**Supplementary Table S1a** Oxylipins scanned but below the level of detection (0 to <3 times baseline)

**ARA Oxylipins**

2,3-dinor-11β-PGF2α; 2,3-dinor-TxB2; 5,6-dihydroxy eicosatetraenoic acid; 5-hydroxy eicosatrienoic acid; 5-iso-PGF2αVI; 6,15-diketo-13,14-dihydro PGF1α; 6k-PGE1; 6-LXA4; 6-trans-LTB4; 11β-dihydroketo-PGF2α; 11β-PGE2; 11β-PGF2α; 11-dehydro-TxB2; 12-epi-LTB4; 12-oxo-LTB4; 14,15-LTC4 (EXC4); 14,15-LTD4 (EXD4); 14,15-LTE4 (EXE4); 15-deoxy-PGA2; 15-deoxy-PGJ2; 15k-PGF2α; 19-HETE; 19oh -PGE2; 19oh -PGF2α; 20-carboxy-LTB4; 20-HETE; 20oh-LTB4; 20oh-PGE2; 20oh-PGF2α; bicyclo-PGE2; dihydro-PGF2α; dihydroketo-PGD2; dihydroketo-PGE2; Hepoxilin A3; Hepoxilin B3; LTC4; LTD4; LTE4; LXA5; LXB4; PGA2; PGB2; PGK1; PGK2; tetranor-12-hydroxy-eicosatetraenoic acid; tetranor-PGD metabolite; tetranor-PGE metabolite; tetranor-PGF metabolite.

**Other Oxylipins**

2,3-dinor 8-iso-PGF2α; 8,15-dihydroxy-eicosatetraenoic acid; 8-iso-15k-PGF2β; 8-iso-PGF2αIII; 8-iso-PGF3α; 9,10-EpODE; 9-Nitrooleate; 10-Nitrooleate; 11-hydroxy-eicosapentaenoic acid; 13-oxo-octadecatrienoic acid; 15,16-dihydroxy-octadecadienoic acid; 15,16-epoxy-octadecadienoic acid; 15-oxo-eicosadienoic acid; 17-hydroxy-eicosatetraenoic acid; 17k-DHA; 17k-DPA; dihomo-15-deoxy-PGD2; dihomo-PGD2; dihomo-PGE2; dihomo-PGF2α; dihomo-PGJ2; Protectin D1; PGE1; PGF3α; RvD1; RvD2; RvE1; TxB1; TxB3.

**Supplementary Table S1b** Oxylipins detected but below the level of quantification (>3 to <5 times baseline)

2,3-dinor-6k-PGF1α; 7-Maresin-1; 15k-PGD2; 15k-PGF1α; 15-LXA4; 20-carboxy-ARA; Dhk-PGF2α; PGD1; PGD3; PGE3; PGF2α.

EX, eoxin; k, keto; LT, leukotriene; LX, lipoxilin; oh, hydroxy; PG, prostaglandin; Rv, resolving; Tx, thromboxane.

**Supplementary Table S2** Diet and sex effects on heart n-3 oxylipins in rats given control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diet | Control | | ALA | | EPA | | DHA | | LA | | LA+ALA | | P value | | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Diet | Sex | Int.# |
| ng/g | | | | | | | | | | | | | | | |
| ALA Oxylipins | | | | | | | | | | | | | | | |
| 9-HOTrE | 60.6±9.62C | 62.8±11.6 | 1015±118A | 650±95.8 | 85.9±14.6C | 63.9±11.0 | 99.8±11.6C | 87.2±20.4 | 116±5.25C | 57.5±8.38 | 200±40.6B | 156±37.9 | <0.0001 | 0.0018 |  |
| 9-oxoOTrE | 106±16.6cd | 125±24.8bcd | 1428±155a | 887±130a | 127±24.4bcd | 139±22.2bcd | 84.2±14.1d | 119±14.4bcd | 174±25.1bcd | 83.0±12.6d | 289±67.4b | 259±52.3bc |  |  | 0.0251 |
| 13-HOTrE | 54.9±7.77D | 55.8±11.2 | 1056±117A | 765±149 | 84.9±8.01D | 51.8±8.71 | 70.7±6.80CD | 79.9±13.8 | 151±14.4BC | 81.8±13.5 | 188±22.6B | 157±40.9 | <0.0001 | 0.0022 |  |
| 9,10-DiHODE† | 0.32±0.06 | 0.23±0.03 | 0.36±0.06 | 0.21±0.04 | 0.50±0.16 | 0.33±0.06 | 0.21±0.04 | 0.43±0.10 | 0.46±0.13 | 0.38±0.06 | 0.72±0.23 | 0.38±0.08 | 0.20 | 0.33 |  |
| 12,13-EpODE | 2.84±0.83c | 2.55±0.59c | 65.9±5.84a | 15.5±1.84b | 6.74±2.02bc | 3.26±0.48c | 3.68±0.69c | 3.82±1.01c | 3.57±1.13c | 2.10±0.51c | 9.48±2.79bc | 6.10±1.68c |  |  | <0.0001 |
| 12,13-DiHODE | 0.29±0.03C | 0.29±0.04 | 2.14±0.23A | 1.29±0.13 | 0.30±0.04C | 0.31±0.05 | 0.47±0.11BC | 0.32±0.06 | 0.45±0.05BC | 0.41±0.03 | 0.65±0.09B | 0.45±0.05 | <0.0001 | 0.0188 |  |
| EPA Oxylipins | | | | | | | | | | | | | | | |
| Δ17-6k-PGF1α | 0.51±0.16C | 0.53±0.12 | 2.86±0.49B | 2.64±0.69 | 14.2±1.64A | 18.1±2.45 | 2.54±0.49B | 1.91±0.39 | 0.53±0.14C | 0.30±0.06 | 0.90±0.39C | 0.79±0.21 | <0.0001 | 0.52 |  |
| 5-HEPE | 27.8±3.92C | 29.7±5.71 | 515±110B | 323±33.9 | 3840±282A | 3121±565 | 364±17.0B | 353±57.0 | 30.4±6.02C | 22.5±1.83 | 40.5±4.72C | 39.3±3.56 | <0.0001 | 0.06 |  |
| 8-HEPE | 14.0±2.14CD | 13.6±3.42 | 170±23.1B | 127±17.4 | 931±18.3A | 915±169 | 153±9.69B | 133±20.0 | 10.57±1.82D | 14.8±1.78 | 19.8±1.52C | 18.8±2.66 | <0.0001 | 0.46 |  |
| 9-HEPE | 34.8±6.12D | 31.9±4.17 | 656±141B | 503±93.4 | 3340±129A | 4017±386 | 459±48.7B | 474±81.7 | 57.1±11.3CD | 27.3±5.38 | 61.7±11.5C | 53.6±6.93 | <0.0001 | 0.12 |  |
| 12-HEPE | 8.22±1.13D | 7.04±1.60 | 129±15.5B | 99.0±13.3 | 749±43.4A | 572±134 | 114±9.40B | 101±14.6 | 8.35±1.48D | 5.22±0.77 | 13.0±1.57C | 12.4±2.12 | <0.0001 | 0.0041 |  |
| 15-HEPE | 4.49±0.49D | 4.69±0.93 | 103±10.9B | 94.9±16.8 | 745±41.4A | 782±103 | 94.9±11.5B | 96.8±14.8 | 6.16±0.87D | 5.26±0.71 | 11.4±1.29C | 9.38±1.82 | <0.0001 | 0.33 |  |
| 14,15-EpETE | –¥b | –b | 2.06±0.48b | 0.52±0.11b | 24.8±8.13a | 15.8±4.07a | 1.40±0.32b | 1.51±0.40b | –b | –b | –b | –b |  |  | <0.0001$ |
| 17,18-EpETE | 0.28±0.06d | 0.39±0.06d | 5.18±0.93b | 1.53±0.42c | 38.5±8.43a | 40.9±7.90a | 3.04±0.69bc | 3.06±0.42bc | 0.20±0.05d | 0.16±0.04d | 0.39±0.06d | 0.33±0.07d |  |  | 0.0093 |
| 18-HEPE | 4.42±0.54d | 3.79±0.25d | 102±10.8b | 44.7±4.89c | 871±57.9a | 1230±218a | 86.8±12.3bc | 59.7±12.5bc | 3.86±0.67d | 0.93±0.26e | 5.36±0.92d | 3.34±0.33d |  |  | 0.0002 |
| DHA Oxylipins | | | | | | | | | | | | | | | |
| 4-HDoHE | 585±86.9B | 236±40.3 | 694±99.1B | 194±22.7 | 416±45.1B | 253±50.9 | 2417±246A | 2008±268 | 277±45.9B | 182±37.0 | 503±110B | 198±47.3 | <0.0001 | <0.0001 |  |
| 7-HDoHE | 318±34.7bcd | 119±9.91e | 443±42.6b | 163±28.6de | 266±19.8bcd | 190±43.8cde | 1558±174a | 998±121a | 390±67.3bc | 97.4±18.4e | 369±62.8bc | 163±35.7de |  |  | 0.0245 |
| 8-HDoHE | 180±35.8B | 96.8±31.0 | 307±30.0B | 93.8±19.6 | 149±13.9B | 124±30.7 | 960±114A | 534±62.9 | 202±48.2B | 81.5±24.0 | 227±42.3B | 92.6±26.5 | <0.0001 | <0.0001 |  |
| 10-HDoHE | 165±24.4c | 86.4±34.8c | 234±29.2c | 97.1±19.9c | 139±13.7c | 91.6±25.5c | 838±81.6a | 440±33.4b | 229±46.4c | 83.4±22.4c | 189±35.7c | 85.8±28.9c |  |  | 0.0005 |
| 11-HDoHE | 170±23.2cd | 86.4±27.0d | 288±40.7c | 89.2±18.8d | 139±14.6cd | 94.3±24.6d | 934±68.1a | 620±90.2b | 200±30.9cd | 65.2±17.8d | 207±45.2cd | 77.3±13.7d |  |  | 0.0158 |
| 13-HDoHE | 134±14.8bc | 40.2±2.85e | 199±25.1b | 75.4±14.9cde | 125±14.3bc | 120±34.2bcd | 714±109a | 511±63.0b | 112±21.3bcd | 48.5±3.12de | 158±35.8bc | 50.8±7.97de |  |  | 0.0101 |
| 14-HDoHE | 126±17.9cdef | 36.0±4.00h | 196±25.3bc | 55.1±5.23fgh | 132±23.9cde | 78.1±18.2defgh | 579±71.8a | 416±23.2ab | 108±23.5cdefg | 55.3±3.95efgh | 195±43.2bcd | 50.6±11.0gh |  |  | 0.0081 |
| 16-HDoHE | 206±22.9BC | 67.6±8.11 | 306±44.9B | 83.1±7.17 | 189±29.5BC | 102±22.8 | 914±130A | 661±65.7 | 151±28.2C | 53.8±10.0 | 197±46.4BC | 81.0±13.8 | <0.0001 | <0.0001 |  |
| 17-HDoHE | 668±66.3B | 235±30.0 | 1049±134B | 357±44.2 | 645±94.6B | 467±119 | 3186±472A | 2403±198 | 556±94.1B | 259±22.5 | 666±157B | 279±36.2 | <0.0001 | <0.0001 |  |
| PDX | 11.3±2.28cd | 4.69±0.75d | 15.9±1.50bc | 8.13±1.59cd | 10.6±1.49cd | 7.59±2.03cd | 47.5±3.54a | 27.0±2.20b | 15.2±3.50c | 8.46±1.90cd | 10.6±1.22cd | 9.04±2.56cd |  |  | 0.0034 |
| 15*t* PD1† | 3.44±0.44cd | 1.41±0.26d | 5.70±0.64c | 2.22±0.40d | 3.55±0.42cd | 2.16±0.52d | 16.3±0.56a | 9.75±0.98b | 3.60±0.69cd | 1.87±0.50d | 3.20±0.32cd | 2.05±0.54d |  |  | 0.0001 |
| RvD5† | 2.49±0.45B | 0.82±0.19 | 3.51±0.34B | 1.31±0.21 | 2.15±0.46B | 1.36±0.26 | 8.86±0.85A | 7.30±1.59 | 3.07±0.76B | 0.93±0.24 | 1.96±0.28B | 1.41±0.39 | <0.0001 | <0.0001 |  |
| 16,17-EpDPE | 40.6±6.53B | 12.7±1.51 | 45.1±11.0BC | 8.26±1.36 | 34.6±9.72B | 18.6±4.23 | 143±22.9A | 113±19.9 | 13.1±2.50C | 7.28±2.27 | 34.8±10.8BC | 11.3±2.27 | <0.0001 | <0.0001 |  |
| 19,20-EpDPE | 4.04±0.81B | 1.11±0.20 | 4.17±1.02B | 0.56±0.15 | 2.60±0.97B | 1.04±0.39 | 9.92±1.98A | 7.36±1.82 | 2.69±1.14B | 0.69±0.35 | 4.24±1.10B | 0.85±0.25 | <0.0001 | <0.0001 |  |
| 19,20-DiHDoPE | 4.29±0.45b | 2.20±0.27cd | 4.09±0.41b | 2.13±0.18cd | 3.46±0.24bc | 2.64±0.46bcd | 19.9±1.39a | 21.6±0.98a | 2.45±0.36bcd | 2.02±0.34cd | 3.56±0.62bc | 1.85±0.25d |  |  | 0.0409 |
| 20-HDoHE | 312±48.5cd | 137±10.9degf | 419±62.7bc | 118±11.1fg | 314±54.2cd | 283±54.7cde | 1392±189a | 751±84.6ab | 225±20.3cdef | 84.5±10.6g | 423±80.5bc | 127±12.5efg |  |  | 0.0047 |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Different upper-case superscripts on the female values within a row indicate significant main effects of diet (P< 0.05). Different lower-case superscripts within a row indicate simple effect differences between means (P< 0.05). P values for sex effects are shaded pink when levels are higher in female hearts. #Int. represents interaction between diet and sex unless noted with superscript $ which denotes that Pvalues were obtained from the Kruskal-Wallis test because the data were not normally distributed. †Denotes no primary standard, so not quantified. ¥Denotes not detected. ALA, alpha-linolenic acid; DiHDoPE, dihydroxy-docosapentaenoic acid; DiHODE, dihydroxy-octadecadienoic acid; EpDPE, epoxy-docosapentaenoic acid; EpETE, epoxy-eicosatetraenoic acid; EpODE, epoxy- octadecadienoic acid; HDoHE, hydroxy-docosahexaenoic acid; HEPE, hydroxy-eicosapentaenoic acid; HOTrE, hydroxy-octadecatrienoic acid; LA, linoleic acid; oxoOTrE, oxo- octadecatrienoic acid; PD, protectin; Rv, resolvin.

**Supplementary Table S3** Diet and sex effects on the heart n-6 oxylipins in rats given control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diet | Control | | ALA | | EPA | | DHA | | LA | | LA+ALA | | P value | | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Diet | Sex | Int.# |
| ng/g | | | | | | | | | | | | | | | |
| LA Oxylipins | | | | | | | | | | | | | | | |
| 9-HODE | 2428±391 | 2114±392 | 3747±494 | 1651±180 | 3782±815 | 2570±383 | 2446±347 | 3247±681 | 5176±1266 | 3131±702 | 5275±1265 | 3557±873 | 0.07 | 0.0117 |  |
| 9-oxoODE | 945±213abc | 1037±413abc | 1120±157abc | 594±209bc | 1762±535abc | 1265±249abc | 400±88.9c | 904±191abc | 3243±1032a | 615±154abc | 2469±801ab | 1313±420abc |  |  | 0.0157 |
| 13-HODE | 1076±119bc | 1090±201bc | 1547±157bc | 972±111c | 1686±213abc | 1326±189bc | 945±120c | 1180±94.1bc | 3456±497a | 1820±374abc | 2168±276ab | 2357±612ab |  |  | 0.0476 |
| 13-oxoODE | 6294±672BC | 5921±1252 | 7660±475BC | 5947±1105 | 9385±2063ABC | 7581±963 | 3419±463C | 5982±757 | 18486±3433A | 8421±1786 | 12496±3214AB | 8712±2886 | 0.0004 | 0.0259 |  |
| 9,10,13-TriHOME | 1238±237C | 1210±241 | 1774±274BC | 2174±279 | 1321±206C | 1447±346 | 2121±391AB | 3248±474 | 3302±344A | 2513±406 | 3290±293A | 3043±669 | <0.0001 | 0.65 |  |
| 9,12,13-TriHOME | 534±140e | 1184±138bcde | 1150±143cde | 1576±218abcde | 889±145de | 1086±125cde | 1002±184cde | 2028±267abcd | 2683±277a | 1991±247abcd | 2188±263abc | 2468±671ab |  |  | 0.0313 |
| 9,10-EpOME | 13.9±3.44b | 13.0±2.76b | 23.3±2.25b | 5.33±1.78b | 14.5±4.83b | 16.3±2.65b | 13.0±2.63b | 16.0±4.99b | 20.8±6.45b | 17.3±3.91b | 61.7±4.17a | 13.7±2.58b |  |  | <0.0001 |
| 9,10-DiHOME | 4.11±0.68B | 3.58±0.29 | 3.99±0.43B | 2.34±0.36 | 3.80±0.33B | 3.87±0.39 | 3.69±0.14B | 4.48±0.90 | 9.70±1.04A | 7.15±1.03 | 6.41±1.11A | 6.45±1.30 | <0.0001 | 0.07 |  |
| 12,13-EpOME | 4.55±0.91bcd | 5.21±1.17bcd | 9.88±0.92b | 2.00±0.75d | 6.19±1.98bcd | 7.47±1.29bcd | 5.67±1.28bcd | 2.92±0.42cd | 9.71±2.32bc | 5.72±1.18bcd | 26.1±1.36a | 5.74±1.11bcd |  |  | <0.0001 |
| 12,13-DiHOME | 4.68±0.67BC | 3.26±0.28 | 4.00±0.59C | 2.09±0.42 | 4.42±0.53BC | 3.61±0.37 | 3.60±0.27C | 3.51±0.76 | 8.07±0.69A | 6.07±0.88 | 6.42±1.06AB | 5.51±1.11 | <0.0001 | 0.0043 |  |
| GLA Oxylipins | | | | | | | | | | | | | | | |
| 13-HOTrEγ | 6.82±0.71BC | 5.44±0.90 | 6.83±0.29C | 3.71±0.47 | 3.58±0.20D | 2.43±0.42 | 3.09±0.30D | 3.02±0.38 | 14.3±2.23A | 8.49±1.01 | 11.1±1.50AB | 6.14±1.25 | <0.0001 | <0.0001 |  |
| DGLA Oxylipins | | | | | | | | | | | | | | | |
| PGF1α | 0.76±0.11 | 0.78±0.11 | 0.42±0.07 | 0.54±0.11 | 0.76±0.16 | 0.58±0.04 | 0.67±0.09 | 0.56±0.06 | 0.75±0.11 | 0.59±0.09 | 0.69±0.09 | 0.63±0.08 | 0.11 | 0.29 |  |
| 8-HETrE | 17.1±1.76bc | 13.5±3.19c | 24.2±3.34abc | 15.5±2.83bc | 21.1±2.69abc | 17.8±3.48abc | 11.5±1.23c | 14.6±2.87bc | 31.7±3.10a | 18.1±2.61abc | 27.9±4.01ab | 15.1±2.93bc |  |  | 0.0493 |
| 15-HETrE | 5.44±0.87bc | 4.07±0.29c | 6.39±0.82bc | 4.17±0.55c | 9.45±1.51ab | 4.50±1.19c | 3.93±0.58c | 4.23±0.86c | 7.96±1.32abc | 6.00±1.09bc | 11.8±1.87a | 3.88±0.35c |  |  | 0.0029 |
| ARA Oxylipins | | | | | | | | | | | | | | | |
| PGD2 | 11.7±0.90A | 9.82±1.33 | 6.13±0.78B | 4.01±0.73 | 6.01±1.36B | 5.28±0.61 | 1.96±0.28C | 2.59±0.61 | 10.1±1.06A | 8.58±1.04 | 7.73±1.29A | 10.7±0.67 | <0.0001 | 0.40 |  |
| 15d-PGD2 | 1.36±0.15bcd | 1.00±0.15cd | 1.10±0.11cd | 0.56±0.09cd | 2.54±0.41ab | 2.66±0.50a | 0.37±0.10d | 0.53±0.09cd | 1.57±0.34abc | 0.94±0.18cd | 1.05±0.18cd | 0.57±0.08cd |  |  | <0.0001$ |
| PGJ2 | 2.87±0.34ab | 1.91±0.27bc | 1.82±0.35bc | 1.97±0.30bc | 0.40±0.07c | 0.37±0.13c | 2.26±0.28ab | 3.82±0.51a | 2.65±0.44ab | 2.66±0.49ab | 2.09±0.26abc | 1.92±0.27bc |  |  | 0.0298 |
| 6k-PGF1α | 16.6±2.09A | 17.0±1.82 | 8.84±2.29B | 6.29±1.30 | 2.52±0.55C | 3.35±0.62 | 1.99±0.53C | 1.51±0.27 | 21.4±2.74A | 25.1±4.71 | 14.8±1.73A | 20.8±2.81 | <0.0001 | 0.73 |  |
| PGE2 | 5.63±0.46A | 4.08±0.43 | 3.20±0.26B | 1.73±0.21 | 4.02±0.37A | 3.56±0.32 | 1.17±0.17C | 1.35±0.21 | 4.26±0.75A | 3.78±0.59 | 4.64±1.10A | 3.63±0.63 | <0.0001 | 0.0159 |  |
| 15k-PGE2 | 4.21±0.46B | 2.51±0.33 | 2.44±0.22BC | 1.45±0.22 | 5.72±1.15A | 4.33±0.70 | 1.17±0.17C | 2.19±0.46 | 3.25±0.32BC | 2.68±0.48 | 3.12±0.64BC | 2.23±0.31 | <0.0001 | 0.0159 |  |
| TxB2 | 1.83±0.16ab | 1.99±0.12a | 1.13±0.05cde | 0.68±0.06de | 0.72±0.13de | 0.63±0.05e | –¥b | –b | 1.67±0.12abc | 2.27±0.07a | 1.28±0.14bcd | 2.11±0.27a |  |  | <0.0001$ |
| 12-HHTrE | 616±77.6A | 581±42.2 | 405±32.6B | 392±54.9 | 218±31.8C | 260±40.0 | 90.7±21.0C | 128±10.4 | 715±38.0A | 575±49.1 | 550±53.0A | 589±98.7 | <0.0001 | 0.70 |  |
| 5-HETE | 662±39.8A | 460±74.5 | 516±52.1B | 230±36.4 | 365±60.2B | 264±51.1 | 119±14.5C | 147±34.8 | 782±90.5A | 448±73.8 | 583±102AB | 366±76.5 | <0.0001 | <0.0001 |  |
| 5-oxoETE | 367±46.3A | 199±29.1 | 231±35.0AB | 82.4±16.4 | 291±69.6A | 216±47.7 | 42.1±8.82B | 47.2±9.51 | 216±41.6AB | 160±35.1 | 242±84.5A | 174±53.3 | 0.0002 | 0.0035 |  |
| 5,15-DiHETE | 6.62±1.09ab | 4.46±1.05abc | 5.97±0.81ab | 1.55±0.35c | 4.73±1.21abc | 3.54±0.66bc | 1.92±0.39c | 1.69±0.65c | 8.49±0.58a | 3.24±0.65bc | 4.15±1.08abc | 5.01±1.12abc |  |  | 0.0050 |
| 8-HETE | 1286±143ab | 999±179bcd | 1083±98.1bc | 554±94bcd | 733±121bcd | 591±141bcd | 243±37.3d | 306±67.5cd | 2035±351a | 1053±172bc | 1353±210ab | 858±160bcd |  |  | 0.0488 |
| 9-HETE | 623±58.4ab | 363±66.4bc | 513±29.5b | 299±53.3bc | 349±44.7bc | 304±86.2bc | 118±18.7c | 154±31.9c | 958±109a | 509±99.3b | 620±105ab | 421±81.6bc |  |  | 0.0229 |
| 11-HETE | 1578±139b | 1067±209bcde | 1404±131bc | 728±120cde | 1071±194bcd | 649±177cde | 280±50.5e | 381±94.7de | 2504±277a | 1141±211bcd | 1436±238bc | 972±196bcde |  |  | 0.0063 |
| 12-HETE | 139±20.7AB | 87.2±12.8 | 91.7±7.38B | 47.3±6.32 | 89.8±18.5B | 61.2±14.1 | 26.6±3.54C | 29.7±7.26 | 144±27.6A | 107±17.8 | 94.4±23.1AB | 75.8±16.0 | <0.0001 | 0.0036 |  |
| 12-oxoETE | 34.0±3.85AB | 23.0±4.11 | 21.3±2.05ABC | 22.8±2.84 | 14.0±3.11D | 15.1±4.69 | 6.94±1.60D | 6.25±1.10 | 42.3±8.28A | 24.9±6.74 | 16.0±2.80BCD | 17.4±5.53 | <0.0001 | 0.11 |  |
| 15-HETE | 648±55.2AB | 375±43.7 | 541±70.3AB | 266±35.6 | 444±89.1BC | 269±58.1 | 129±22.5C | 184±40.0 | 661±119A | 500±85.4 | 551±104AB | 385±55.4 | <0.0001 | 0.0001 |  |
| 15-oxoETE | 559±50.1A | 438±102 | 342±22.6BC | 232±50.5 | 348±74.6AB | 348±89.1 | 102±32.0C | 149±27.1 | 433±60.1AB | 301±65.4 | 366±112ABC | 234±80.1 | <0.0001 | 0.07 |  |
| 6t,12epi-LTB4 | 10.4±1.71A | 5.16±0.96 | 8.99±1.23A | 3.76±0.92 | 7.65±1.76A | 4.22±1.00 | 1.29±0.47B | 2.21±0.80 | 10.3±2.62A | 6.64±1.59 | 5.57±1.82AB | 4.07±1.31 | 0.0002 | 0.0005 |  |
| LTB4 | 9.91±1.40a | 5.73±1.00abc | 8.11±0.80ab | 3.13±0.60bcd | 5.09±0.85abc | 5.11±1.28abc | 1.69±0.24d | 2.36±0.38cd | 7.66±1.18ab | 5.76±1.38abc | 8.66±2.23ab | 4.08±1.11abcd |  |  | 0.0324 |
| 5,6-EpETrE | 4.70±0.67b | 3.44±0.63bcd | 3.97±0.94bc | 0.56±0.06d | 2.42±0.54bcd | 2.44±0.51bcd | 1.15±0.27cd | 1.26±0.31cd | 2.83±0.72bcd | 1.90±0.34bcd | 8.17±1.43a | 2.83±0.50bcd |  |  | 0.0003 |
| 5,6-DiHETrE | 13.0±1.27A | 9.34±0.89 | 7.53±0.48CD | 5.13±0.84 | 6.76±1.13CD | 5.66±0.80 | 3.66±0.42D | 3.86±0.40 | 9.65±1.04AB | 9.95±1.43 | 8.12±0.54BC | 8.27±1.04 | <0.0001 | 0.05 |  |
| 8,9-EpETrE | 14.4±3.11A | 8.03±1.05 | 13.0±2.61A | 3.47±0.85 | 11.2±3.50A | 7.37±1.92 | 2.75±0.44B | 3.16±0.58 | 7.52±1.46A | 6.44±1.07 | 12.7±3.77A | 6.88±1.44 | <0.0001 | 0.0019 |  |
| 8,9-DiHETrE | 1.17±0.13A | 0.97±0.16 | 0.73±0.08B | 0.41±0.08 | 0.47±0.11BC | 0.35±0.11 | 0.17±0.09C | 0.21±0.07 | 1.07±0.11A | 0.93±0.14 | 1.21±0.21A | 0.97±0.15 | <0.0001 | 0.0284 |  |
| 11,12-EpETrE | 7.49±1.66A | 3.73±0.41 | 5.84±1.15AB | 1.47±0.44 | 4.86±1.54A | 3.00±0.65 | 1.37±0.24B | 1.49±0.35 | 5.26±1.61A | 3.25±0.56 | 6.26±1.83A | 3.25±0.62 | <0.0001 | 0.0007 |  |
| 11,12-DiHETrE | 2.16±0.18A | 1.60±0.19 | 1.36±0.11BC | 0.78±0.10 | 1.11±0.13BC | 0.97±0.08 | 0.61±0.12C | 0.64±0.09 | 1.77±0.12A | 1.89±0.29 | 1.36±0.09AB | 1.64±0.30 | <0.0001 | 0.17 |  |
| 14,15-EpETrE | 22.9±5.75a | 8.58±1.42cd | 12.3±2.78abc | 2.79±0.89cd | 5.81±1.40cd | 7.21±1.47cd | 2.70±0.61d | 3.30±0.98cd | 9.90±1.59bcd | 7.00±1.50cd | 19.5±3.93ab | 6.76±1.58d |  |  | 0.0007 |
| 14,15-DiHETrE | 6.70±0.74A | 4.46±0.25 | 3.84±0.38B | 2.19±0.28 | 3.40±0.41B | 2.87±0.30 | 1.69±0.34B | 1.64±0.28 | 4.55±0.48A | 4.91±0.69 | 5.05±0.91A | 4.87±0.80 | <0.0001 | 0.0217 |  |
| 16-HETE | 52.4±5.10A | 32.4±1.66 | 31.3±3.47BC | 24.5±2.70 | 23.4±3.07CD | 20.7±2.43 | 13.6±1.57D | 17.3±1.47 | 53.9±9.17A | 35.9±4.08 | 41.2±5.70AB | 34.4±5.84 | <0.0001 | 0.0080 |  |
| 18-HETE | 1.35±0.11 | 1.05±0.13 | 1.09±0.16 | 1.04±0.27 | 1.18±0.52 | 1.32±0.32 | 0.87±0.22 | 1.03±0.34 | 1.67±0.34 | 1.85±0.26 | 1.39±0.31 | 1.08±0.08 | 0.10 | 0.87 |  |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Different upper-case superscripts on the female values within a row indicate significant main effects of diet (P< 0.05). Different lower-case superscripts within a row indicate simple effect differences between means (P< 0.05). P values for sex effects are shaded pink when levels are higher in female hearts. #Int. represents interaction between diet and sex unless noted with superscript $ which denotes that Pvalues were obtained from the Kruskal-Wallis test because the data were not normally distributed. ¥Denotes not detected. ALA, alpha-linolenic acid; d, deoxy; DGLA, dihomo-gamma-linolenic acid; DiHETE, dihydroxy-eicosatetraenoic acid; DiHETrE, dihydroxy-eicosatrienoic acid; DiHOME, dihydroxy-octadecenoic acid; EpETrE, epoxy-eicosatrienoic acid; EpOME, epoxy-octadecenoic acid; GLA, gamma-linoleic acid; HETE, hydroxy-eicosatetraenoic acid; HETrE, hydroxy-eicosatrienoic acid; HHTrE, hydroxy-heptadecatrienoic acid; HODE, hydroxy-octadecadienoic acid; k, keto; LA, linoleic acid; LT, leukotriene; oxoETE, oxo-eicosatetraenoic acid; oxoODE, oxo-octadecadienoic acid; TriHOME, trihydroxy-octadecenoic acid; Tx, thromboxane; γ, gamma.

**Supplementary Table S4** Distributions of heart oxylipins and PUFA mass in rats provided the control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | % of total oxylipins /PUFA | | | | | | |
| Diet | Sex | Oxylipin  /PUFA | ALA | | EPA | DHA | Other n-3 | LA | ARA | Other n-6 |
| Control | Female | Oxylipin | 1.00 | | 0.42 | 13.0 |  | 55.8 | 29.8 | 0.13 |
| PUFA-PL | 0.18 | | 0.04 | 19.5 | 2.40 | 34.0 | 38.9 | 5.04 |
| -NL | 3.26 | |  | 9.18 | 1.85 | 62.2 | 19.5 | 4.08 |
| Male | Oxylipin | 1.31 | | 0.49 | 6.19 |  | 66.9 | 25.1 | 0.13 |
| PUFA-PL | 0.26 | | 0.10 | 14.8 | 1.77 | 39.8 | 38.1 | 5.25 |
| -NL | 4.60 | |  | 3.31 | 2.16 | 72.3 | 13.5 | 4.14 |
| ALA | Female | Oxylipin | 11.2 | | 5.31 | 13.3 |  | 53.6 | 16.6 | 0.12 |
| PUFA-PL | 2.64 | | 2.07 | 19.9 | 7.35 | 41.4 | 25.0 | 1.70 |
| -NL | 33.1 | | 2.33 | 5.79 | 5.05 | 44.9 | 8.01 | 0.88 |
| Male | Oxylipin | 11.2 | | 5.78 | 6.51 |  | 62.4 | 14.1 | 0.12 |
| PUFA-PL | 3.19 | | 1.76 | 14.1 | 7.11 | 48.2 | 23.9 | 1.74 |
| -NL | 32.6 | | 1.55 | 4.48 | 5.24 | 47.3 | 7.78 | 1.11 |
| EPA | Female | Oxylipin | 0.84 | | 29.1 | 7.08 |  | 52.0 | 11.1 | 0.10 |
| PUFA-PL | 0.37 | | 9.89 | 12.3 | 13.8 | 42.9 | 19.5 | 1.29 |
| -NL | 3.94 | | 16.7 | 3.38 | 9.42 | 60.1 | 5.12 | 1.29 |
| Male | Oxylipin | 0.83 | | 34.4 | 5.89 |  | 49.1 | 9.82 | 0.08 |
| PUFA-PL | 0.40 | | 10.1 | 10.1 | 12.5 | 44.5 | 21.2 | 1.30 |
| -NL | 3.82 | | 17.2 | 4.03 | 6.38 | 60.4 | 6.86 | 1.37 |
| DHA | Female | Oxylipin | 0.97 | | 4.77 | 51.2 |  | 38.6 | 4.47 | 0.07 |
| PUFA-PL | 0.14 | | 1.67 | 45.8 | 2.16 | 40.7 | 8.19 | 1.38 |
| -NL | 2.84 | | 2.43 | 39.4 | 3.92 | 48.7 | 1.69 | 1.01 |
| Male | Oxylipin | 0.99 | | 4.19 | 32.6 |  | 56.8 | 5.42 | 0.08 |
| PUFA-PL | 0.28 | | 1.89 | 38.3 | 2.20 | 45.6 | 9.76 | 1.90 |
| -NL | 2.37 | | 1.77 | 59.3 | 3.41 | 29.2 | 3.02 | 0.90 |
| LA | Female | Oxylipin | 0.93 | | 0.24 | 5.18 |  | 75.7 | 18.0 | 0.12 |
| PUFA-PL | 0.08 | | 0.01 | 13.5 | 1.44 | 41.9 | 34.7 | 8.43 |
| -NL | 2.32 | |  | 2.50 | 0.54 | 81.1 | 9.33 | 4.21 |
| Male | Oxylipin | 0.91 | | 0.31 | 4.16 |  | 74.7 | 20.0 | 0.13 |
| PUFA-PL | 0.19 | | 0.03 | 8.89 | 1.64 | 45.3 | 35.5 | 8.50 |
| -NL | 2.12 | |  | 2.51 | 0.80 | 77.8 | 11.7 | 5.06 |
| LA+ALA | Female | Oxylipin | 1.81 | | 0.40 | 8.41 |  | 73.7 | 15.7 | 0.14 |
| PUFA-PL | 0.45 | | 0.08 | 18.9 | 6.01 | 39.2 | 31.4 | 4.02 |
| -NL | 4.68 | | 0.05 | 4.80 | 1.98 | 74.9 | 10.5 | 3.15 |
| Male | Oxylipin | 2.09 | | 0.50 | 4.45 |  | 77.7 | 15.3 | 0.10 |
| PUFA-PL | 0.61 | | 0.09 | 11.5 | 3.73 | 46.0 | 33.4 | 4.65 |
| -NL | 4.85 | |  | 3.27 | 1.03 | 76.2 | 11.2 | 3.41 |

ALA, α-linolenic acid; LA, linoleic acid; NL, neutral lipid; PL, phospholipid.

**Supplementary Table S5** Heart weights at termination in rats given control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diet | Control | | ALA | | EPA | | DHA | | LA | | ALA+LA | | P Value | | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Diet | Sex | Int.# |
| Heart, g | 1.09±0.04b | 1.47±0.02a | 1.03±0.04b | 1.52±0.05a | 0.99±0.05b | 1.56±0.02a | 1.12±0.04b | 1.45±0.02a | 0.99±0.03b | 1.53±0.05a | 1.03±0.04b | 1.49±0.06a |  |  | 0.0411 |
| Heart/Body, mg/g | 3.44±0.12 | 2.89±0.06 | 3.41±0.10 | 3.07±0.08 | 3.23±0.05 | 3.04±0.06 | 3.29±0.06 | 3.15±0.05 | 3.41±0.05 | 3.11±0.11 | 3.19±0.12 | 3.02±0.09 | 0.37 | <0.0001 |  |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Mean values within a row with differing superscript letters are significantly different (P<0.05). P value for sex effect is shaded in pink when oxylipins are higher in female hearts. #Int. represents interaction between diet and sex (P<0.05). Body weight data have been published in references 23 and 24. ALA, α-linolenic acid; LA, linoleic acid.

**Supplementary Table S6** Diet and sex effects on heart PL PUFA in rats given control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diet  Sex | Control | | ALA | | EPA | | DHA | | LA | | LA + ALA | | P Value | | |
| Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Diet | Sex | Int.# |
| µg/g | | | | | | | | | | | | | | | |
| SFA | | | | | | | | | | | | | | | |
| 14:0 | 9.59±4.14B | 11.8±2.71 | 17.5±3.57A | 20.9±2.70 | 20.6±3.47A | 20.9±2.70 | 13.4±1.57A | 25.8±4.49 | 9.42±1.69AB | 17.6±3.90 | 17.7±2.85A | 19.2±4.93 | 0.0006 | 0.0057 |  |
| 16:0 | 1049±123 | 1238±136 | 1077±117 | 1340±124 | 1150±108 | 1090±136 | 1094±36.5 | 1523±265 | 864±90.6 | 1156±86.4 | 1377±79.8 | 1346±120 | 0.05 | 0.0197 |  |
| 18:0 | 2126±280ab | 2380±281ab | 2351±293ab | 2807±273ab | 2503±300ab | 2053±266ab | 1806±72.6b | 2354±369ab | 1947±181b | 2275±169ab | 3101±172a | 2765±196ab |  | | 0.0130$ |
| 20:0 | 38.0±6.22AB | 44.4±4.53 | 35.8±4.53AB | 44.9±3.62 | 39.1±5.74B | 31.3±4.58 | 26.4±1.47B | 35.4±5.98 | 34.8±3.93AB | 41.2±3.26 | 50.2±2.71A | 50.0±3.33 | 0.0005 | 0.11 |  |
| 22:0 | 33.8±5.94B | 31.7±4.59 | 41.9±6.00B | 39.9±2.60 | 45.4±8.16B | 32.6±5.60 | 32.3±1.95B | 36.4±6.50 | 37.0±3.72B | 36.4±2.86 | 69.0±2.29A | 52.1±4.07 | <0.0001 | 0.14 |  |
| 24:0 | 18.9±1.68B | 23.7±4.24 | 34.8±4.46A | 35.9±4.49 | 27.7±1.25B | 25.2±1.98 | 28.1±1.64B | 25.9±1.61 | 23.3±2.58B | 26.2±2.95 | 38.4±1.70A | 34.9±3.96 | 0.0001 | 0.97 |  |
| MUFA | | | | | | | | | | | | | | | |
| 16:1t | 6.06±1.99ab | 8.69±1.08a | 6.73±1.15ab | 7.96±0.90ab | 5.74±0.99ab | 3.55±0.79b | 5.26±0.39b | 5.82±1.47ab | 3.63±0.56b | 5.30±0.54ab | 6.00±0.74ab | 6.42±0.57ab |  |  | 0.0061$ |
| 16:1n7 | 19.2±2.95abc | 46.9±8.08a | 26.3±3.56abc | 41.4±5.81ab | 17.8±3.23bc | 21.8±4.27abc | 13.5±3.25cd | 27.5±8.96abc | 6.21±0.85d | 30.5±3.14abc | 25.2±2.65abc | 32.0±5.38abc |  |  | 0.0054$ |
| 18:1n9 | 542±111A | 726±84.1 | 423±44.7A | 628.±69.9 | 375±54.9BC | 346±52.3 | 244±11.8C | 311±58.3 | 245±28.5C | 357±29.8 | 465±25.7AB | 470±38.1 | <0.0001 | 0.0044 |  |
| 18:1n7 | 368±30.9A | 505±47.5 | 277±29.7ABC | 424±41.1 | 287±31.0BC | 318±35.7 | 207±7.57C | 334±59.2 | 233±23.0BC | 400±27.6 | 353±29.2AB | 463±42.9 | <0.0001 | <0.0001 |  |
| 20:1n9 | 8.57±2.86abc | 12.3±2.63a | 6.49±1.37abc | 10.1±1.90ab | 5.80±1.93abc | 4.04±1.08bc | 2.19±0.26c | 5.06±1.77abc | 4.12±0.57bc | 6.61±0.50abc | 8.64±1.23abc | 8.92±1.64abc |  | | 0.0005$ |
| 24:1n9 | 6.15±1.76bc | 15.8±2.74a | 7.52±1.59abc | 12.8±2.61ab | 5.11±1.72bc | 4.00±0.88c | 4.17±0.21c | 9.69±2.80abc | 6.14±0.76bc | 9.51±0.71abc | 7.75±0.79abc | 8.44±1.60abc |  | | 0.0002$ |
| N-3 PUFA | | | | | | | | | | | | | | | |
| 18:3n3 | 9.42±4.14D | 15.8±4.00 | 151±23.6A | 232±28.1 | 22.9±5.78C | 21.7±5.13 | 6.67±1.11D | 16.3±5.25 | 3.47±0.37D | 10.2±4.05 | 35.7±2.76B | 41.9±4.04 | <0.0001 | 0.0020 |  |
| 20:3n3 | 2.82±0.85b | 4.07±1.22b | 16.8±2.98a | 19.2±2.96a | 6.02±1.86b | 2.27±0.53b | 2.73±0.30b | 3.55±0.65b | 2.65±0.26b | 2.46±0.47b | 7.26±1.04b | 6.36±1.48b |  |  | <0.0001$ |
| 20:5n3 | 2.34±0.51b | 5.98±1.44b | 118.5±21.4b | 128±16.3b | 611±82.7a | 538±71.8a | 80.9±8.46b | 110±24.4b | 0.50±0.24b | 1.37±0.38b | 6.66±1.06b | 5.95±1.12b |  |  | <0.0001$ |
| 22:5n3 | 123±60.5cd | 105±11.5cd | 404±78.0bcd | 498±145abc | 847±108a | 667±103ab | 102±3.25cd | 124±23.6cd | 60.2±5.10d | 87.3±8.44cd | 467±173abcd | 250±72.4bcd |  |  | <0.0001$ |
| 22:6n3 | 1021±128B | 915±205 | 1138±130B | 1029±99.5 | 763±94.9C | 538±63.6 | 2213±108A | 2225±143 | 587±47.9C | 487±54.0 | 1494±171B | 790±85.2 | <0.0001 | 0.0006 |  |
| N-6 PUFA | | | | | | | | | | | | | | | |
| 18:2n6 | 1778±289B | 2456±220 | 2371±299AB | 3505±415 | 2651±312AB | 2378±268 | 1966±117B | 2647±405 | 1822±207B | 2478±164 | 3089±233A | 3164±280 | 0.0009 | 0.0015 |  |
| 18:3n6 | 2.30±1.29ab | 4.56±2.43ab | 3.25±1.30ab | 7.67±2.16ab | 6.51±2.06ab | 6.52±1.05ab | 0.82±0.54b | 8.69±1.48ab | 2.19±0.72ab | 4.30±1.50ab | 5.07±1.91ab | 10.0±2.99a |  | | 0.0128$ |
| 20:2n6 | 6.31±0.98B | 10.8±2.03 | 10.0±1.63B | 13.7±1.98 | 13.2±2.70B | 12.3±2.90 | 7.71±0.93B | 14.8±2.78 | 19.7±2.47A | 25.4±2.62 | 27.3±1.69A | 30.2±4.02 | <0.0001 | 0.0095 |  |
| 20:3n6 | 34.2±4.58AB | 55.2±7.75 | 47.5±6.57A | 69.2±7.47 | 36.3±5.05BC | 36.9±5.76 | 32.3±1.52BC | 44.6±6.90 | 25.4±2.71C | 33.5±2.25 | 49.3±3.03AB | 42.3±6.29 | <0.0001 | 0.0055 |  |
| 20:4n6 | 2036±252ab | 2351±252a | 1431±195bcd | 1740±163abcd | 1203±180cde | 1134±144def | 396±14.2f | 566±91.2ef | 1509±118bcd | 1943±145abcd | 2474±125a | 2300±183a |  |  | <0.0001$ |
| 22:2n6 | 3.09±1.41ab | 24.2±9.19ab | 13.5±7.26ab | 10.1±2.21ab | 10.9±5.86ab | 5.53±1.69ab | 0.72±0.33b | 4.45±1.92ab | 5.56±1.49ab | 15.2±8.40ab | 18.3±10.4ab | 29.2±4.48a |  |  | 0.0216$ |
| 22:4n6 | 97.8±18.1b | 101±12.0b | 18.1±3.11c | 20.3±3.63c | 9.41±2.22c | 5.53±1.27c | 2.04±0.48c | 3.40±0.73c | 134±11.3ab | 151±9.53a | 122±10.0ab | 129±9.07ab |  |  | <0.0001$ |
| 22:5n6 | 120±19.4bc | 131±21.2bc | 4.83±1.53f | 5.43±1.43ef | 3.11±0.69f | 2.82±0.64f | 23.0±1.28def | 34.4±5.80def | 180±26.3ab | 236±32.9a | 95.5±8.90cd | 78.8±9.14cde |  |  | <0.0001$ |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Different upper-case superscripts on the female values within a row indicate significant main effects of diet (P< 0.05). Different lower-case superscripts within a row indicate (simple effect) differences between means (P< 0.05). P values for main sex effects are shaded blue and pink when oxylipins are higher in male and female hearts, respectively. #Int. represents interaction between diet and sex unless noted with superscript $ which denotes that Pvalues were obtained from the Kruskal-Wallis test because data were not normally distributed. ALA, alpha-linolenic acid; LA, linoleic acid; SFA, saturated fatty acid.

**Supplementary Table S7** Diet and sex effects on heart NL PUFA in rats given control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diet  Sex | Control | | ALA | | EPA | | DHA | | LA | | LA + ALA | | P Value | | |
| Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Diet | Sex | Int.# |
| µg/g | | | | | | | | | | | | | | | |
| SFA | | | | | | | | | | | | | | | |
| 16:0 | –¥d | 482±83.0b | –d | 278±83.0bcd | 234±96.8bc | –d | –d | –d | –d | –d | 603±77.6a | 349±65.4b |  |  | 0.0003$ |
| 20:0 | –d | 3.06±1.27b | –d | 1.45±0.72c | –d | –d | –d | –d | –d | –d | 5.53±0.81a | 2.94±0.81b |  |  | <0.0001$ |
| 22:0 | 0.21±0.21b | 0.58±0.49b | 0.44±0.35b | 0.77±0.34b | 2.07±0.94ab | –b | 0.64±0.41b | 0.14±0.14b | 1.42±0.88ab | 0.70±0.39b | 3.77±0.86a | 1.50±0.46ab |  |  | 0.00694 |
| MUFA | | | | | | | | | | | | | | | |
| 16:1t | 6.04±1.10A | 8.84±1.27 | 6.85±1.85AB | 4.95±0.54 | 4.70±0.79B | 2.52±0.60 | 4.36±0.40B | 2.95±1.70 | 4.36±1.19AB | 4.82±0.63 | 6.75±0.58AB | 6.58±1.40 | 0.0044 | 0.55 |  |
| 16:1n7 | 13.59±3.83B | 27.4±4.64 | 26.8±5.19B | 35.7±6.57 | 21.4±4.57B | 23.9±8.24 | 22.0±5.27B | 9.28±4.65 | 21.5±8.61B | 32.2±10.1 | 36.4±5.95A | 70.8±14.3 | <0.0001 | 0.0284 |  |
| 18:1n9 | 327±98.1ab | 238±143ab | 403±86.3ab | 378±66.5ab | 276±62.1ab | 176±69.1b | 236±86.6ab | 159±80.7b | 201±80.1ab | 251±51.7ab | 552±61.1a | 423±79.7ab |  |  | 0.0216$ |
| 18:1n7 | 30.3±13.1b | 53.4±9.38a | –c | 15.1±9.13bc | –c | –c | –c | –c | 15.2±8.86bc | 15.4±2.95bc | 19.6±5.25b | 20.0±8.44b |  |  | 0.0002$ |
| 20:1n9 | 4.33±1.16abc | 5.47±1.52ab | 3.36±0.94abc | 4.80±1.18ab | 2.22±0.61bc | 1.89±1.09bc | 0.65±0.21c | 1.66±1.13bc | 1.54±0.39bc | 3.36±0.34abc | 6.82±0.74a | 5.41±0.34ab |  |  | 0.0001$ |
| N-3 PUFA | | | | | | | | | | | | | | | |
| 18:3n3 | 6.67±2.27b | 13.7±2.31b | 148±22.6a | 133±21.3a | 19.8±3.61b | 10.0±1.47b | 11.2±2.95b | 9.22±3.61b | 12.1±2.79b | 8.77±0.84b | 37.3±3.39b | 24.5±3.22b |  |  | <0.0001$ |
| 20:3n3 | 0.11±0.07d | 0.22±0.05d | 1.51±0.09b | 3.35±0.13a | 0.20±0.07d | 0.16±0.06d | 0.27±0.07d | –d | 0.14±0.06d | 0.19±0.06d | 0.80±0.04c | 0.62±0.10c |  |  | <0.0001 |
| 20:5n3 | 018±0.18c | 0.29±0.26c | 8.02±1.39c | 8.38±1.26c | 89.9±7.60a | 58.5±2.35b | 9.60±1.00c | 11.0±4.40c | 1.44±0.78c | 0.12±0.12c | 0.53±0.15c | 0.17±0.13c |  |  | <0.0001$ |
| 22:5n3 | 3.67±1.66b | 4.19±2.00b | 19.7±3.73ab | 25.7±4.93ab | 47.1±7.60a | 46.6±16.3a | 15.2±0.65b | 21.1±7.34ab | 2.58±0.61b | 3.85±1.59b | 15.0±3.42b | 5.73±1.74b |  |  | 0.0026$ |
| 22:6n3 | 18.8±3.06bc | 12.0±2.91c | 25.9±5.08bc | 24.2±3.64bc | 17.0±1.91bc | 13.7±4.54c | 155±5.47a | 367±66.7a | 13.0±0.96c | 12.7±2.40c | 38.2±1.43b | 19.7±4.42bc |  |  | 0.0023$ |
| N-6 PUFA | | | | | | | | | | | | | | | |
| 18:2n6 | 127±39.4d | 261±40.6bcd | 201±29.1cd | 256±60.0bcd | 302±61.2bcd | 206±41.6cd | 192±17.9cd | 181±43.7cd | 421±86.8abc | 393±56.2abcd | 597±43.3a | 460±74.4ab |  |  | <0.0001$ |
| 18:3n6 | –b | –b | –b | –b | –b | –b | –b | –b | –b | –b | 2.78±0.90a | 2.74±1.10a |  |  | <0.0001$ |
| 20:2n6 | 1.02±0.26C | 2.50±0.74 | 1.65±0.62C | 1.58±0.37 | 2.65±0.71C | 1.62±0.58 | 1.17±0.26C | 1.43±0.49 | 3.75±0.98B | 4.61±0.70 | 6.39±0.38A | 5.66±0.78 | <0.0001 | 0.72 |  |
| 20:3n6 | 1.64±0.57 | 3.58±1.41 | 2.06±0.96 | 4.17±1.24 | 3.33±0.96 | 2.76±1.05 | 1.43±0.33 | 2.26±0.91 | 3.83±1.14 | 3.57±0.67 | 6.53±0.79 | 4.10±0.86 |  |  | 0.0514$ |
| 20:4n6 | 39.8±8.89bcde | 48.6±10.0abcd | 35.9±6.50bcde | 42.1±9.67bcde | 25.7±4.59cde | 23.4±8.69cde | 6.65±2.26e | 18.7±9.48de | 48.5±6.66abcd | 59.2±11.1abc | 83.6±4.66a | 67.9±10.6ab |  |  | <0.0001$ |
| 22:4n6 | 3.43±0.80de | 4.32±0.98cd | 0.23±0.09f | 0.28±0.10f | 0.50±0.30ef | 0.28±0.19f | 0.20±0.03f | 0.08±0.05f | 9.80±1.03a | 9.93±0.76a | 7.70±0.76ab | 6.52±0.81bc |  |  | <0.0001$ |
| 22:5n6 | 2.25±0.27bc | 3.45±1.37bc | –c | –c | –c | –c | 1.20±0.40bc | 1.80±0.88bc | 4.51±1.37ab | 7.43±1.15a | 1.69±0.51bc | 1.55±0.45bc |  |  | <0.0001$ |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Different upper-case superscripts on the female values within a row indicate significant main effects of diet (P< 0.05). Different lower-case superscripts within a row indicate simple effect differences between means (P< 0.05). P values for main sex effects are shaded blue when oxylipins are higher in male hearts. #Int. represents interaction between diet and sex unless noted with superscript $ which denotes that Pvalues were obtained from the Kruskal-Wallis test because data were not normally distributed. ¥Not detected. ALA, alpha-linolenic acid; LA, linoleic acid; SFA, saturated fatty acid.

**Supplementary Table S8** Heart oxylipin to PUFA ratios for enzymes in rats provided control, ALA, EPA, DHA, LA and LA+ALA diets for 6 weeks

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| **a. 5-Lipoxygenase** | | | | | | | | | | | | |
| Ratio | 5-HETE/ARA | | 9-HODE/LA | | 9-HOTrE/ALA | | 5-HEPE/EPA | | 7-HDoHE/DHA | | P Value | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Ratio | Sex |
| Diet | nmol/mmol | | | | | | | | | | | |
| Control | 281±43.2C | 193±31.7 | 1264±189B | 889±201 | 7550±1128A | 4308±1588 | 10407±2844A | 5572±1240 | 265±40.7C | 185±36.4 | <0.0001 | 0.0009 |
| ALA | 379±61.8C | 133±28.2 | 1750±434B | 483±87.9 | 5541±935A | 2874±570 | 3534±340A | 2489±307 | 406±69.0C | 154±24.1 | <0.0001 | <0.0001 |
| EPA | 311±65.6D | 231±47.6 | 1412±386C | 1092±225 | 3827±1140B | 2349±402 | 6414±805A | 4612±771 | 360±55.1D | 335±72.1 | <0.0001 | 0.0440 |
| DHA | 284±31.3D | 302±97.1 | 1213±191C | 1381±411 | 16110±2918A | 6890±2134 | 4499±491B | 3441±635 | 675±72.3C | 762±301 | <0.0001 | 0.0316 |
| LA | 530±116c | 224±39.4c | 2679±580c | 1204±277c | 29931±4426a | 10749±3025b | –¥ | 15019±2965b | 577±117c | 253±54.7c | <0.0001$ | |
| LA+ALA | 235±49.1C | 211±53.2 | 1754±480B | 1102±254 | 5734±1441A | 3558±746 | 6352±1024A | 8923±1774 | 254±54.8C | 261±79.8 | <0.0001 |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **b. 12-Lipoxygenase** | | |  |  |  |  |  |  |
| Ratio | 12-HETE/ARA | | 12-HEPE/EPA | | 14-HDoHE/DHA | | P value | |
| Sex | Female | Male | Female | Male | Female | Male | Ratio | Sex |
| Diet | nmol/mmol | | | | | | | |
| Control | 56.2±4.12C | 36.1±3.93 | 2503±304A | 1494±166 | 103±17.6B | 59.4±2.05 | <0.0001 | <0.0001 |
| ALA | 79.6±15.8C | 26.7±4.29 | 1129±142A | 745±83.0 | 181±31.9B | 67.3±14.1 | <0.0001 | <0.0001 |
| EPA | 76.3±18.9C | 53.2±12.6 | 1252±160A | 995±202 | 176±37.1B | 144±49.8 | <0.0001 |  |
| DHA | 63.6±7.66C | 56.9±19.5 | 1391±157A | 956±159 | 253±34.3B | 128±24.2 | <0.0001 | 0.0066 |
| LA | 129±39.4C | 53.6±9.78 | 9079±2851A | 3792±843 | 257±77.8B | 122±26.8 | <0.0001 | 0.0024 |
| LA+ALA | 59.4±16.6B | 42.7±10.2 | 2170±483A | 2121±326 | 102±32.6B | 104±36.3 | <0.0001 |  |

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| **c. 15-Lipoxygenase** | |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ratio | 15-HETE/ARA | | 13-HODE/LA | | 15-HETrE/DGLA | | 13-HOTrE/ALA | | 15-HEPE/EPA | | 17-HDoHE/DHA | | P value | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Ratio | Sex |
| Diet | nmol/mmol | | | | | | | | | | | | | |
| Control | 277±46.9D | 189±29.2 | 574±33.4C | 445±88.0 | 159±25.5D | 92.1±15.2 | 7406±1497A | 4671±1505 | 2190±708B | 1152±232 | 560±85.3C | 480±100 | <0.0001 | 0.0009 |
| ALA | 394±67.9D | 152±26.6 | 714±167C | 277±42.7 | 170±36.0E | 59.0±8.53 | 7493±1507A | 3285±658 | 1041±164B | 703±103 | 954±158BC | 343±46.0 | <0.0001 | <0.0001 |
| EPA | 381±96.0E | 305±86.7 | 626±100CD | 569±119 | 236±51.5E | 167±51.1 | 4913±1308A | 2200±383 | 1231±126B | 1548±572 | 864±152BC | 713±187 | <0.0001 | 0.0347 |
| DHA | 306±47.8C | 377±115 | 471±69.4C | 482±90.0 | 117±17.9D | 147±52.0 | 11575±1934A | 7651±2378 | 1146±150B | 1163±281 | 1381±199B | 1822±748 | <0.0001 |  |
| LA | 591±176D | 248±43.3 | 1577±315C | 696±147 | 382±80.6D | 177±38.9 | 38330±7955A | 22658±2457 | 8304±3333B | 4126±441 | 1243±303C | 582±126 | <0.0001 | <0.0001 |
| LA+ALA | 266±66.1E | 215±46.7 | 705±126C | 641±166 | 181±51.1E | 130±32.4 | 5231±881A | 4960±1378 | 1882±410B | 1920±358 | 439±130CD | 384±64.3 | <0.0001 |  |

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| **d. Cytochrome P450-hydroxylase** | | | | | | | | |
| Ratio | 18-HETE/ARA | | 18-HEPE/EPA | | 20-HDoHE/DHA | | P value | |
| Sex | Female | Male | Female | Male | Female | Male | Ratio | Sex |
| Diet | nmol/mmol | | | | | | | |
| Control | 0.66±0.08C | 0.52±0.04 | 1364±92.7A | 1086±128 | 214±19.5B | 237±30.8 | <0.0001 |  |
| ALA | 0.78±0.17C | 0.74±0.18 | 945±166A | 378±40.8 | 384±76.9B | 122±18.9 | <0.0001 | 0.0004 |
| EPA | 1.41±0.56C | 1.40±0.27 | 1600±215A | 1664±475 | 417±77.8B | 436±94.8 | <0.0001 |  |
| DHA | 2.07±0.52C | 2.11±0.89 | 914±141A | 746±152 | 555±93.1B | 375±147 | <0.0001 |  |
| LA | 1.11±0.25C | 0.90±0.11 | 4791±954A | 798±250 | 408±82.9B | 199±49.4 | <0.0001 | 0.0004 |
| LA+ALA | 0.67±0.09C | 0.46±0.05 | 607±142A | 773±48.3 | 220±68.4B | 184±39.5 | <0.0001 |  |

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| **e. Cytochrome P450-epoxygenase** | | | |  |  |  |  |  |  |  |  |  |
| Ratio | 14,15-EpETrE/ARA | | 12,13-EpOME/LA | | 12,13-EpODE/ALA | | 14,15-EpETE/EPA | | 16,17-EpDPE/DHA | | P value | |
| Sex | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Ratio | Sex |
| Diet | nmol/mmol | | | | | | | | | | | |
| Control | 9.34±2.44c | 5.18±0.34c | 4.81±1.44c | 2.27±0.62c | 325±50.0a | 176±74.0b | 29.5±5.28bc | – | 28.6±5.13bc | 21.9±1.76bc | <0.0001$ | |
| ALA | 8.96±2.34C | 1.78±0.72 | 4.97±1.63D | 0.69±0.35 | 239±38.1A | 64.0±11.7 | 19.5±4.81BC | 3.76±1.26 | 41.2±11.0B | 8.55±2.19 | <0.0001 | <0.0001 |
| EPA | 10.3±3.78C | 6.42±1.45 | 2.93±0.91D | 3.16±0.72 | 172±50.7A | 177±36.1 | 41.3±14.8B | 23.0±8.94 | 44.8±10.9B | 36.0±9.78 | <0.0001 |  |
| DHA | 7.29±1.29C | 3.40±1.40 | 3.43±0.62D | 1.11±0.33 | 887±86.5A | 475±124 | 15.3±3.23C | 7.80±3.06 | 62.2±10.1B | 42.5±13.6 | <0.0001 | <0.0001 |
| LA | 4.66±1.40C | 3.48±0.73 | 5.32±1.40C | 2.83±0.73 | 1126±247A | 398±140 | – | – | 19.5±5.36B | 8.85±1.22 | <0.0001 | 0.0087 |
| LA+ALA | 6.83±1.97b | 3.32±0.81b | 7.58±1.57b | 2.70±0.58b | 276±86.0a | 145±40.0ab | 8.18±2.57b | – | 10.8±3.24b | 11.1±1.27b | <0.0001$ | |

Data were analyzed by 2-way ANOVA when normally distributed and by Kruskal-Wallis when not, followed by Tukey’s post hoc test. Different upper-case superscripts on the female values within a row indicate significant main effects of ratio (P< 0.05). Different lower-case superscripts within a row indicate simple effect differences between means (P< 0.05). P values for sex effects are shaded pink when ratios are higher in female hearts. P values centred between the ratio and sex columns denote interaction effects. $Denotes that Pvalues were obtained from the Kruskal-Wallis test because data were not normally distributed. ¥Indicates zero value (not detected) for the numerator or denominator, therefore the ratio could not be calculated. ARA, arachidonic acid; ALA, α-linolenic acid; EpDPE, epoxy-docosapentaenoic acid; EpETE, epoxy-eicosatetraenoic acid; EpETrE, epoxy-eicosatrienoic acid; EpODE, epoxy- octadecadienoic acid; EpOME, epoxy-octadecenoic acid; HDoHE, hydroxy-docosahexaenoic acid; HEPE, hydroxy-eicosapentaenoic acid; HETE, hydroxy-eicosatetraenoic acid; HETrE, hydroxy-eicosatrienoic acid; HODE, hydroxy-octadecadienoic acid; HOTrE, hydroxy-octadecatrienoic acid; LA, linoleic acid.