**Supplemental Data**

**EXTENDED METHODS**

**INCLUSION & EXCLUSION CRITERIA**

***PET Imaging of Giant Cell and Takayasu Arteritis (PITA):***

ClinicalTrials.gov Identifier: NCT04071691

Inclusion Criteria:

* Male or female participants >18 years old
* Able to give written, informed consent and to lie flat
* Either:
1. New clinical diagnosis or acute flare of large vessel vasculitis (Giant-cell arteritis or Takayasu's arteritis) within ~1 week of treatment initiation, and
2. Clinical indication for 18F-FDG positron emission tomography (PET) imaging determined by the referring physician, or
3. Undergoing surgery for large vessel vasculitis, or
4. Diagnosis of large vessel vasculitis in remission

Exclusion Criteria:

* Women of childbearing potential not using adequate contraception
* Contra-indication to magnetic resonance imaging
* Contrast allergy or contrast-nephropathy
* Chronic kidney disease (eGFR <30 mL/min/1.73 m2)
* Any medical condition, in the opinion of the investigator, that prevents the participant from lying flat during scanning, or from participating in the study
* History of recent malignancy deemed relevant to the study by the investigator

***Vascular Inflammation Imaging Using Somatostatin Receptor Positron Emission Tomography (VISION):***

ClinicalTrials.gov Identifier: NCT02021188

Inclusion Criteria:

* Age ≥40 years of age
* Can provide written, fully informed consent
* Have had a transient ischemic attack or stroke within the preceding four weeks due to carotid artery atherosclerosis; or have ≥30% carotid artery or epicardial coronary artery stenosis

Exclusion Criteria:

* Renal impairment (eGFR<30mL/min)
* History of contrast nephropathy
* Atrial fibrillation
* Any condition, in the opinion of the investigator, which prevents the participant from lying flat during scanning
* Women of childbearing potential
* Inability to provide written informed consent
* Hemorrhagic stroke within 3 months of study entry
* Total occlusion of a culprit carotid artery
* Any medical condition, vital sign or laboratory value that, in the opinion of the investigator, makes the subject ineligible for inclusion

***Residual Inflammation and Plaque Progression Long-term Evaluation (RIPPLE):***

ClinicalTrials.gov Identifier: NCT04073810

Inclusion Criteria:

* Male or female participants >18 years old
* Able to give written, informed consent and to lie flat
* First-presentation of myocardial infarction within ~2 weeks
* At least mild non-culprit coronary artery disease on angiography, managed medically

Exclusion Criteria:

* Women of child-bearing potential not using adequate contraception
* Contrast allergy or contrast-nephropathy
* Uncontrolled atrial fibrillation
* Chronic kidney disease (eGFR <30 mL/min/1.73 m2)
* Any medical condition, in the opinion of the investigator, that prevents the participant from lying flat during scanning, or from participating in the study
* Uncontrolled chronic inflammatory disorder
* History of recent malignancy deemed relevant to the study by the investigator
* Current use of systemic corticosteroids
* Previous coronary artery bypass grafting surgery (CABG) or percutaneous coronary intervention (PCI) before the index event
* Contraindication to coronary angiography
* Requires CABG or staged non-culprit artery PCI

**ADDITIONAL FIGURES**

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**Figure S1.** Study flow chart

Red: Takayasu arteritis (TAK); Blue: atherosclerotic coronary artery disease (CAD); Gray: Controls; CCTA: Coronary computed tomography angiography; FDG: Fluorodeoxyglucose; PET: Positron Emission Tomography



**Figure S2.** Distribution of PCAT density within the coronary tree

Color heatmap displaying median PCAT values (HU) around individual coronary segments from all subjects in each group.

**ADDITIONAL TABLES**

**Table S1.** PCAT & PAAT values by group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | **CAD+TAK** | **TAK** | **CAD** | **Control** | **p value**  |
| **mPCATtotal (IQR), HU** | -72.93 (-79.40, -67.46) | -73.31 (-76.62, -69.95) | -77.42 (-84.86, -73.09) | -82.99 (-86.96, -77.97) | **p<0.0001** |
| **mPCATprox (IQR), HU** | -68.91 (-75.38, -61.37) | -66.19 (-70.98, -60.36) | -72.08 (-78.37, -60.36) | -80.65 (-86.02, -74.35) | **p<0.0001** |
| **mPCATpRCA (IQR), HU** | -70.05 (-77.30, -63.81) | -65.79 (-71.53, -61.53) | -77.57 (-82.74, -66.09) | -85.65 (-90.01, -72.43) | **p<0.0001** |
| **PAAT (IQR), HU** | -65.55 (-71.35, -60.29) | -71.29 (-74.44, -63.16) | -74.30 (-79.85, -64.62) | -75.15 (-83.52, -70.27) | **p=0.0001** |

**Table S2.** PCAT & PAAT ROC analyses

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   | **TAK+CAD vs** **Stable CAD** | **TAK vs** **Controls** | **Active vs** **Inactive TAK** | **Active TAK vs Controls** | **Recent MI vs** **Stable CAD** | **TAK vs Non-TAK** |
| **mPCATtotal** |   |   |   |  |   |  |
| Lower threshold (HU) | -77.4 | -76.2 | -71.8 | -74.1 | -77.4 | -76.2 |
| Sensitivity (%) | 72 | 78 | 73 | 1 | 79 | 0.70 |
| Specificity (%) | 72 | 86 | 74 | 0.95 | 72 | 0.67 |
| AUC (95% CI) | 0.76 (0.60-0.88) | 0.86 (0.72-0.97) | 0.82 (0.7-0.92) | 0.99 (0.97-1) | 0.77 (0.58-0.92) | 0.73 (0.63-0.82) |
| **mPCATprox**  |  |  |  |  |  |  |
| Lower threshold (HU) | -72.7 | -72.2 | -66.9 | -72.1 | -69.8 | -71.5 |
| Sensitivity (%) | 61 | 0.83 | 73 | 0.95 | 78 | 0.67 |
| Specificity (%) | 61 | 0.95 | 66 | 1 | 64 | 0.70 |
| AUC (95% CI) | 0.69 (0.54-0.82) | 0.88 (0.76-0.98) | 0.74 (0.59-0.86) | 0.97 (0.90-1) | 0.72 (0.52-0.89) | 0.72 (0.63-0.81) |
| **mPCATpRCA**  |  |  |  |  |  |  |
| Lower threshold (HU) | -77.1 | -74.9 | -65.5 | -71.3 | -76.6 | -71.5 |
| Sensitivity (%) | 67 | 0.83 | 67 | 0.93 | 64 | 0.67 |
| Specificity (%) | 75 | 0.77 | 79 | 0.86 | 67 | 0.74 |
| AUC (95% CI) | 0.7 (0.55-0.83) | 0.91 (0.81-0.98) | 0.76 (0.62-0.88) | 0.96 (0.89-1) | 0.69 (0.49-0.87) | 0.73 (0.63-0.82) |
| **PAAT** |  |  |  |  |  |  |
| Lower threshold (HU) | -71.9 | -72.9 | -65.1 | -69.9 | -75.1 | -71.2 |
| Sensitivity (%) | 72 | 0.64 | 60 | 0.8 | 57 | 0.67 |
| Specificity (%) | 78 | 0.61 | 63 | 0.82 | 50 | 0.67 |
| AUC (95% CI) | 0.75 (0.61-0.88) | 0.73 (0.57-0.87) | 0.63 (0.45-0.79) | 0.86 (0.72-0.98) | 0.58 (0.37-0.77) | 0.73 (0.64-0.82) |
|  |  |  |  |  |  |  |

**Table S3.** Spearman’s correlations for PCAT density vs clinical data

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|   | **ITAS-CRP**  | **CRP** | **ESR** | **WCC** | **Neut** | **Total Chol** | **LDL** | **BMI** | **% TPB** | **% CV risk** |
| **mPCATtotal** |  |  |  |  |  |  |  |  |  |
| r value (95% CI) | 0.43(0.17-0.64) | 0.41(0.22-0.57) | 0.41(0.16-0.61) | 0.19(-0.01-0.37) | 0.21(0.01-0.40) | 0.05(-0.16-0.26) | 0.02(-0.18-0.22) | 0.11(-0.10-0.32) | 0.04(-0.20-0.28) | 0.08(-0.11-0.28) |
| p value  | **0.001** | **<0.0001** | **0.002** | 0.05 | **0.03** | 0.61 | 0.84 | 0.29 | 0.72 | 0.38 |
| **mPCATprox** |  |  |  |  |  |  |  |  |  |  |
| r value (95% CI) | 0.39(0.12-0.60) | 0.39(0.20-0.56) | 0.38(0.12-0.59) | 0.24 (0.04-0.42) | 0.24(0.04-0.42) | 0.005(-0.21-0.22) | -0.05(-0.25-0.16) | 0.08(-0.14-0.29) | 0.005(-0.24-0.25 | 0.07(-0.13-0.26) |
| p value  | **0.004** | **<0.0001** | **0.004** | **0.02** | **0.02** | 0.96 | 0.65 | 0.45 | 0.97 | 0.46 |
| **mPCATpRCA** |  |  |  |  |  |  |  |  |  |  |
| r value (95% CI) | 0.39(0.12-0.60) | 0.35(0.15-0.52) | 0.31(0.04-0.53) | 0.22 (0.02-0.41) | 0.26(0.06-0.44) | 0.09(-0.12-0.30) | 0.003(-0.19-0.21) | 0.11(-0.11-0.31) | 0.04(-0.21-0.28) | -0.03(-0.22-0.16) |
| p value  | **0.004** | **0.0006** | **0.02** | **0.03** | **0.009** | 0.38 | 0.97 | 0.31 | 0.75 | 0.76 |
| **PAAT** |  |  |  |  |  |  |  |  |  |  |
| r value (95% CI) | 0.04(-0.24-0.34) | 0.16(-0.05-0.36) | 0.05 (-0.22-0.31) | 0.25 (0.06-0.43) | 0.29 (0.10-0.47) | 0.18(-0.12-0.30) | 0.17(-0.03-0.36) | 0.09(-0.13-0.29) | -0.04(-0.28-0.21) | -0.03(-0.23-0.16) |
| p value  | 0.78 | 0.12 | 0.72 | **0.01** | **0.003** | 0.38 | 0.08 | 0.42 | 0.75 | 0.71 |

**Table S4.** PCAT values for active vs inactive/stable disease

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   | **Active TAK** | **Inactive TAK** | **p value** | **Recent MI** | **Stable CAD** | **p value** |
| **mPCATtotal (HU)** | -68.24 (-73.52, -66.16) | -75.44 (-80.43, -70.90) | **0.0002** | -73.82 (-77.76, -69.80) | -81.49 (-86.37, -75.37) | **0.008** |
| **mPCATprox (HU)** | -64.20 (-68.79, -58.21) | -71.05 (-76.13, -62.99) | **0.004** | -73.65 (-84.52, -62.95) | -86.37 (-91.86, -81.49) | **0.0002** |
| **mPCATpRCA (HU)** | -63.99 (-66.17, - 61.20) | -70.29 (-77.59, -65.76) | **0.0002** | -76.68 (-80.57, -61.15) | -83.15 (-92.18, -80.97) |  0.24 |
| **PAAT (HU)** | -64.07 (-69.71, -60.18) | -68.72 (-74.34, -62.41) |  0.15 | -74.30 (-79.17, -64.39)  | -74.50 (-82.56, -67.91) |  0.46 |

**Table S5.** Associations between PCAT density and potential confounding factors

|  |  |
| --- | --- |
| **Potential confounder** | **Fixed effects** |
| Coronary artery1  | ANOVA p<0.0001 |
| Proximal, mid or distal segment1 | ANOVA p<0.0001 |
| Gender | p=0.18 |
| Age2 | -0.13 ± SEM 0.05 HU, p=0.008 |
| Body mass index | p=0.51 |
| Current statin use | p=0.42 |
| Current steroid use3 | 3.19 ± SEM 1.43 HU, p=0.03 |
| Total cholesterol | p=0.58 |
| LDL cholesterol | p=0.95 |
| HDL cholesterol | p=0.33 |
| Hypertension | p=0.46 |
| Diabetes mellitus | p=0.48 |
| Current or ex smoking habit | p=0.86 |
| Angina | p=0.19 |
| Previous myocardial infarction | p=0.51 |
| Recent myocardial infarction3 | 3.86 ± SEM 2.02 HU, p=0.06 |
| Culprit vessel | p=0.91 |
| % 10-year cardiovascular risk score | p=0.78 |
| % total plaque burden | p=0.93 |
| kV2 | 0.26 ± SEM 0.04 HU, p<0.0001 |

Fixed effects are reported as estimate ± SEM where p<0.1

1For categorical variables with multiple stems, the ANOVA p-value is reported

2Reported as the difference in PCAT density per unit of change

3Reported as the difference of PCAT density in samples with the condition versus those without