev. 2020

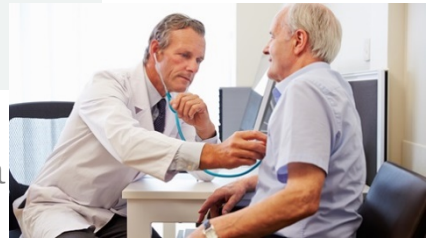
Ketogenic Diet: Inflammation and Oxidation



La dieta chetogenica migliora lo stress ossidativo attraverso l'attivazione del fattore di trascrizione nucleare eritroide-2 (Nrf2) che regola l'espressione genica di una grande varietà di enzimi citoprotettivi antiossidanti

Multidisciplinary approach to the patient with severe psoriasis





TAKE-HOME-MESSAGE

La nutrizione è considerata un fattore chiave nella gestione delle malattie infiammatorie croniche della pelle, inclusa la psoriasi. La perdita di peso è associata al miglioramento della gravità clinica della psoriasi e delle sue comorbidità, ma meno si sa circa l'effetto della VLCKD sulla psoriasi.

Le prove suggeriscono che le VLCKD, attraverso la riduzione dell'infiammazione, dell'ossidazione e dell'obesità, potrebbe avere effetti benefici di *per sé* importanti

Attraverso la perdita di peso e riduzione dell'infiammazione, le VLCKD in pazienti psoriasici potrebbero ripristinare una rapida risposta alla terapia medica sistemica

Considerando l'intensa restrizione calorica e di nutrienti, le VLCKD dovrebbe essere considerato come una vera e propria «terapia medica dietetica» proposto a specifici pazienti psoriasici, come parte della terapia farmacologica ma soprattutto sotto stretta supervisione clinica di un nutrizionista qualificato.

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Nutrizione Endocrinologica ed Obesità
UOC di Endocrinologia
AOU Federico II
-Napoli-

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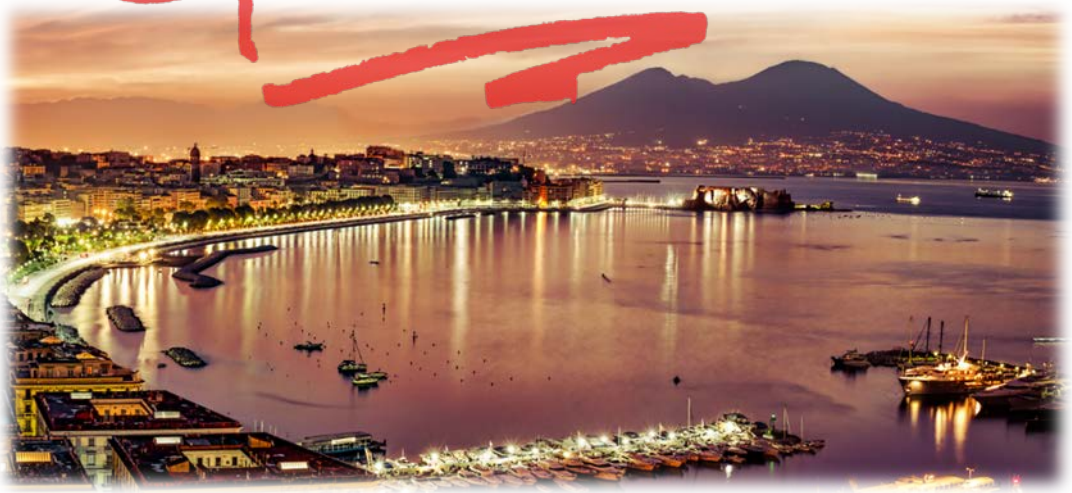
Grazie



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