

the fat attenuation index of perivascular tissue (FAI_{PVAT}), is positively associated with the presence of coronary artery disease (CAD) and the volume of fibrous plaque in the proximal RCA independently of the presence of coronary calcium. As part of the same study, the present inventors also showed that FAI_{PVAT} changes in a dynamic way in response to local rupture of a culprit lesion in patients with acute MI and can distinguish culprit from non-culprit lesions. These observations supported the inventors' hypothesis that FAI_{PVAT} could function as a dynamic biomarker of vascular inflammation and cardiovascular risk and offer diagnostic and prognostic information beyond that of traditional biomarkers, such as coronary calcium.

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However, there remains an urgent need for the identification and development of functional biomarkers that will describe vascular inflammation, rather than structural and non-reversible changes in the vascular wall, and diagnostic tools to aid non-invasive detection of vascular inflammation and enable stratification of patients who are at risk of suffering serious cardiac events.

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Summary

According to a first aspect, the present disclosure is directed to a use of perivascular water index (PVWi) as a functional biomarker of vascular inflammation, wherein the perivascular water index (PVWi) of a blood vessel, comprising

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(i) using data gathered from a computer tomography scan along a length of the vessel to determine the total volume of voxels of water within an attenuation window around the attenuation of water within the perivascular space a pre-determined distance from the outer wall of the vessel, and

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(ii) correcting the total volume of the voxels of water for the volume of the vessel by dividing the total volume of voxels of water determined in step (i) by the total perivascular volume.

As described herein, the present disclosure provides a method for determining the perivascular water index (PVWi) of a blood vessel, comprising (i) using data gathered from a computer tomography scan along a length of the vessel to determine the total volume of voxels of water within an attenuation window around the attenuation of water within the perivascular space a pre-determined

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distance from the outer wall of the vessel, and (ii) correcting the total volume of the voxels of water for the size of the vessel by dividing the total volume of voxels of water determined in step (i) by the total perivascular volume.

5 According to an example, the present disclosure is directed to the use of perivascular water index (PVWi), as defined according to the method of the first aspect of the disclosure, as a functional biomarker of vascular inflammation. According to this aspect, PVWi can be used alone, or in combination with one or more other biomarkers, to predict all-cause or cardiac mortality risk in a patient.

10 In particular, PVWi can be used in combination with one or more of calcium index, fibrous plaque index, fat attenuation index of the perivascular adipose tissue, volumetric perivascular characterisation index, fat attenuation index and total volume of the epicardial adipose tissue to predict all-cause or cardiac mortality risk in a patient.

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According to a second aspect, the present disclosure is directed to a method for predicting the mortality risk or risk of a patient suffering a cardiovascular event, said method comprising:

(a) using data gathered from a computer tomography (CT) scan along a length
20 of a blood vessel to determine:

(i) calcium index (Calcium-i); and/or

(ii) fibrous plaque index (FPI);

and at least one of

(iii) fat attenuation index of the perivascular adipose tissue (FAI_{PVAT});

25 (iv) perivascular water index (PVWi); and/or

(v) fat attenuation index of the epicardial adipose tissue (FAI_{EPAT}); and

(b) comparing each of the values determined in (a) to a pre-determined cut-off value or using the absolute value of each variable in order to generate an output value that indicates the patient's risk of suffering a cardiovascular event.

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Further described herein, is a method for predicting the risk of a patient suffering a cardiovascular event, said method comprising:

- (a) using data gathered from a computer tomography scan along a length of a blood vessel to determine:
- (i) calcium index (Calcium-i); and/or
 - (ii) fibrous plaque index (FPI);
- 5 and at least one of
- (iii) fat attenuation index of the perivascular adipose tissue (FAI_{PVAT}); and/or
 - (iv) perivascular water index (PVWi); and
- 10 with the possible addition of any of the following:
- (v) volumetric perivascular characterisation index (VPCI)
 - (vi) total epicardial adipose tissue volume (EpAT-vol);
 - (vii) fat attenuation index (FAI) of epicardial adipose tissue (FAI_{EpAT});
- 15 (b) comparing each of the values determined in (a) to a pre-determined cut-off value or using the absolute value of each variable in order to generate an output value that indicates the patient's risk of suffering a cardiovascular event.
- 20 According to a third aspect, the present disclosure is directed to use of the method according to the third aspect for non-invasive monitoring of aortic aneurysms and/or carotid plaques, wherein said method does not include determining EpAT volume or FAI_{EpAT} .
- 25 In a preferred example of the method of the third aspect of the disclosure, both FAI_{PVAT} and PVWi are determined in step (a) of the method.
- In one example, the method according to the third aspect of the disclosure further comprises determining one or more of (vi) fat attenuation index of total volume of the epicardial adipose tissue (EpAT-vol), (vii) the epicardial adipose
- 30 tissue (FAI_{EpAT}), (viii) age and (ix) gender of the patient.

Claims

1. Use of perivascular water index (PVWi) as a functional biomarker of vascular inflammation, wherein the perivascular water index is determined by a method comprising
 - (i) using data gathered from a computer tomography scan along a length of the vessel to determine the total volume of voxels of water within an attenuation window around the attenuation of water within the perivascular space a pre-determined distance from the outer wall of the vessel, and
 - (ii) correcting the total volume of the voxels of water for the volume of the vessel by dividing the total volume of voxels of water determined in step (i) by the total perivascular volume.
2. Use of PVWi as a functional biomarker according to claim 1, wherein the attenuation window around the attenuation of water is from -30 to +30 Hounsfield units (HU).
3. Use of PVWi as a functional biomarker according to claim 2, wherein the attenuation window around the attenuation of water is from -15 to +15 HU.
4. Use of PVWi as a functional biomarker according to any preceding claim, wherein the pre-determined distance from the outer wall of the vessel is a standard distance that is not equal to or related to the diameter or radius of the underlying vessel.
5. Use of PVWi as a functional biomarker according to any of claims 1 to 3, wherein the pre-determined distance from the outer wall of the vessel is either a distance equal to the radius or diameter of the underlying vessel or a distance that is representative of a dimension of the underlying vessel.
6. Use of PVWi as a functional biomarker according to any preceding claim, wherein the data is gathered from a computerised tomography scan along a

length of the right coronary artery, left anterior descending artery, left circumflex artery, aorta, carotid arteries or femoral arteries.

7. Use of PVWi as a functional biomarker according to claim 6, wherein the
5 data is gathered from a computerised tomography scan along a 4cm length, starting 1cm distally to the origin of the right coronary artery.

8. Use of PVWi as a functional biomarker according to any of claims 1 to 5,
10 wherein the data is gathered from a computerised tomography scan along a length of the aorta.

9. Use of PVWi as a functional biomarker according to any preceding claim,
wherein the biomarker is used to predict all-cause or cardiac mortality risk in a
15 patient.

10. Use of PVWi as a functional biomarker according to claim 9, wherein
PVWi is used in combination with additional functional and/or biomarkers of
vascular inflammation.

20 11. Use of PVWi as a functional biomarker according to claim 10, wherein the structural biomarkers of vascular inflammation include one or more of calcium index and fibrous plaque index, and/or wherein the additional functional biomarkers of vascular inflammation include one or more of the fat attenuation index of the perivascular adipose tissue (FAI_{PVAT}), fat attenuation index of the
25 epicardial adipose tissue (FAI_{EPAT}) and volumetric perivascular characterisation index (VPCI).

12. A method for predicting the mortality risk or risk of a patient suffering a cardiovascular event, said method comprising:

30 (a) using data gathered from a computer tomography (CT) scan along a length of a blood vessel to determine:

(i) calcium index (Calcium-i); and/or

(ii) fibrous plaque index (FPI);

and at least one of

(iii) fat attenuation index of the perivascular adipose tissue (FAI_{PVAT});

(iv) perivascular water index (PVWi); and/or

5 (v) fat attenuation index of the epicardial adipose tissue (FAI_{EpAT}); and

(b) comparing each of the values determined in (a) to a pre-determined cut-off value or using the absolute value of each variable in order to generate an output value that indicates the patient's risk of suffering a cardiovascular event.

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13. A method according to claim 12, both FAI_{PVAT} and PVWi are determined in step (a).

14. A method according to claims 12 or 13, wherein the data is gathered from
15 a computerised tomography scan along a length of the right coronary artery, left anterior descending artery, left circumflex artery, aorta, carotid arteries or femoral arteries.

15. The method according to claim 14 wherein the data is gathered from a
20 computerised tomography scan along a 4 cm length, starting 1 cm distally to the origin of the right coronary artery.

16. The method according to claims 12 or 13, wherein the data is gathered from a computerised tomography scan along a length of the aorta.

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17. The method according to any of claims 12 to 16, wherein step (a) further comprises using the data gathered from a computer tomography scan along a length of a blood vessel to determine (v) volumetric perivascular characterisation index (VPCI), and wherein the value of (v) is included in step (b) of claim 12.

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18. The method according to any of claims 12 to 17, further comprising determining one or more of (vi) epicardial adipose tissue volume (EpAT-vol) and

(vii) fat attenuation index of the epicardial adipose tissue (FAI_{EpAT}) and wherein the value of (vi) and/or (vii) is included in step (b) of claim 12.

19. The method according to any of claims 12 to 18, further comprising
5 determining one or more of (viii) the age and (ix) gender of the patient and wherein the value of (viii) and/or (ix) is included in step (b) of claim 12.

20. The method according to any of claims 12 to 19, wherein coefficients for each of (i) to (vii) are derived from Cox hazard or logistic regression models.

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21. The method according to any of claims 12 to 19, wherein the cut-off points for each of (i) to (vii) are derived from receiver operating characteristic (ROC) curves.

15 22. The method according to any of claims 12 to 21, wherein the output value is a continuous single value function or a value that falls within one of three discrete brackets corresponding to low, medium and high risk of a cardiac event, cardiac death or all-cause mortality.

20 23. The method according to any of claims 12 to 22, wherein the method is used to stratify patients according to their risk of all-cause or cardiac mortality.

24. The method according to any of claims 12 to 23, wherein the patient has been diagnosed with vascular inflammation, or a condition known to be
25 associated with vascular inflammation.

25. Use of the method according to any of claims 12 to 24 for non-invasive monitoring of aortic aneurysms and/or carotid plaques, wherein said method does not include determining $EpAT$ volume or FAI_{EpAT} .

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