Table 4.10 Studies on chronic inflammation and coffee drinking in exposed humans

Tissue	Cell type	End-point	Test	Description of exposure[a] and controls	Response[b]/significance	Comments	Reference
Cross-sectional studies							
Serum	-	hs CRP	Immunonephelometric Detection limit: 0.05 µg/ml	Cross-sectional study; 10 325 (4407 M, 5918 F) healthy Japanese (49–76 y); quintiles of coffee intake (0; < 1 cup/d; 1–3 cup/d; 4–6 cup/d; ≥ 7 cup/d)	Highest quintile vs lowest Men −20% (95% CI, −36%, −0%) [P trend < 0.05] Women −25% (95% CI, −40%, −3%) [P trend = 0.52]	Effect only in men, and limited to high alcohol consumption (≥ 50 g/d)	Maki et al. (2010), Pham et al. (2011)
Serum	-	hs CRP	Latex Agglutination assay Detection limit: 0.1 µg/ml	Cross-sectional study; 7574 (3664 M, 3910 F) healthy Koreans (40–69 y); coffee pattern derived by factor analysis and divided into quartiles (no data on actual coffee intake);	No difference between Q4 and Q1 [*P* = 0.77]		Lee et al. (2014)
Plasma	-	hs CRP	Immunoturbidimetric Detection limit: no data	Cross-sectional study; 4139 (1921 M, 2218 F) healthy Asians (50 y); quartiles coffee intake (0, < 1 cup/d, 1–2 cup/d, ≥ 3 cup/d)	No effect in multiple regression analysis [*P* = 0.185]	Adjusted a.o. for tea drinking	Rebello et al. (2011)
Plasma	-	hs CRP	Immunonephelometric Detection limit: no data	Cross-sectional study; 344 healthy women (57 y); quartiles of coffee intake (0; 1 cup/mo- 6 cup/wk; 1 cup/d-13 cup/wk; ≥ 2 cup/wk)	Highest quartile vs lowest −30% (95% CI, −40%, −7%) [P trend = 0.005]	CRP positively associated with BMI; hormone replacement therapy increased CRP	Arsenault et al. (2009)
Serum	-	hs CRP	ELISA detection limit: no data	Cross-sectional study; 114 healthy Japanese, age- and sex-matched (60 y); coffee (≥ 1 cup/d) and non-coffee (< 1 cup/d) drinkers	Comparison between coffee and non-coffee drinkers (control) −25% [*P* = 0.05]	Small sample size	Kotani et al. (2010)

Plasma	-	CRP, SAA, IL-6, TNF-α; white blood cell counts	Immunonephelometric (CRP, SAA); ELISA (IL-6, TNF-α)	Cross-sectional study; 1514 healthy men and 1528 healthy women (45 y); quartiles of coffee intake (0; < 200 ml/d; 200–400 ml/d; > 400 ml/d)	Inflammatory markers were positively associated with coffee consumption [P,0.05] Highest quartile vs lowest (no coffee) Men CRP +35% [*P* < 0.01] IL-6 +60% [*P* < 0.01] TNF-α +40% [*P* < 0.01] SAA +15% [*P* < 0.05] WBC + 4% [*P* < 0.05] Women CRP +40% [*P* < 0.05] IL-6 +60% [*P* < 0.01] TNF-α +40% [*P* < 0.01] SAA +50% [*P* < 0.01] WBC + 7% [*P* < 0.05]	Stratification for filtered or unfiltered coffee did not change the effects	Zampelas et al. (2004)
Serum	-	CRP, sICAM, E-selectin, sTNF-α-receptor II	ELISA; turbidimetric (CRP)	Cross-sectional study; 1393 women (43–70 y) Nurses' Health Study I; quartiles coffee intake (< 1 cup/mo; 1 cup/ mo-4 cup/wk; 5–7 cup/wk; ≥ 2 cup/d)	Difference (%) per 1 cup/d increment Caffeinated coffee *non-diabetic* Not significant: CRP, sICAM, E-selectin, TNF-R2 *diabetic* E-selectin ─3% [*P* = 0.05] CRP ─0% [*P* < 0.001] Not significant: sICAM, sTNF-R2	Repeated assessment of coffee intake	Lopez-Garcia et al. (2006)

					Decaffeinated coffee *non-diabetic* CRP ─8% [*P* = 0.02] Not significant: sICAM, E-selectin, sTNF-R2,] *diabetic* Not significant: CRP, sICAM, E-selectin, sTNF-R2		
Plasma	-	IL-6, PAI-1		Cross-sectional study, hypertensives (43 y); heavy coffee drinkers (> 4 cups/d) (*n* = 30) vs light coffee drinkers (< 1 cup/d)(*n* = 30)	IL-6 +120% [*P* < 0.005] PAI-1: +85% [*P* < 0.0001]		Tsioufis et al. (2006)
Serum	-	77 Inflammatory/ immune markers	Luminex bead-based assays	Cross-sectional study with 1728 older US non-Hispanic whites	Coffee drinkers (> 2.5 cups/d) vs non-drinkers sTNF-R2 OR, 0.34; (95% CI: 0.15–0.79)		Loftfield et al. (2015)
Prospective studies							
Serum	-	CRP, TNF-α-receptor II	ELISA; turbidimetric (CRP)	Prospective study; follow-up 6 y; 2040 women Nurses' Health Study; quartiles coffee intake (< 1 cup/wk; 1–6 cup/wk; 1–3 cup/d; ≥ 4 cup/d)	Inverse associations: CRP [*P* = 0.001] TNF-R2 [*P* = 0.03]	Repeated assessment coffee intake	Williams et al. (2008)
Serum /plasma		CRP, IL-6	Turbimetric (CRP), electrochemiluminescence	Prospective nested case-control study; 125 incident cases of hepatocellular carcinoma (HCC); 250 controls; ≥ 4 cups/d vs < 2 cups/d	IL-6 inverse with coffee drinking, β = –0.18 (–0.35, –0.02), [*P* = 0.06] CRP not significant	HCC risk coffee drinkers: 0.25 (95% CI: 0.11–0.62) [P-trend = 0.006]	Aleksandrova et al. (2015)

Randomized controlled trials (RCTs)

Plasma	-	hs CRP, sE-selectin, sVCAM-1, sICAM-1,, IL-1β, IL-6, TNF-α, MCP-1, tPAI-1, fibrinogen,	Immunonephelometric (CRP), Luminex bead-based assay (other markers except fibrinogen	RCT crossover; 20 (6 M, 14 F) healthy non-smoking subjects; 3 cups/d (150 ml) paper-filtered coffee light roasted, 3 cups/d paper-filtered coffee medium roasted; 4 wk, no wash-out in between	Medium roasted vs baseline: fibrinogen + 8% [$P < 0.01$] sVCAM-1 +15% [$P < 0.05$] other markers did not differ Light roasted vs baseline: sVCAM-1 +20% [$P < 0.05$] sE-selectin +10% [$P < 0.05$] other markers did not differ	No placebo	Corrêa et al. (2013)
Serum	-	CRP, IL-6, IL-18, IL-1ra, SAA, MIF	Luminex bead-based assay (IL-18), ELISA (Il-6, IL-1ra, MIF), immunonephelometric (CRP, SAA),	Clinical trial, 3-stage; 47 (11 M, 36 F) subjects (54 y) elevated risk type 2 diabetes; subsequently, no coffee (1 mo), 4 cups/d filtered coffee (1 mo), 8 cups/d filtered coffee (1 mo)	Difference 8 cups vs 0 cups: IL-18 +8% [$P < 0.01$] Not significant: CRP, IL6, IL-1ra, MIF, SAA	No placebo Compliance thoroughly checked	Kempf et al. (2010)
Plasma, serum	-	IL-6, IL-18	ELISA, detection limits: IL-6 0.16 fg/ml; IL-18 ng/ml	RCT, crossover; 16 men (21–39 y); water, 200 ml caffeinated (3 mg caffeine/kg BW), 200 ml decaffeinated coffee; blood drawn every 30 min until 180 min	Serum IL-18 did not change Plasma IL-6 (AUC, IAUC) did not differ between treatments	No placebo	Gavrieli et al. (2011)

[a] unless otherwise specified, the term coffee is used to mean brewed, caffeinated coffee

[b] +, positive; ─, negative; differences: coffee vs control

AUC, area under the curve; CI, confidence interval; CRP, C-reactive protein; d, day; GTT, γ-glutamyltransferase; hs CRP, high-sensitivity CRP; HHQ, hydroxyhydroquinone; F, female; IAUC, incremental AUC; IL, interleukin; IL-1ra, IL-1 receptor antagonist; LR, light roast; M, male; min, minute; mo, month; MR, medium roast; MCP-1, monocyte chemoattractant protein-1; MIF, macrophage migration inhibitory factor; NR, not reported; OR, odds ratio; PAI-1, plasminogen activator inhibitor-1; RCT, randomized clinical trial; SSA, serum amyloid-A; sTNF-R2, sTNF-α-receptor II; sICAM-1, soluble intercellular adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule-1; tPAI-1, total TPAI-1; WBC, white blood cell counts; vs, versus; wk, week; y, year

References

Aleksandrova K, Bamia C, Drogan D, Lagiou P, Trichopoulou A, Jenab M, et al. (2015). The association of coffee intake with liver cancer risk is mediated by biomarkers of inflammation and hepatocellular injury: data from the European Prospective Investigation into Cancer and Nutrition. Am J Clin Nutr. 102(6):1498–508. http://dx.doi.org/10.3945/ajcn.115.116095 PMID:26561631

Arsenault BJ, Earnest CP, Després JP, Blair SN, Church TS (2009). Obesity, coffee consumption and CRP levels in postmenopausal overweight/obese women: importance of hormone replacement therapy use. Eur J Clin Nutr. 63(12):1419–24. http://dx.doi.org/10.1038/ejcn.2009.112 PMID:19756031

Corrêa TA, Rogero MM, Mioto BM, Tarasoutchi D, Tuda VL, César LA, et al. (2013). Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: a clinical trial. Nutrition. 29(7-8):977–81. http://dx.doi.org/10.1016/j.nut.2013.01.003 PMID:23510568

Gavrieli A, Yannakoulia M, Fragopoulou E, Margaritopoulos D, Chamberland JP, Kaisari P, et al. (2011). Caffeinated coffee does not acutely affect energy intake, appetite, or inflammation but prevents serum cortisol concentrations from falling in healthy men. J Nutr. 141(4):703–7. http://dx.doi.org/10.3945/jn.110.137323 PMID:21346100

Kempf K, Herder C, Erlund I, Kolb H, Martin S, Carstensen M, et al. (2010). Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial. Am J Clin Nutr. 91(4):950–7. http://dx.doi.org/10.3945/ajcn.2009.28548 PMID:20181814

Kotani K, Sakane N, Yamada T, Taniguchi N (2010). Association between coffee consumption and the estimated glomerular filtration rate in the general Japanese population: preliminary data regarding C-reactive protein concentrations. Clin Chem Lab Med. 48(12):1773–6. http://dx.doi.org/10.1515/CCLM.2010.347 PMID:20731617

Lee Y, Kang D, Lee SA (2014). Effect of dietary patterns on serum C-reactive protein level. Nutr Metab Cardiovasc Dis. 24(9):1004–11. http://dx.doi.org/10.1016/j.numecd.2014.05.001 PMID:24998076

Loftfield E, Shiels MS, Graubard BI, Katki HA, Chaturvedi AK, Trabert B, et al. (2015). Associations of Coffee Drinking with Systemic Immune and Inflammatory Markers. Cancer Epidemiol Biomarkers Prev. 24(7):1052–60. http://dx.doi.org/10.1158/1055-9965.EPI-15-0038-T PMID:25999212

Lopez-Garcia E, van Dam RM, Qi L, Hu FB (2006). Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr. 84(4):888–93. PMID:17023717

Maki T, Pham NM, Yoshida D, Yin G, Ohnaka K, Takayanagi R, et al. (2010). The relationship of coffee and green tea consumption with high-sensitivity C-reactive protein in Japanese men and women. Clin Chem Lab Med. 48(6):849–54. http://dx.doi.org/10.1515/CCLM.2010.161 PMID:20441477

Pham NM, Zhenjie W, Morita M, Ohnaka K, Adachi M, Kawate H, et al. (2011). Combined effects of coffee consumption and serum γ-glutamyltransferase on serum C-reactive protein in middle-aged and elderly Japanese men and women. Clin Chem Lab Med. 49(10):1661–7. http://dx.doi.org/10.1515/CCLM.2011.652 PMID:21675939

Rebello SA, Chen CH, Naidoo N, Xu W, Lee J, Chia KS, et al. (2011). Coffee and tea consumption in relation to inflammation and basal glucose metabolism in a multi-ethnic Asian population: a cross-sectional study. Nutr J. 10(1):61. http://dx.doi.org/10.1186/1475-2891-10-61 PMID:21631956

Tsioufis C, Dimitriadis K, Vasiliadou C, Taxiarchou E, Vezali E, Tsiamis E, et al. (2006). Heavy coffee consumption in conjunction with smoking is accompanied by increased inflammatory processes and impaired thrombosis/fibrinolysis system in essential hypertensive subjects. J Hum Hypertens. 20(6):470–2. http://dx.doi.org/10.1038/sj.jhh.1002014 PMID:16554843

Williams CJ, Fargnoli JL, Hwang JJ, van Dam RM, Blackburn GL, Hu FB, et al. (2008). Coffee consumption is associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes: a prospective cohort study. Diabetes Care. 31(3):504–7. http://dx.doi.org/10.2337/dc07-1952 PMID:18070989

Zampelas A, Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C (2004). Associations between coffee consumption and inflammatory markers in healthy persons: the ATTICA study. Am J Clin Nutr. 80(4):862–7. PMID:15447891