Supplementary Methods

The design and reporting of this study follows different dedicated guidelines for AI applications in medical imaging, including CLAIM (Checklist for Artificial Intelligence in Medical Imaging)[1], STARD-AI (Standards for Reporting of Diagnostic Accuracy Study-AI)[2], and MINIMAR (Minimum Information for Medical AI Reporting)[3]. Items of the above-listed guidelines documents have been jointly considered appropriate for the development, validation and testing of the AI-based model for automated AAOCA detection and classification in 3D-CCTA.

Evaluation of the models

Supplemental Figure 27 illustrates different strategies for model development and evaluation, which were implemented within our dataset using more labeled data in the model development More specific:

- Strategy 1: Model development was performed on the training dataset; the models were evaluated on the internal and external testing dataset with labeled cases. The external clinical testing dataset was used to evaluate the true and false positives, as the labeling was not available for this dataset.
- Strategy 2: Model training was performed on the entire dataset from Bern University Hospital. The labeled dataset from Zurich University Hospital served as an external testing dataset. The unlabeled open-access CCTA dataset (Guangdong Provincial People's Hospital) was used for external clinical evaluation, similar to Strategy 1.
- Strategy 3: Model training was performed on the entire datasets with labels, including data from Bern and Zurich University Hospitals. Following the previous strategy, external model performance was evaluated in the unlabeled dataset (external clinical evaluation dataset).

We report the results of Strategy 1 (Figure 2 in the main manuscript), while the results of Strategies 2 and 3 are reported in the **Supplementary material**. These additional strategies were explored to enhance the performance of the final model using the entire labeled dataset in different approaches. **Supplemental Figure 3** shows the different options for using the developed model in real clinical settings, from fully automated to semi-automated (physician in loop) approaches.

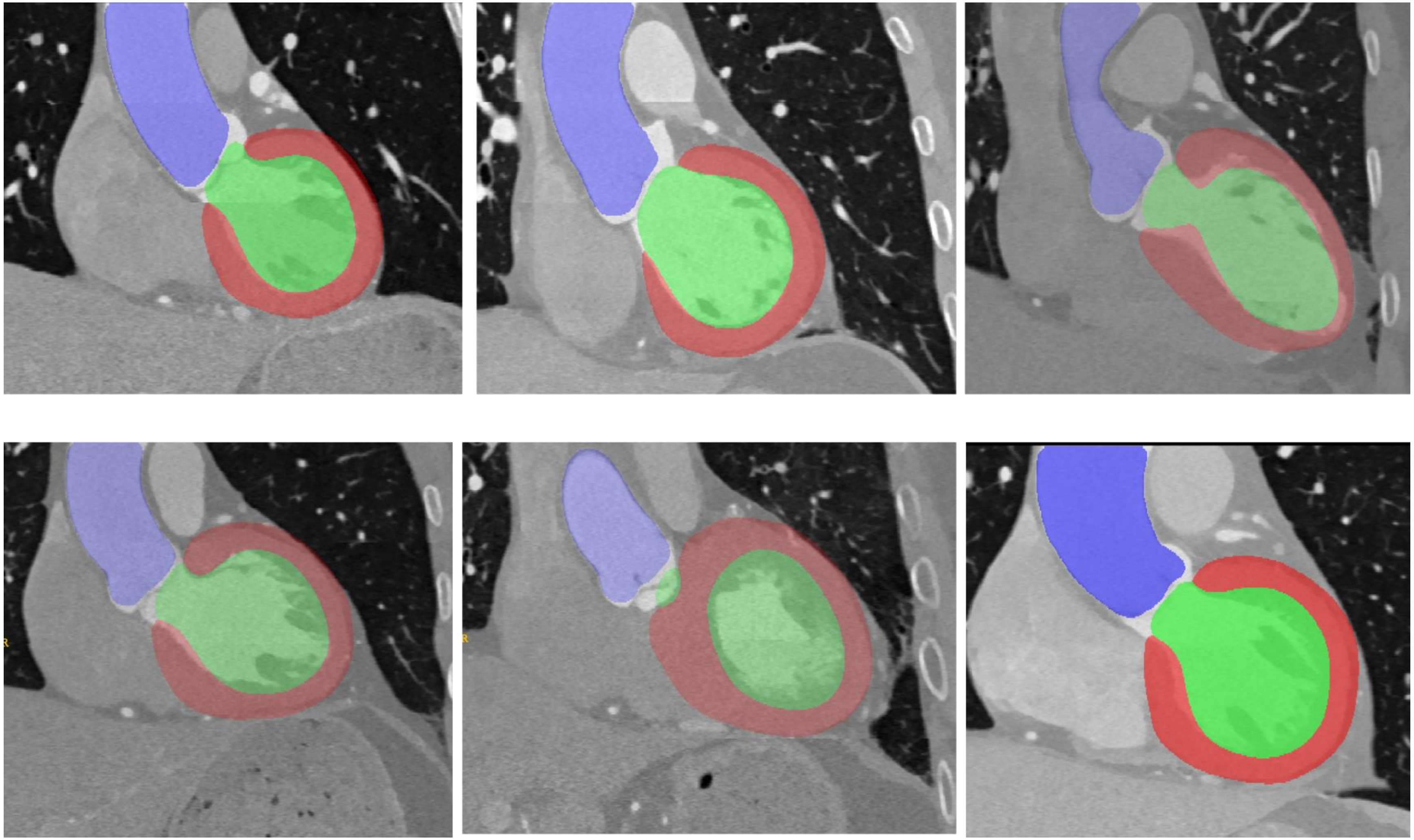
Model development

All data preprocessing and model development were conducted using different libraries in Python such as ITK[4,5], PyTorch[6], TorchIO[7], and MONAI[8] (more details are provided on GitHub)[9,10]. All computational was performed on high-performance servers equipped with 3 A100 GPUs, 250 CPU cores, and 1 TB of VRAM. All developed code and models are made publicly available on our AI-CVI laboratory's GitHub page (https://github.com/AI-in-Cardiovascular-Medicine/AAOCA). In addition, we have also provided a publicly available web service, accessible via the following link (Link to the project: https://mb-neuro.medical-blocks.ch/public_access/projects and link to the WebApp: https://mb-neuro.medical-blocks.ch/public_access/projects/aaoca), which allows users to easily upload images in various desired formats for use to get the report and result based on models developed in the current study.

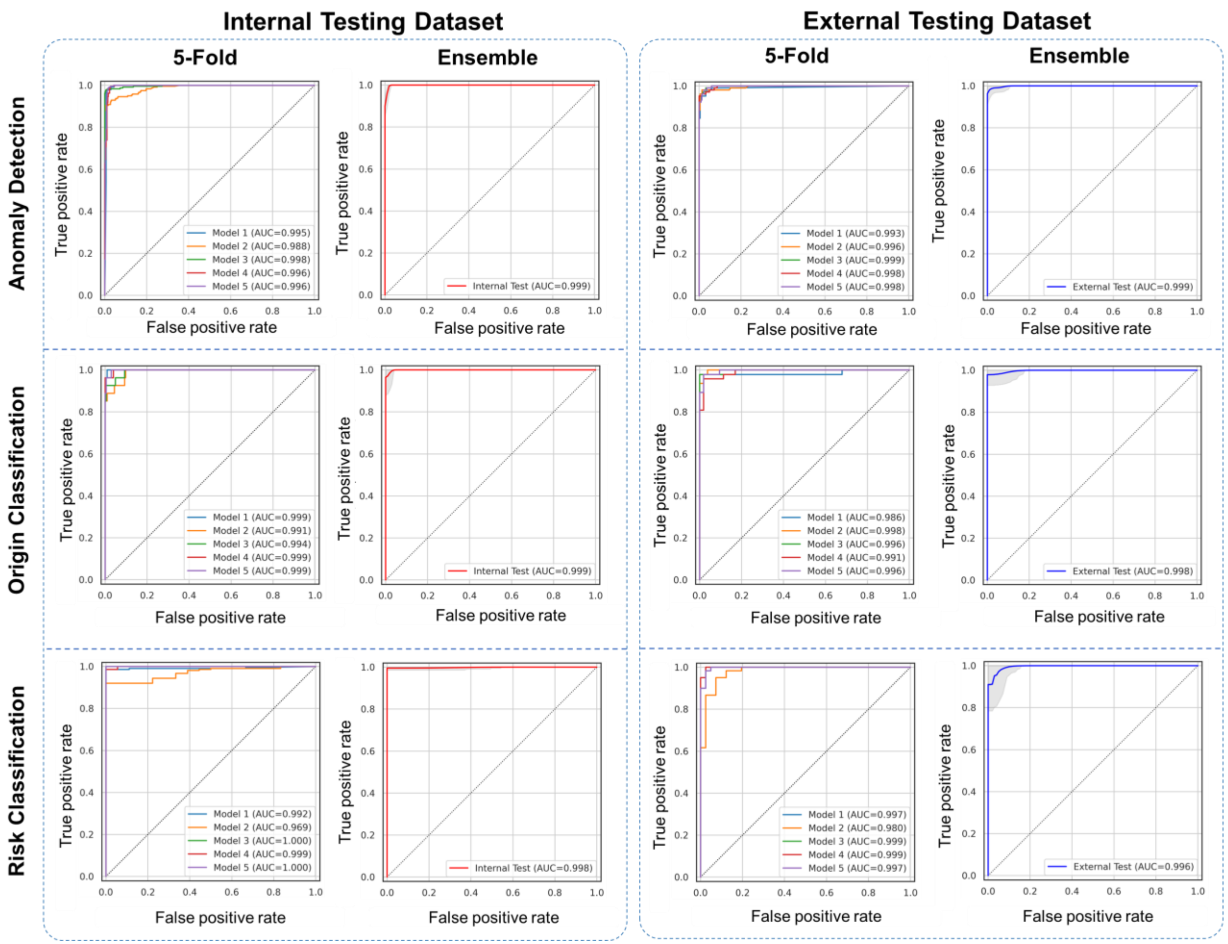
Supplementary Discussion

Although we reported the whole results based on strategy one, our goal was to make it more generalizable and robust by utilizing all available labeled datasets for further use. The performance of the model remained consistent when tested with data from the external test set under the second strategy, and in both the second and third strategies, we did not find more positive cases from the external clinical evaluation dataset; however, the number of false positive cases decreased. This demonstrates the robustness and generalizability of the model developed using the first and main strategy. However, for future applications, we recommend developing the model using the third strategy, as it utilizes the entire dataset from multiple centers and is more likely to produce generalizable results in real-world scenarios.

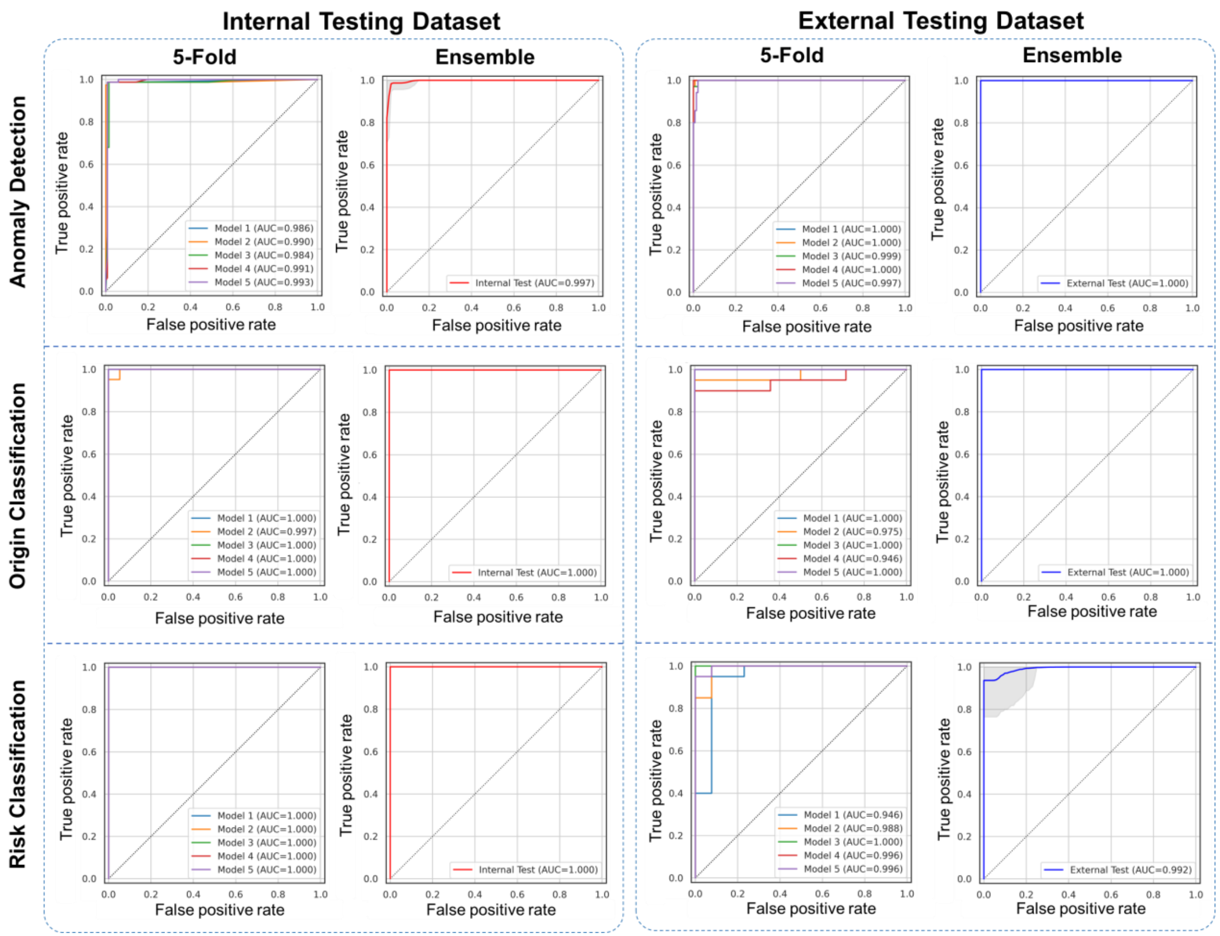
Supplemental Figures



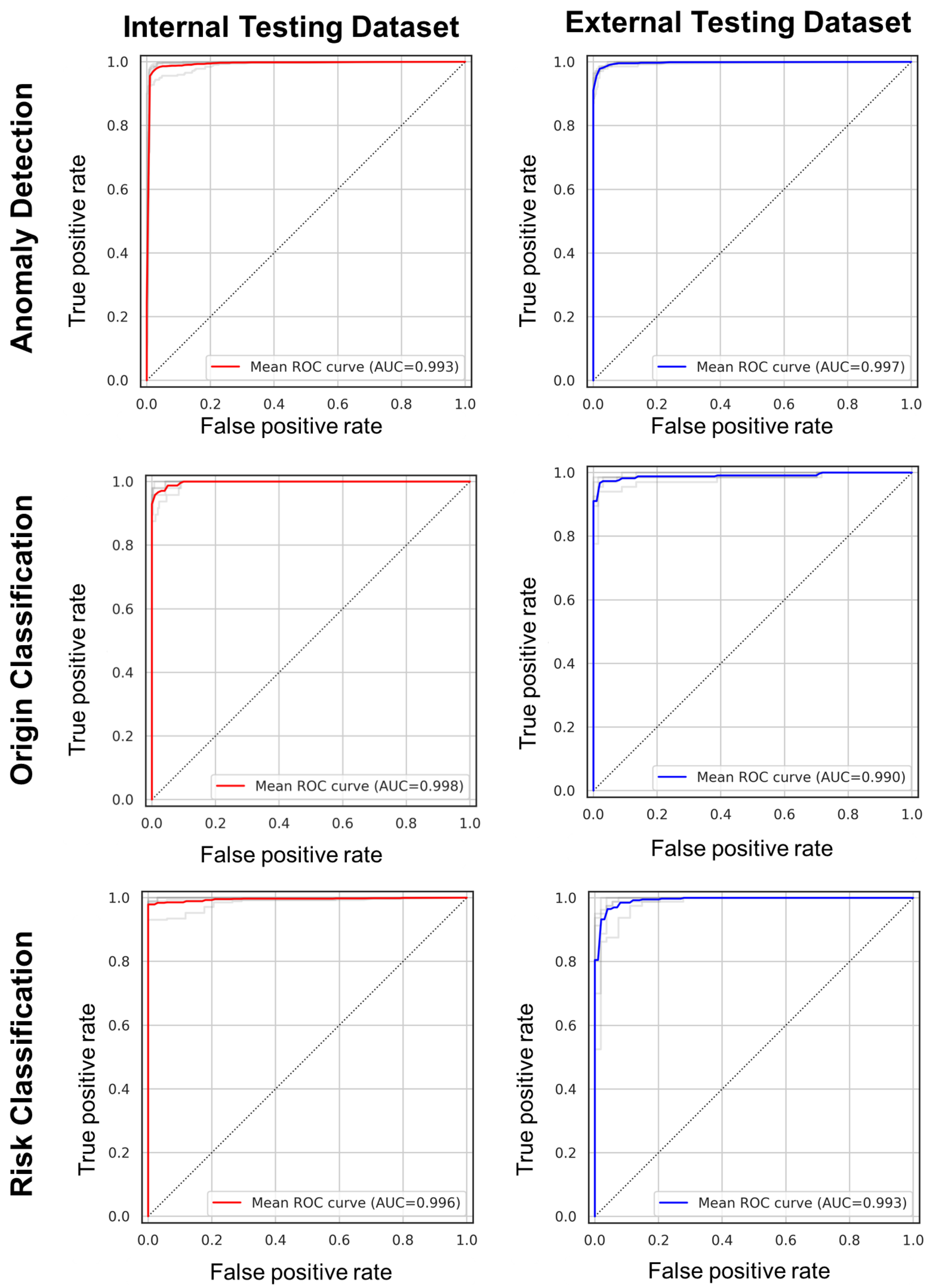
Supplemental Figure 1: Six different cases with their corresponding segmentations of the aorta and left ventricle.



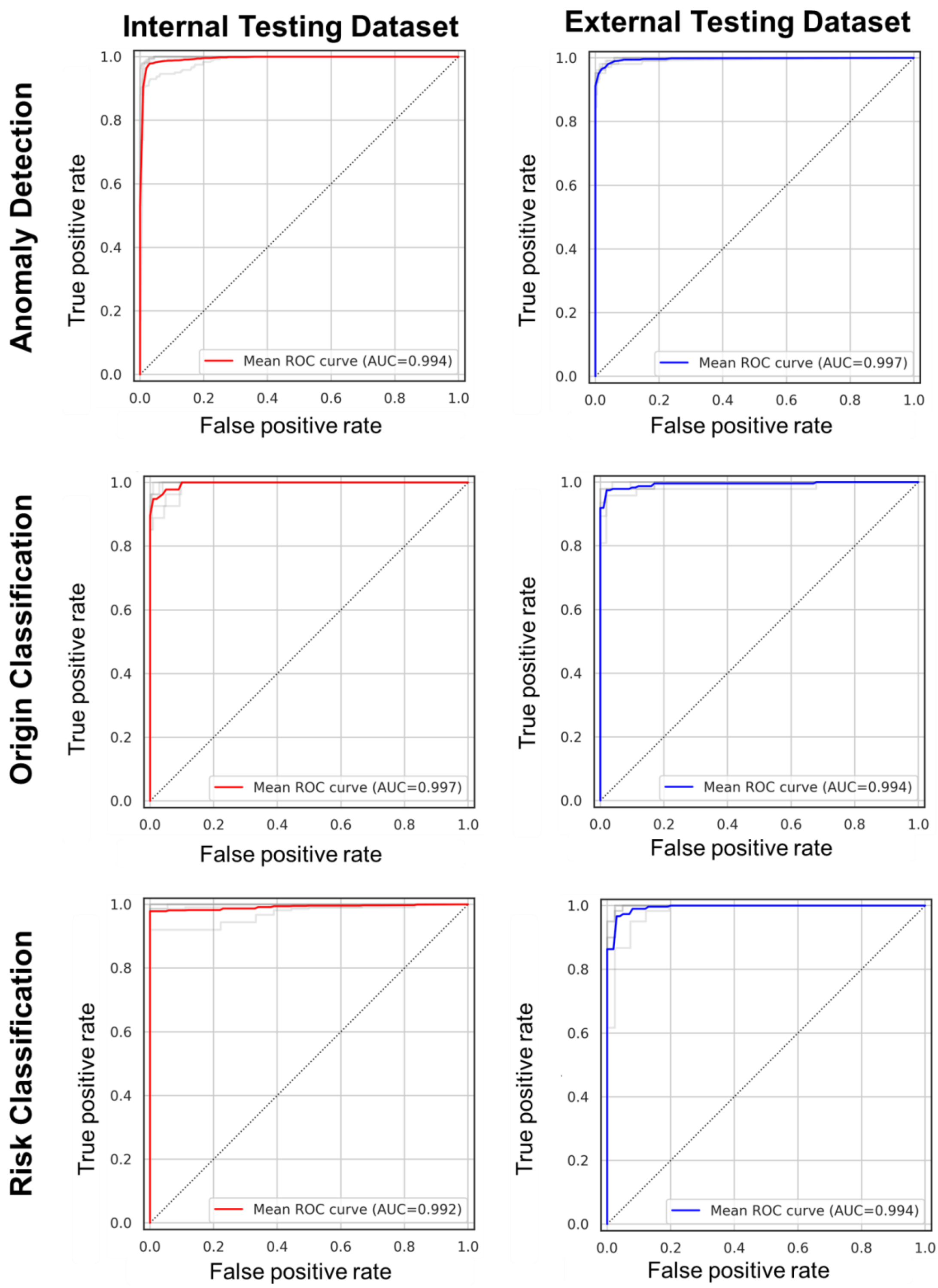
Supplemental Figure 2: ROC curves including the 5 different folds and the ensemble of 5 models across different tasks for various test datasets in the male population. Confidence intervals and tolerance intervals for the ensemble models were computed with the bootstrap method (10,000 iterations), the gray area on the ensemble figures is the tolerance interval. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA); Risk Classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. AUC: area under the curve. Source data are provided as a Source Data file.



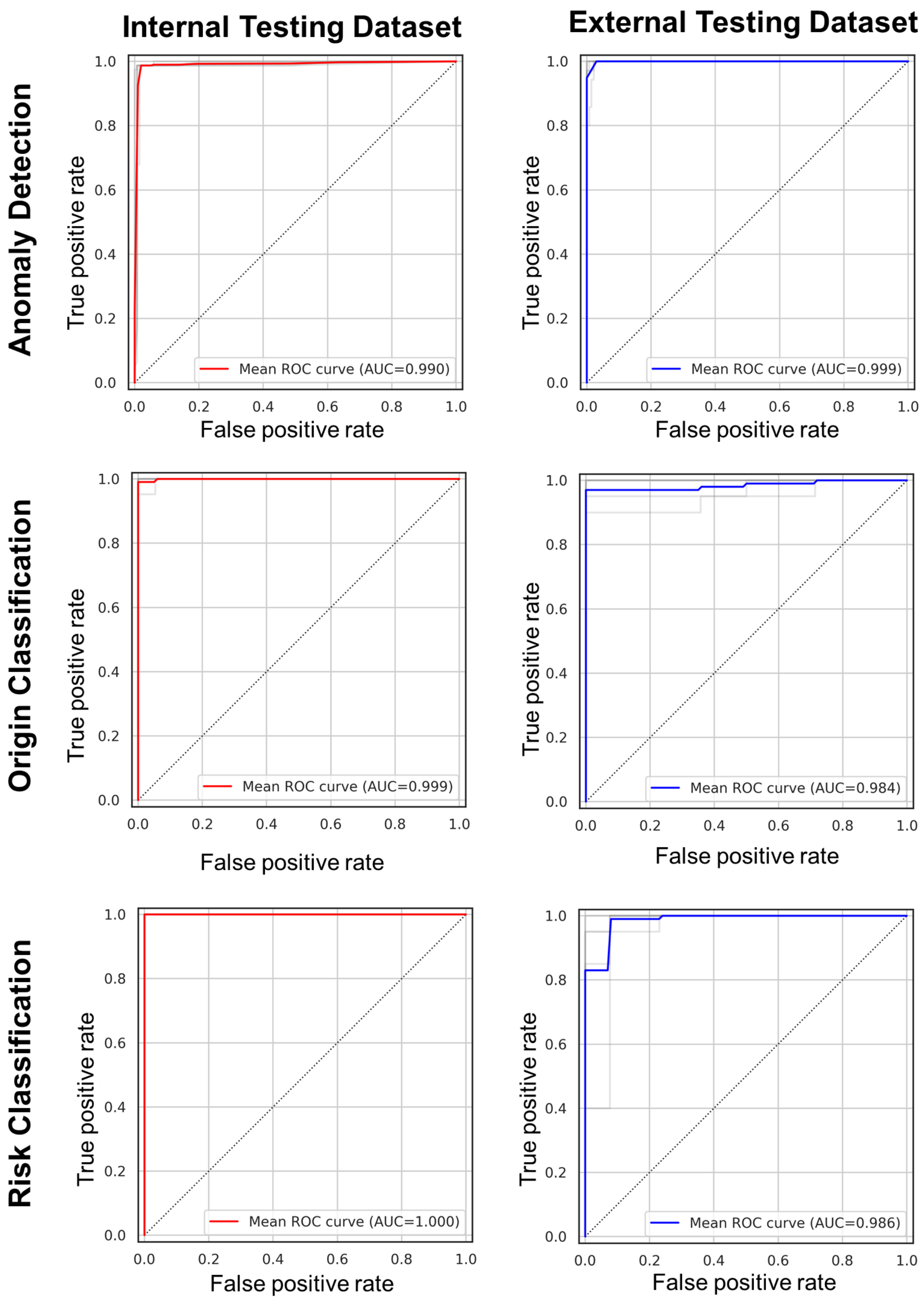
Supplemental Figure 3: ROC curves including the 5 different folds and the ensemble of 5 models across different tasks for various test datasets in the female population. Confidence intervals and tolerance intervals for the ensemble models were computed with the bootstrap method (10,000 iterations), the gray area on the ensemble figures is the tolerance interval. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA); Risk Classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. AUC: area under the curve. Source data are provided as a Source Data file.



Supplemental Figure 4: Mean ROC curves of 5 different folds across different Tasks for various datasets. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA; Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.



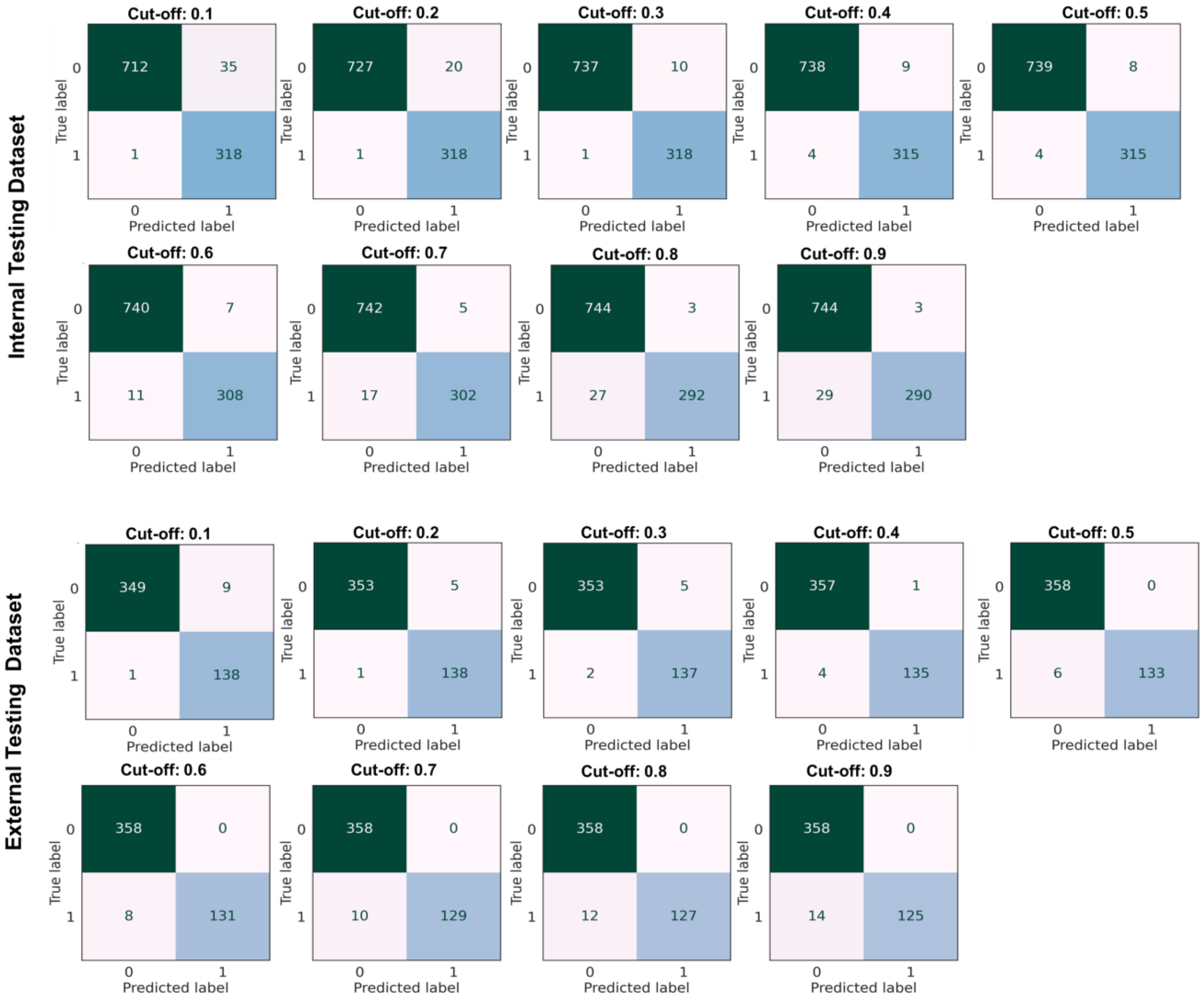
Supplemental Figure 5: Mean ROC curves of 5 different folds across different Tasks for various datasets for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA; Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.



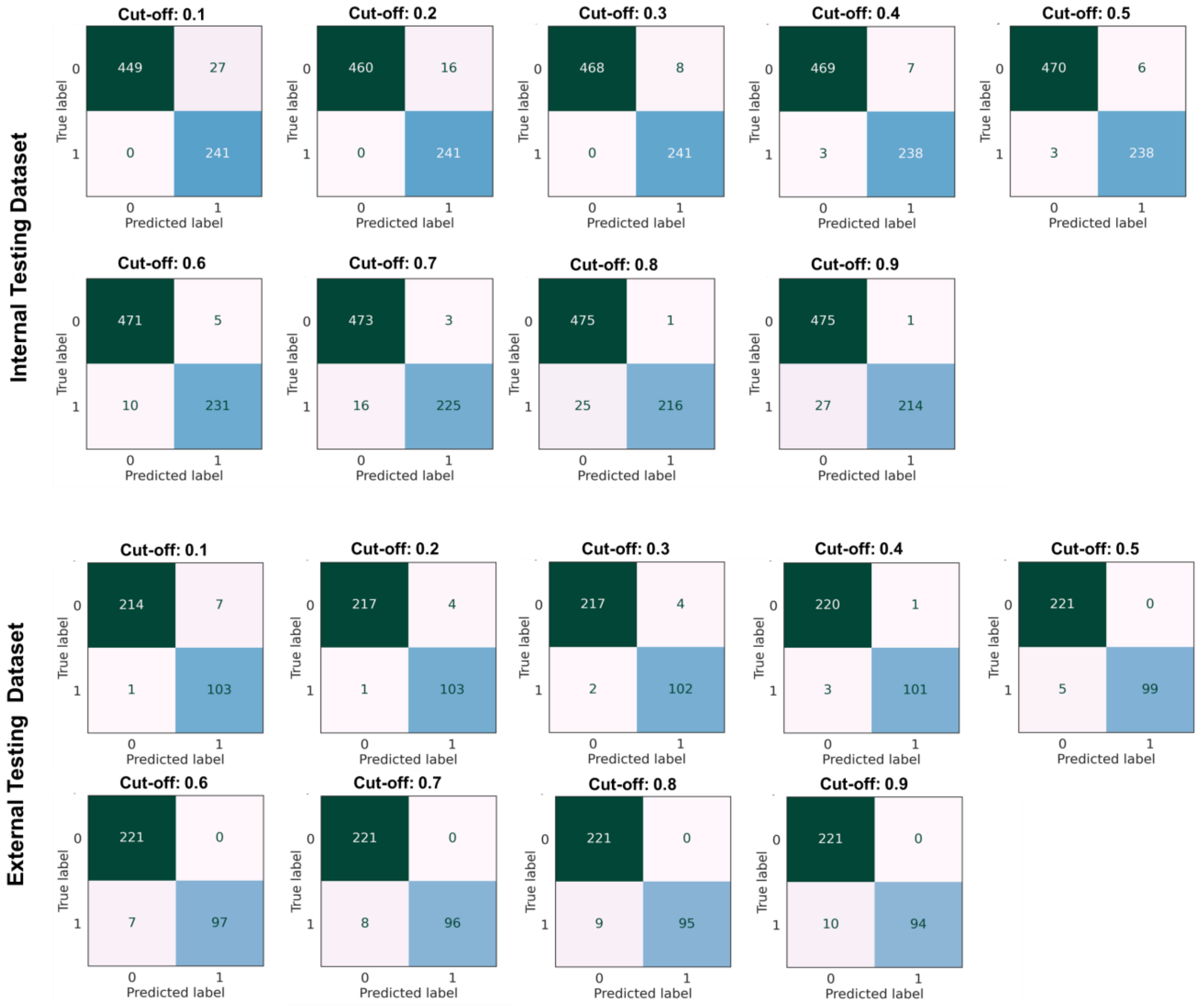
Supplemental Figure 6: Mean ROC curves of 5 different folds across different Tasks for various datasets for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA; Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.

Supplemental Figure 7: Confusion matrices of different models in various Tasks for different datasets in the ensemble model for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA); Risk Classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. Source data are provided as a Source Data file.

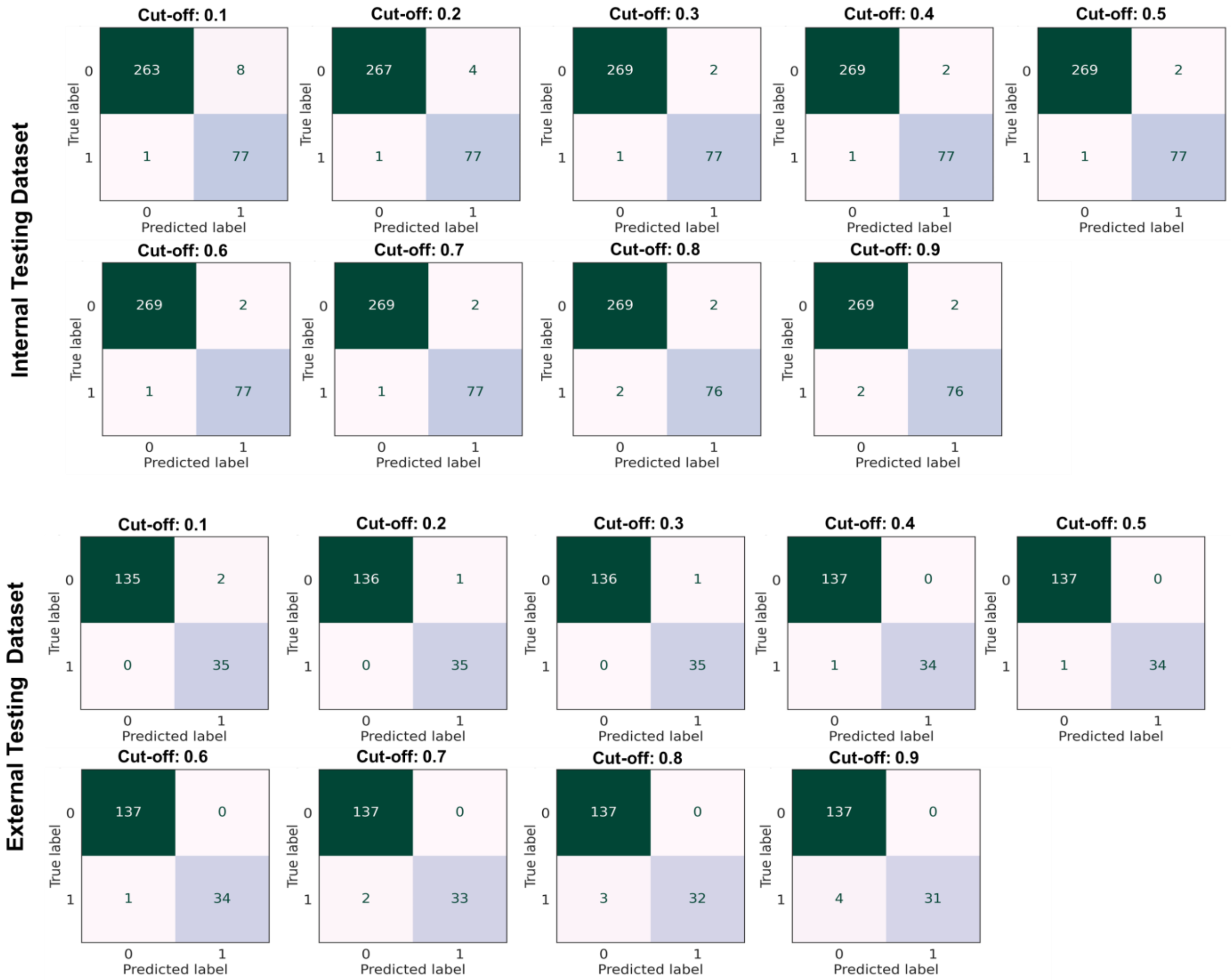
Supplemental Figure 8: Confusion matrices of different models in various Tasks for different datasets in the ensemble model for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA); Risk Classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. Source data are provided as a Source Data file.



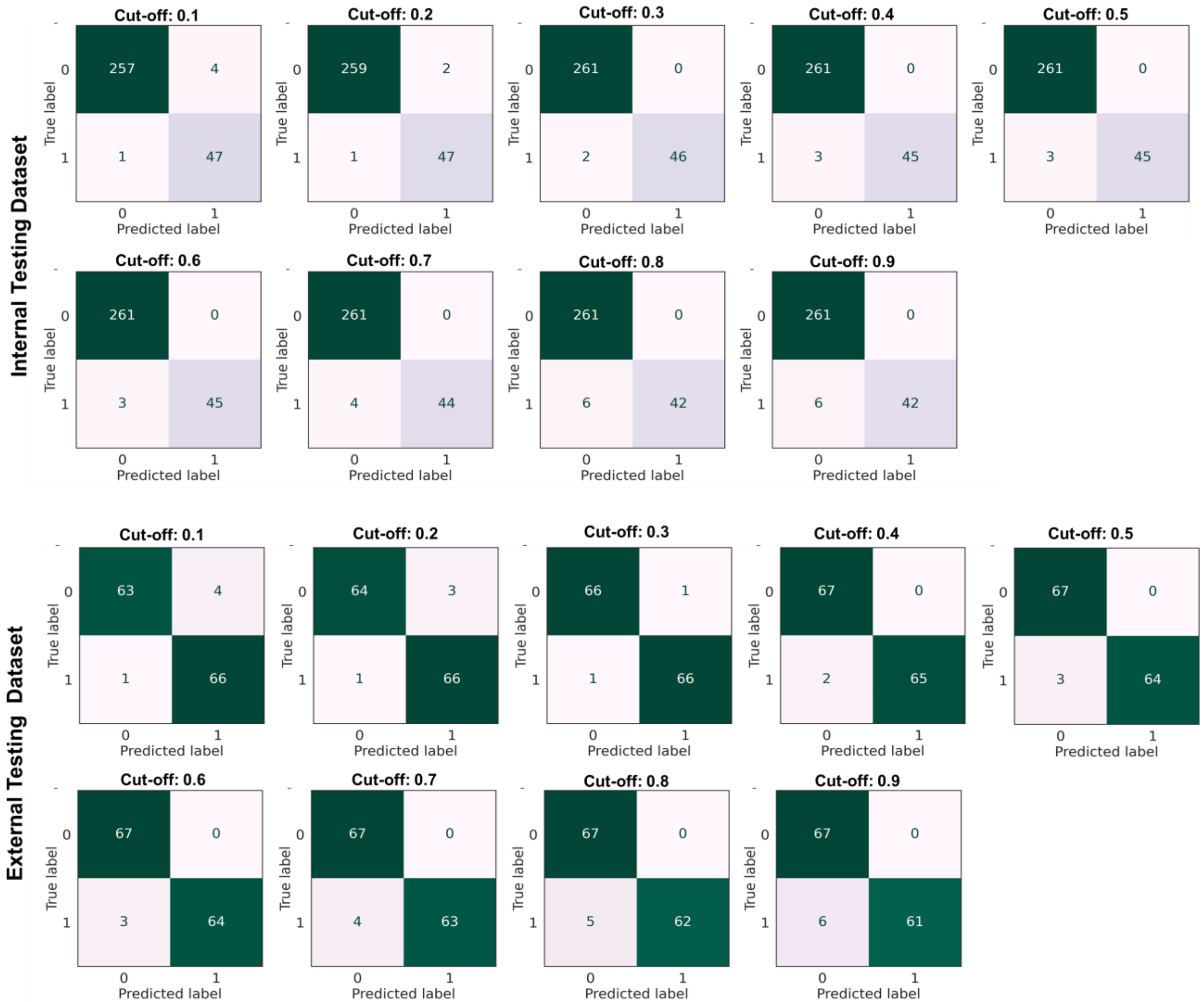
Supplemental Figure 9: Confusion matrices of ensemble model in Anomaly Detection for various datasets at different cut-off points. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



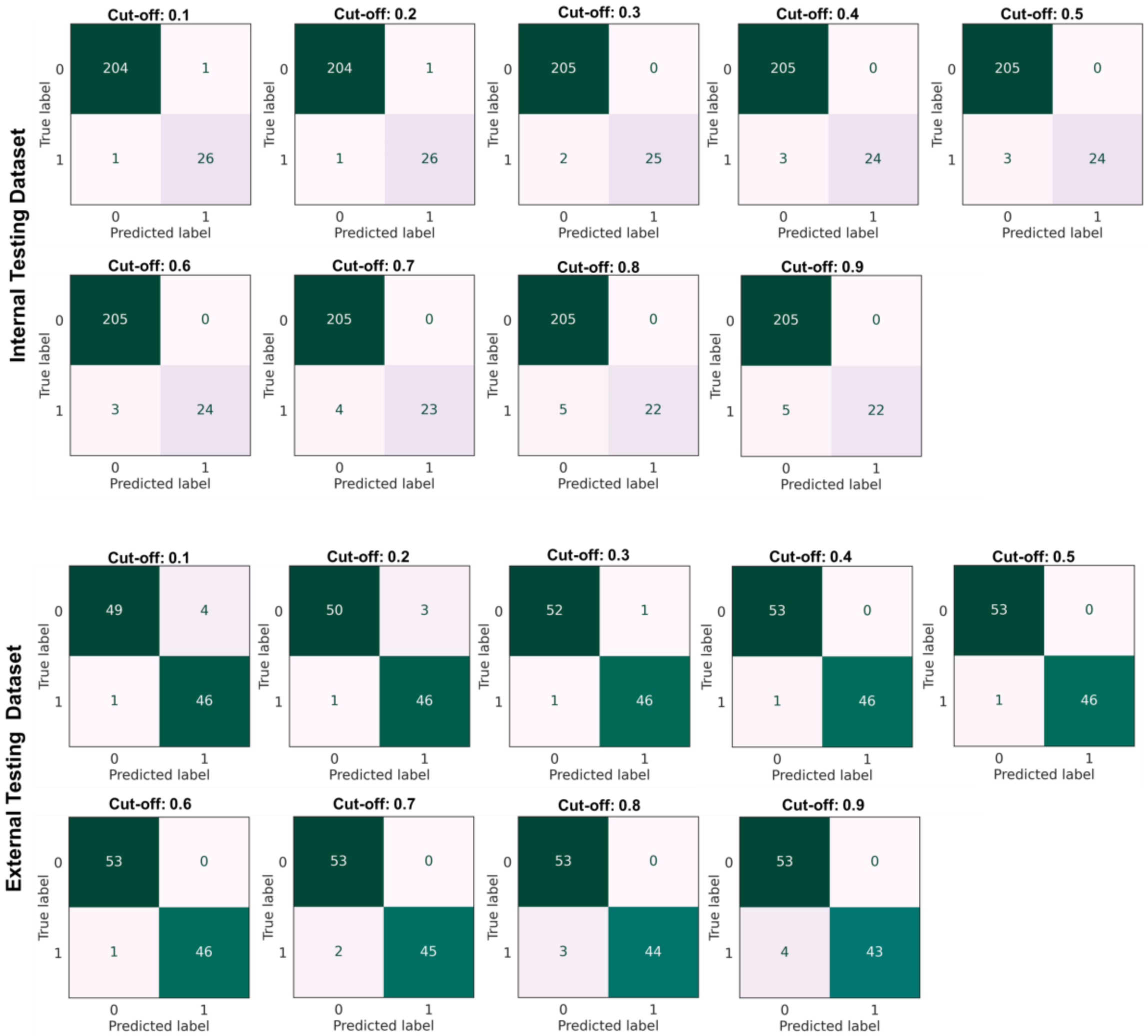
Supplemental Figure 10: Confusion matrices of ensemble model in Anomaly Detection for various datasets at different cut-off points in male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



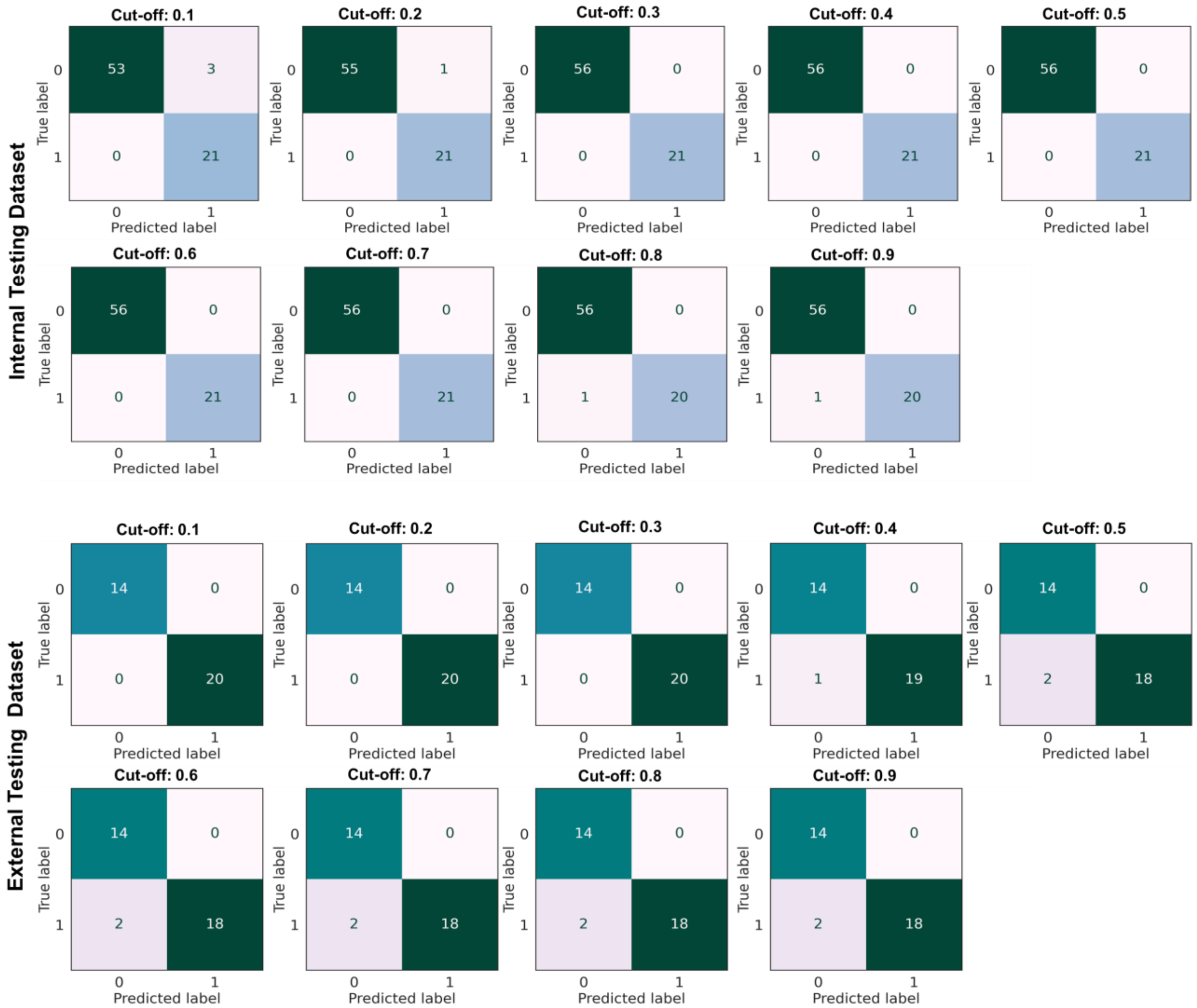
Supplemental Figure 11: Confusion matrices of ensemble model in Anomaly Detection for various datasets at different cut-off points in female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



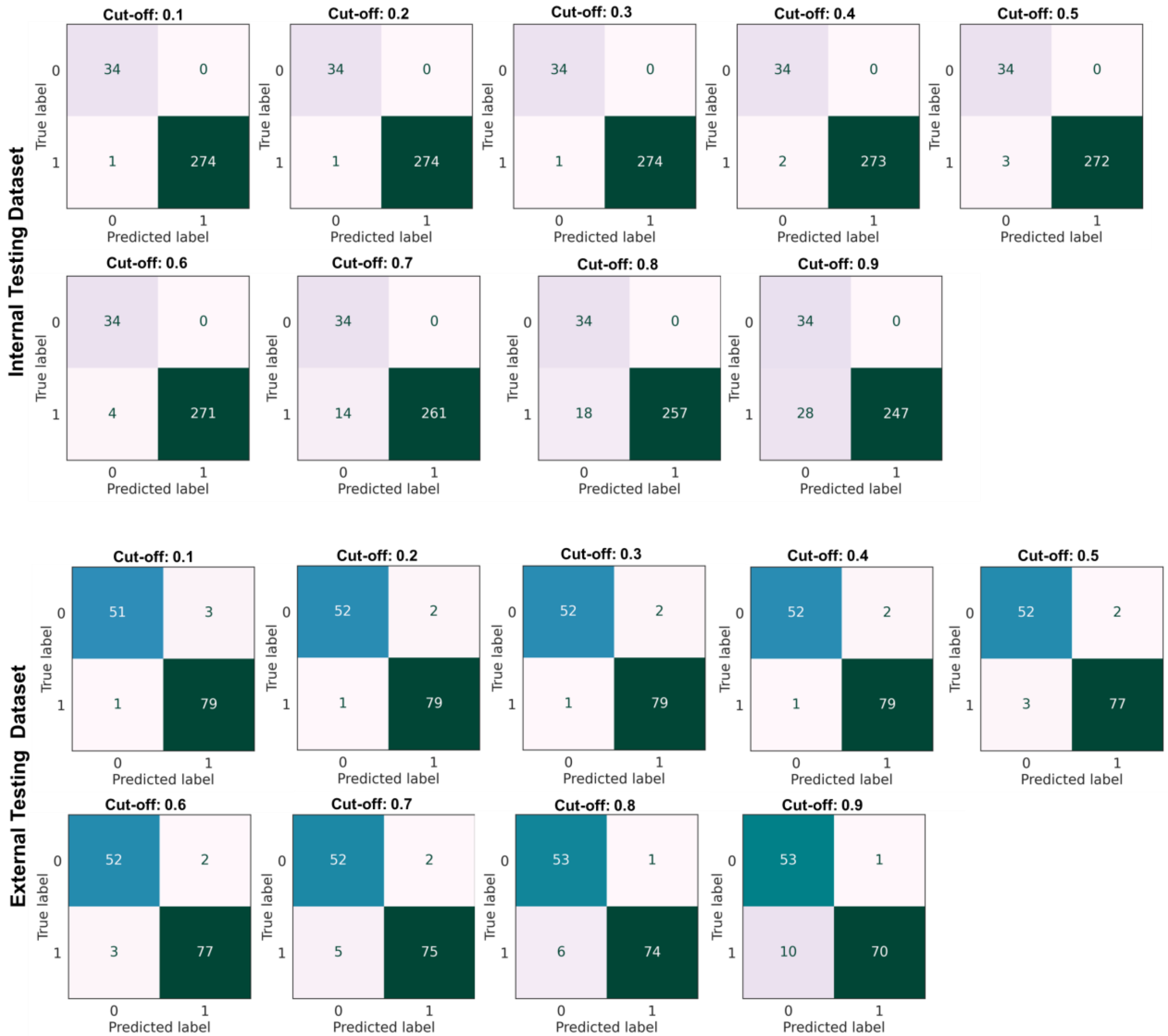
Supplemental Figure 12: Confusion matrices of ensemble model in Origin Classification for various datasets at different cut-off points. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). Source data are provided as a Source Data file.



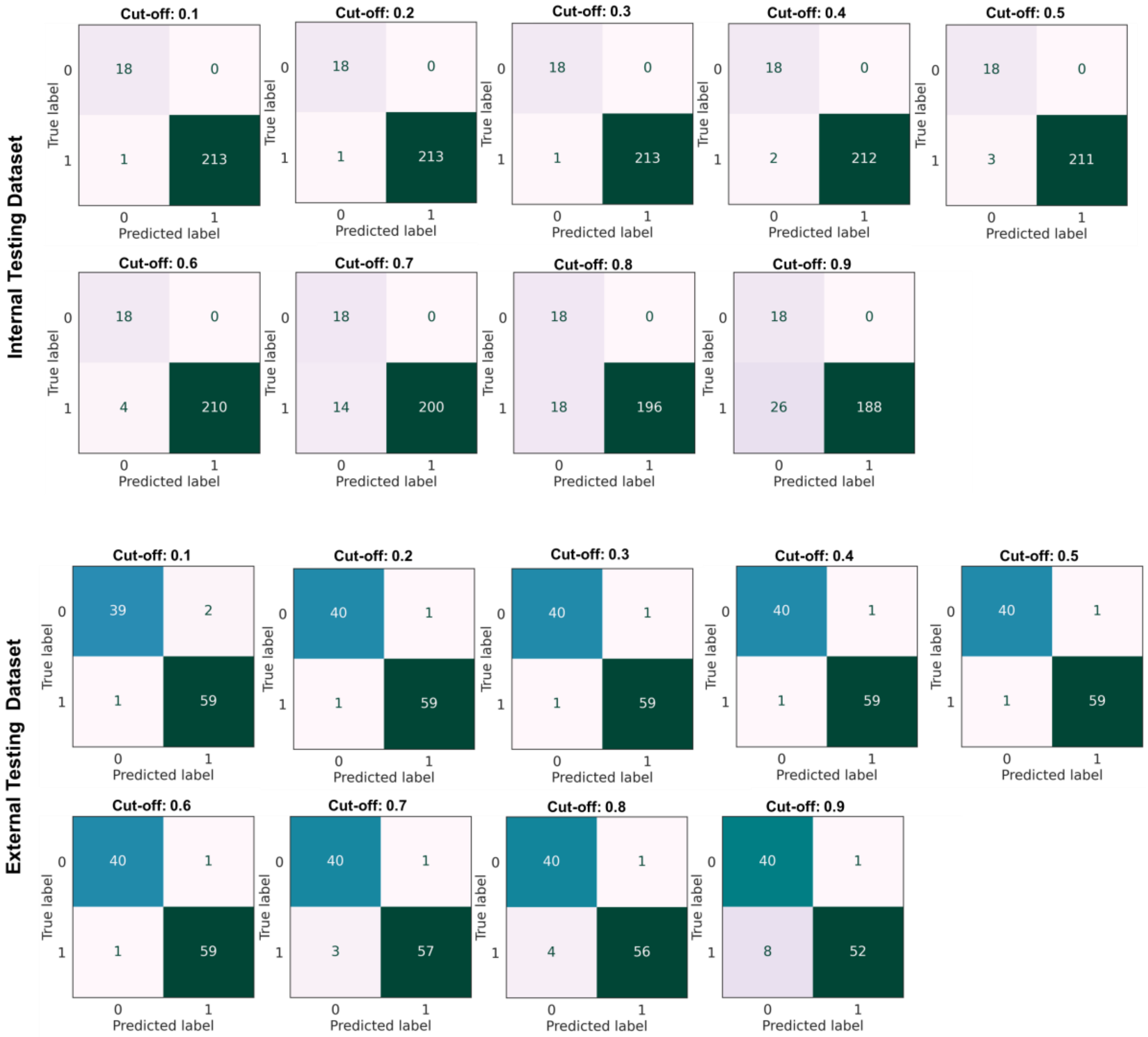
Supplemental Figure 13: Confusion matrices of ensemble model in Origin Classification for various datasets at different cut-off points in male population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). Source data are provided as a Source Data file.



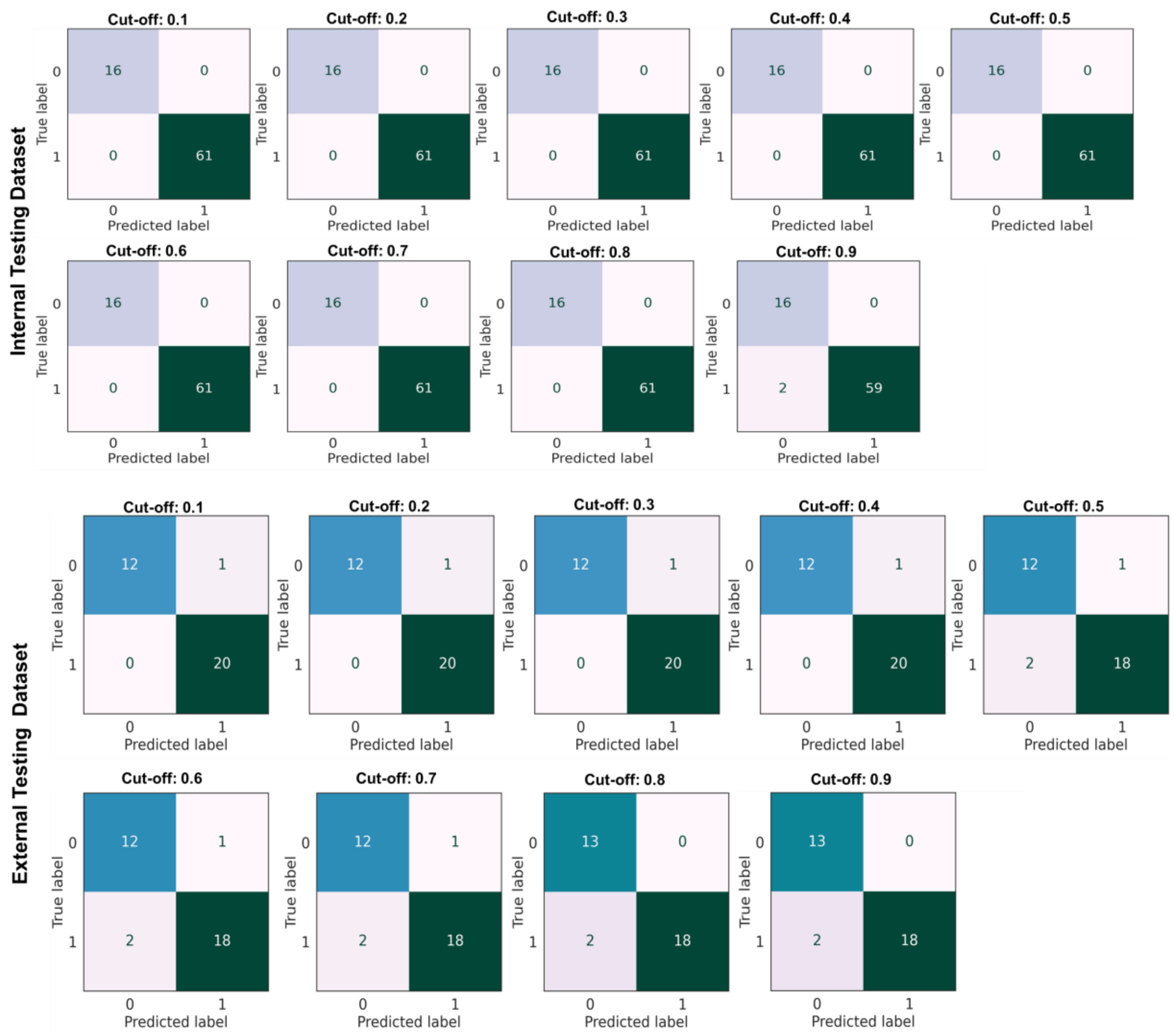
Supplemental Figure 14: Confusion matrices of ensemble model in Origin Classification for various datasets at different cut-off points in female population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). Source data are provided as a Source Data file.



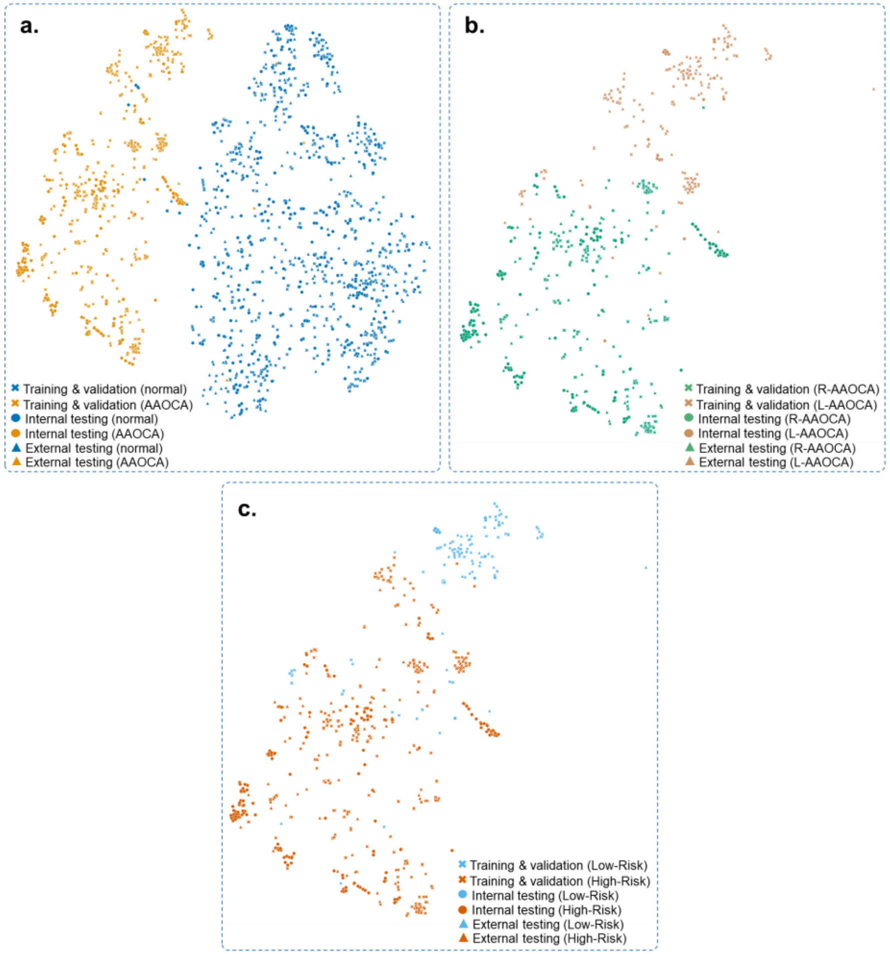
Supplemental Figure 15: Confusion matrices of ensemble model in Risk Classification for various datasets at different cut-off points. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.



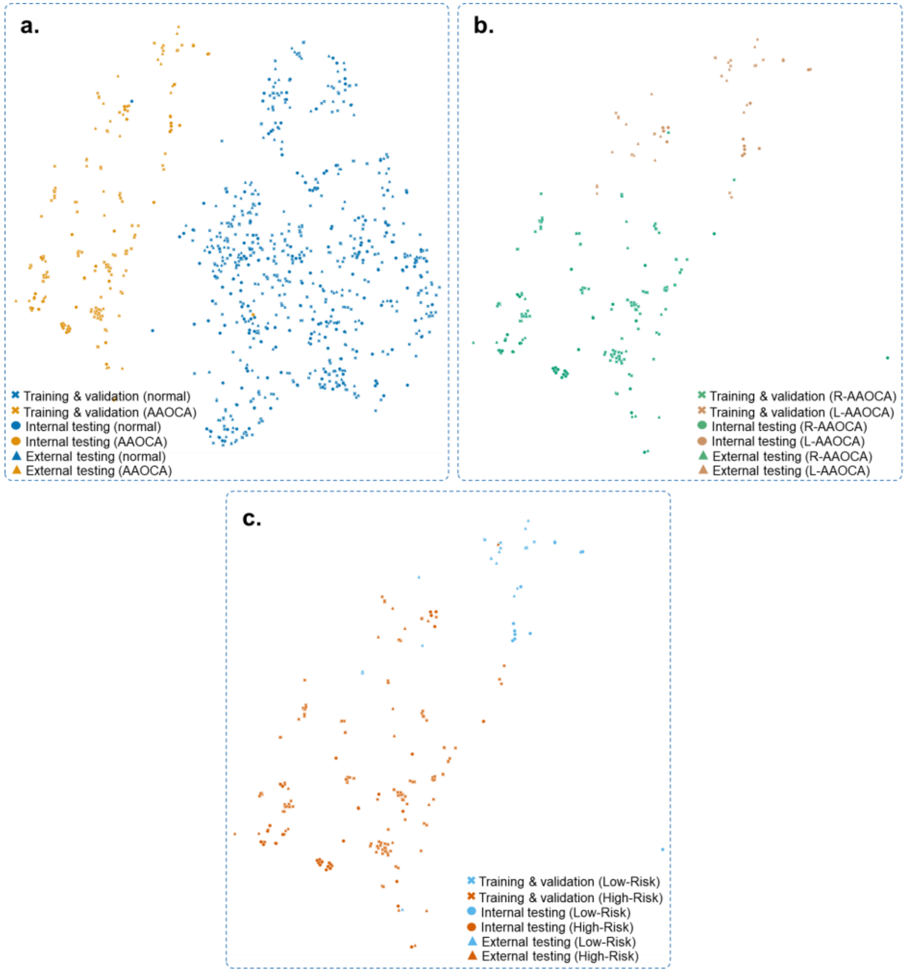
Supplemental Figure 16: Confusion matrices of ensemble model in Risk Classification for various datasets at different cut-off points in male population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.



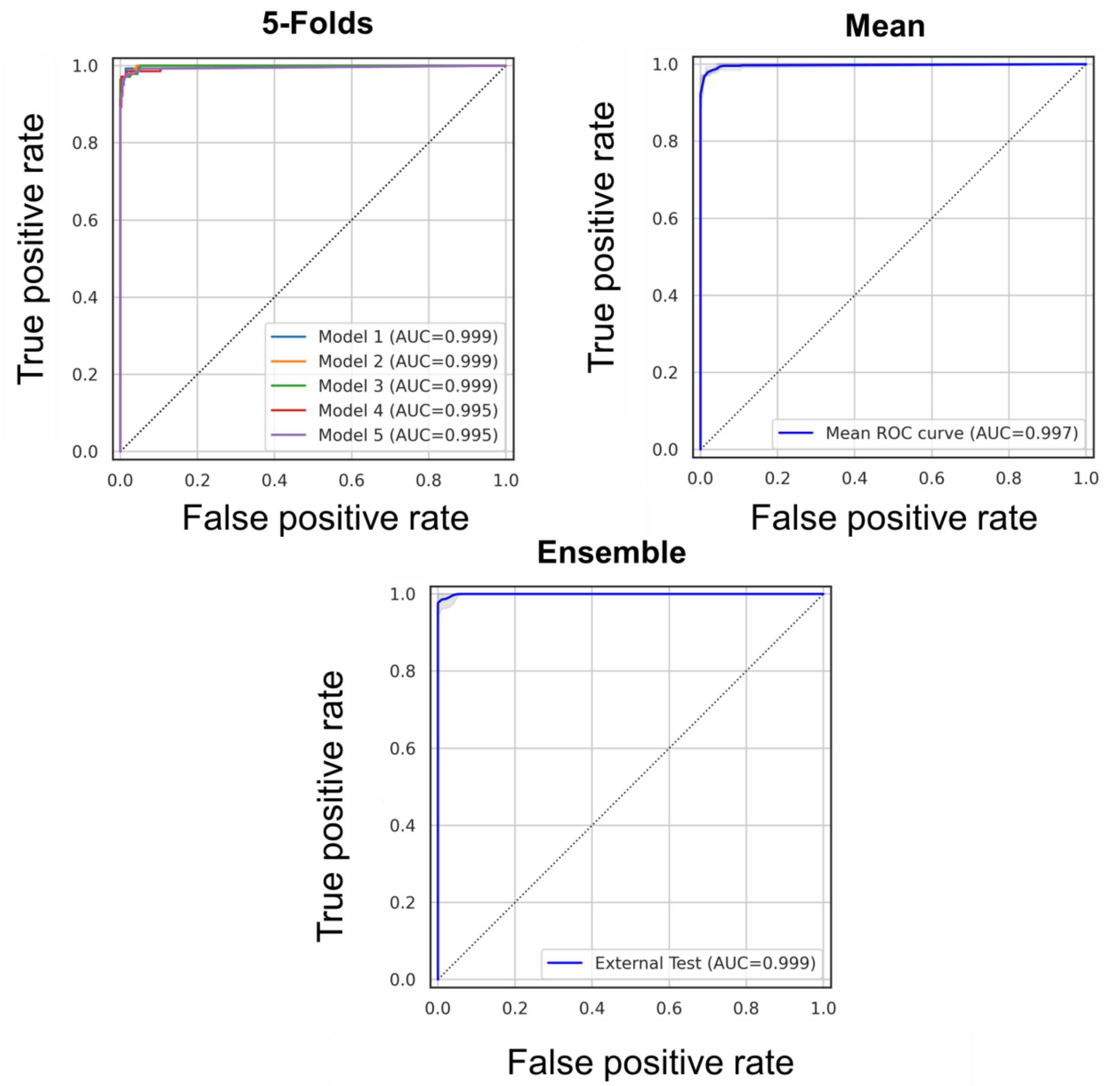
Supplemental Figure 17: Confusion matrices of ensemble model in Risk Classification for various datasets at different cut-off points in female population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.



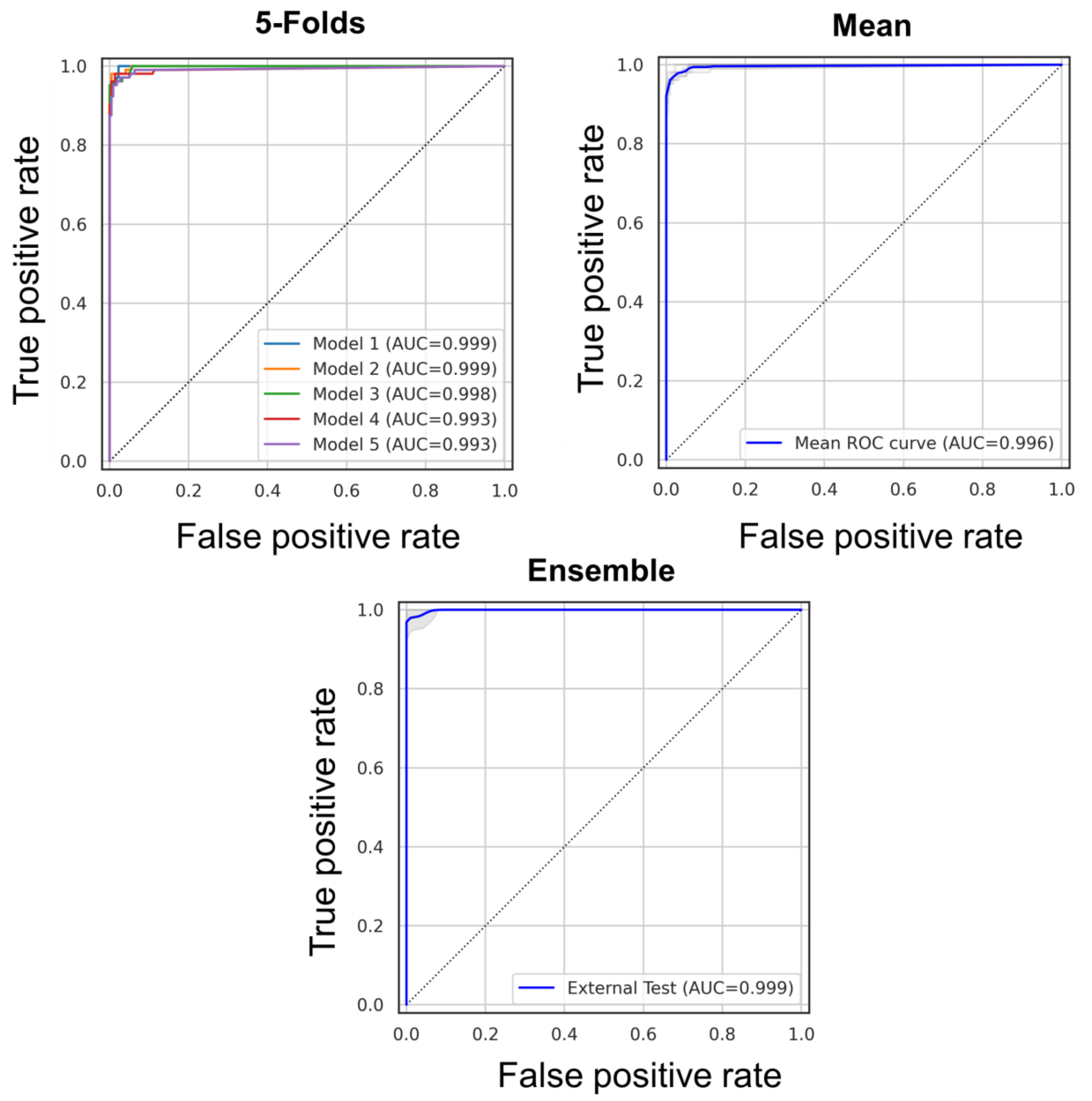
Supplemental Figure 18: t-SNE maps of the Anomaly Detection model in male population colorized for **a)** anomalies and normal cases. Only for the anomaly dataset, **b)** right and left anomalies, and **c)** high and low-risk anomalies. t-SNE: t-distributed stochastic neighbor embedding, AAOCA: Anomalous Aortic Origin of the Coronary Artery, CCTA: Coronary CT Angiography, R-AAOCA: Right AAOCA, L-AAOCA: left AAOCA. Source data are provided as a Source Data file.



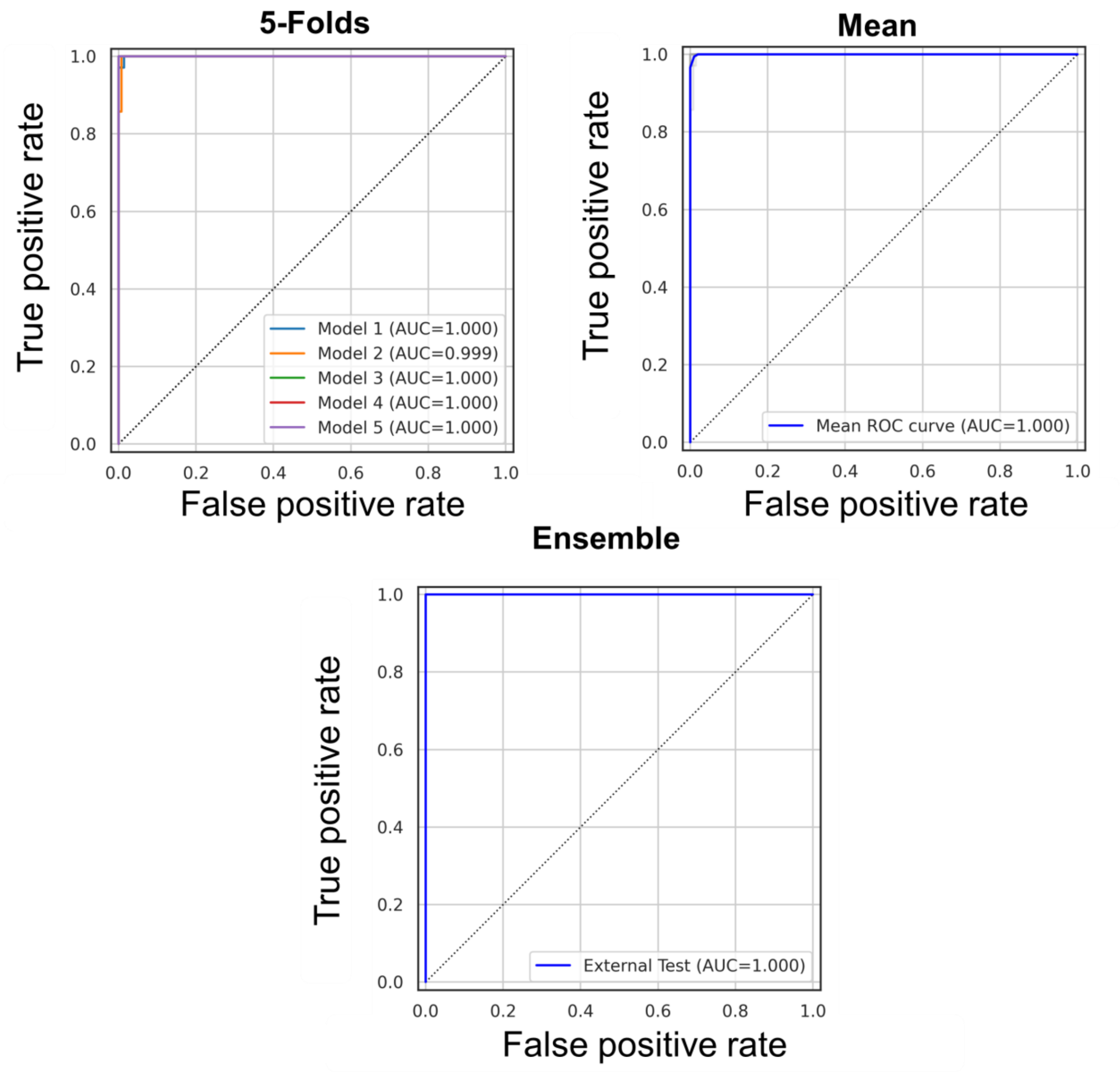
Supplemental Figure 19: t-SNE maps of the Anomaly Detection model in female population colorized for **a)** anomalies and normal cases. Only for the anomaly dataset, **b)** right and left anomalies, and **c)** high and low-risk anomalies. t-SNE: t-distributed stochastic neighbor embedding, AAOCA: Anomalous Aortic Origin of the Coronary Artery, CCTA: Coronary CT Angiography, R-AAOCA: Right AAOCA, L-AAOCA: left AAOCA. Source data are provided as a Source Data file.



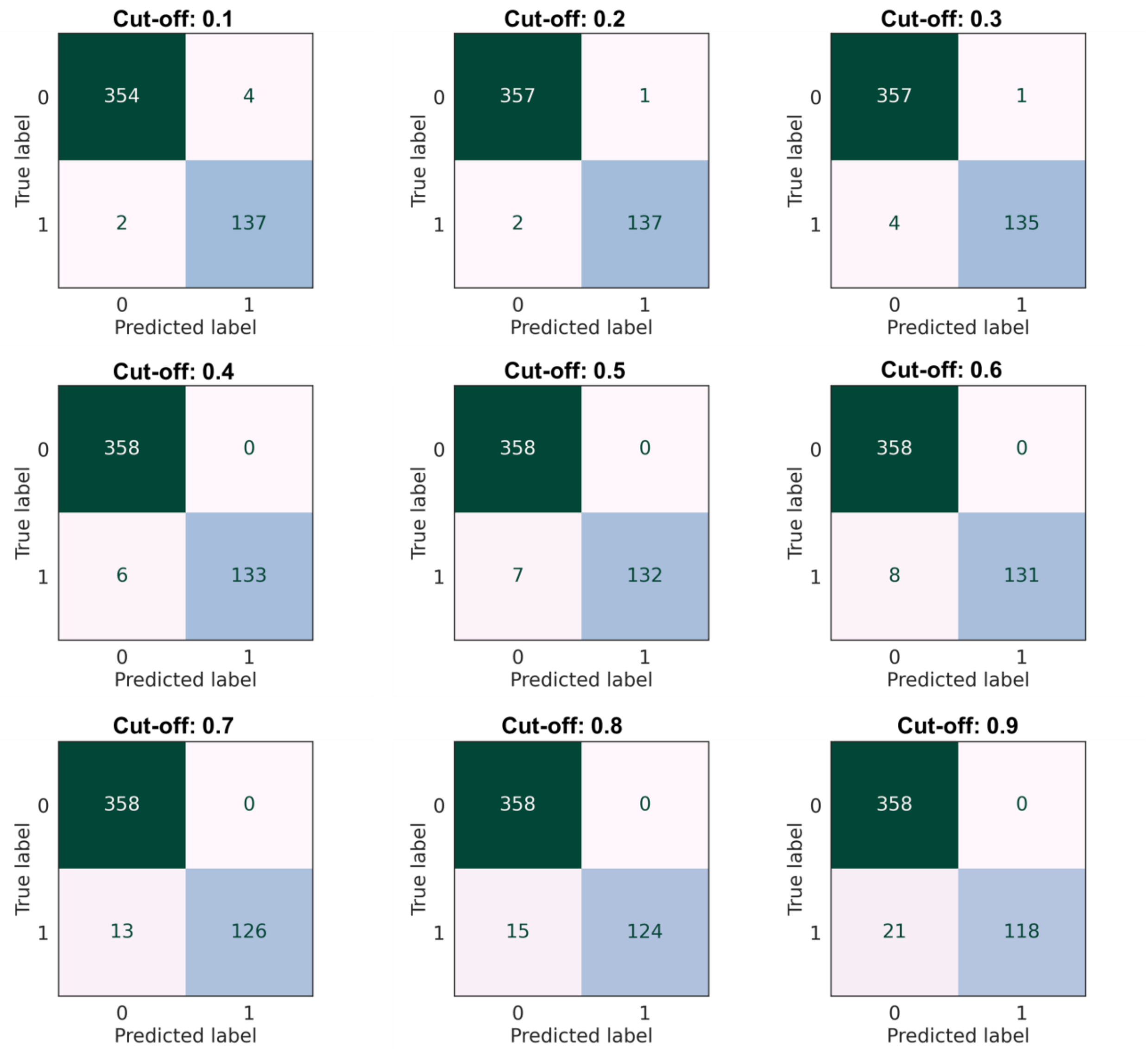
Supplemental Figure 20: ROC curves of 5 folds, mean, and an ensemble of strategy 2 in the external test dataset from external testing dataset. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file. Confidence intervals and tolerance intervals for the ensemble models were computed with the bootstrap method (10,000 iterations), the gray area on the ensemble figures is the tolerance interval



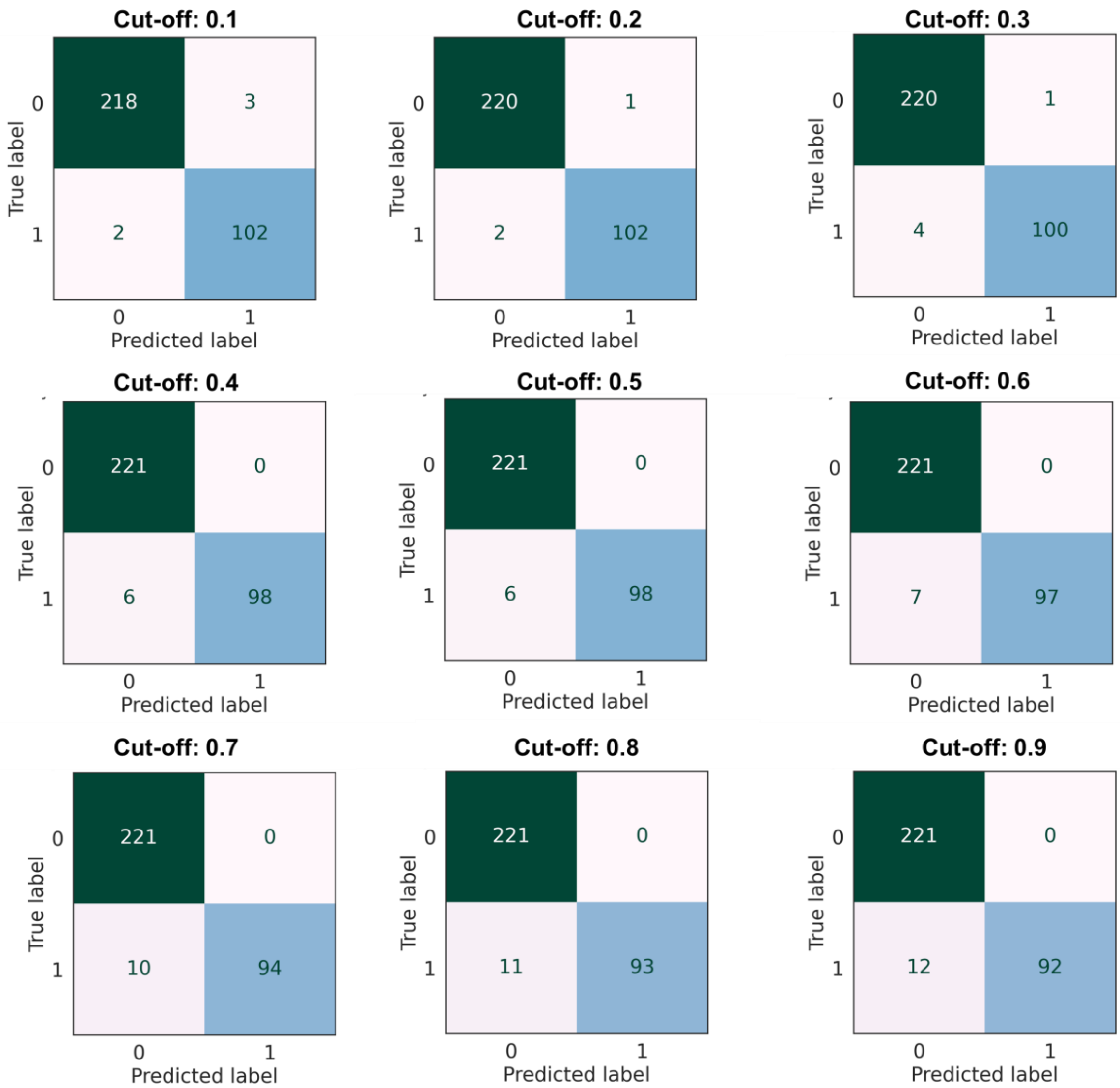
Supplemental Figure 21: ROC curves of 5 folds, mean, and an ensemble of strategy 2 in the external test dataset from external testing dataset for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file. Confidence intervals and tolerance intervals for the ensemble models were computed with the bootstrap method (10,000 iterations), the gray area on the ensemble figures is the tolerance interval



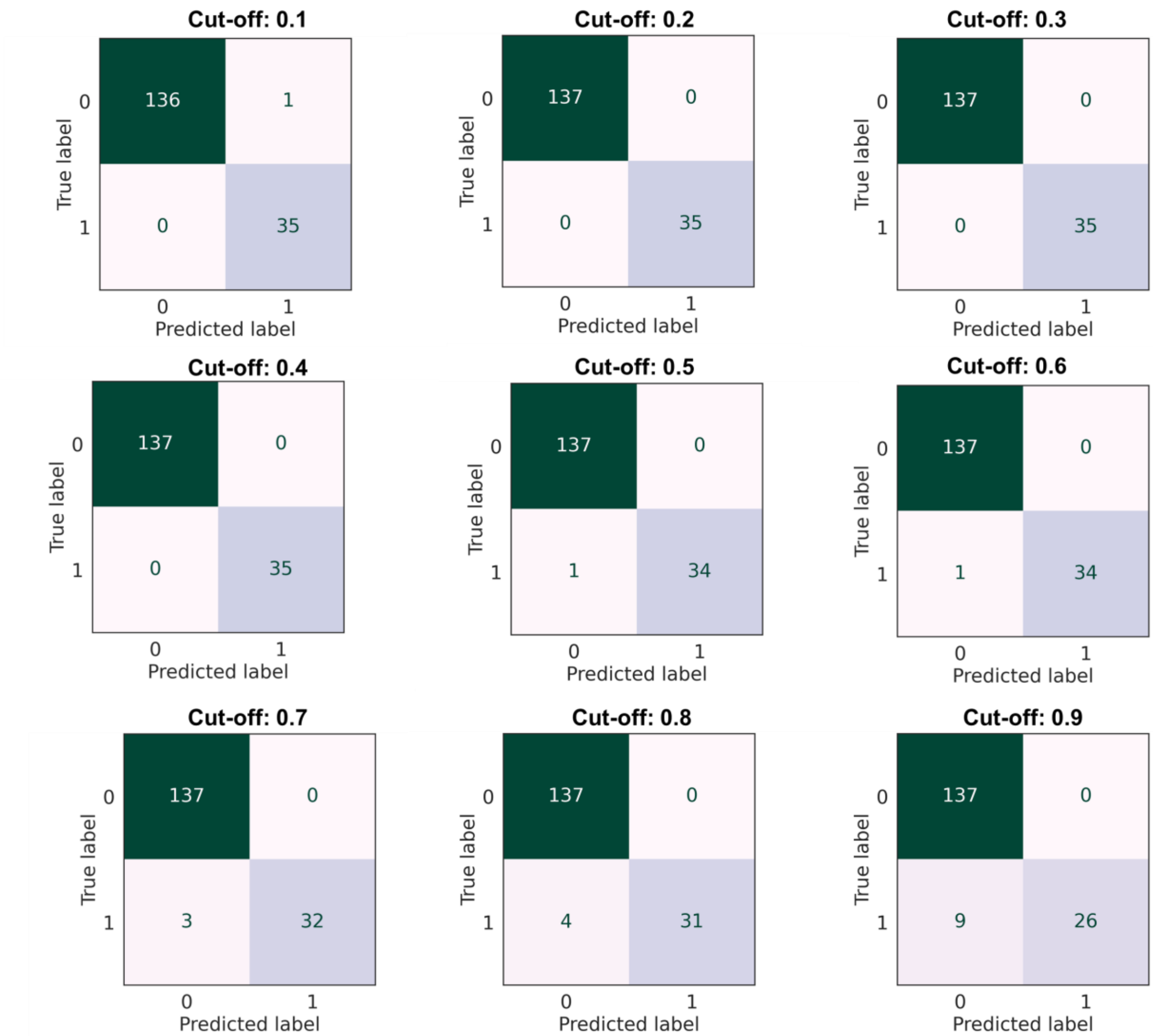
Supplemental Figure 22: ROC curves of 5 folds, mean, and an ensemble of strategy 2 in the external test dataset from external testing dataset for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file. Confidence intervals and tolerance intervals for the ensemble models were computed with the bootstrap method (10,000 iterations), the gray area on the ensemble figures is the tolerance interval



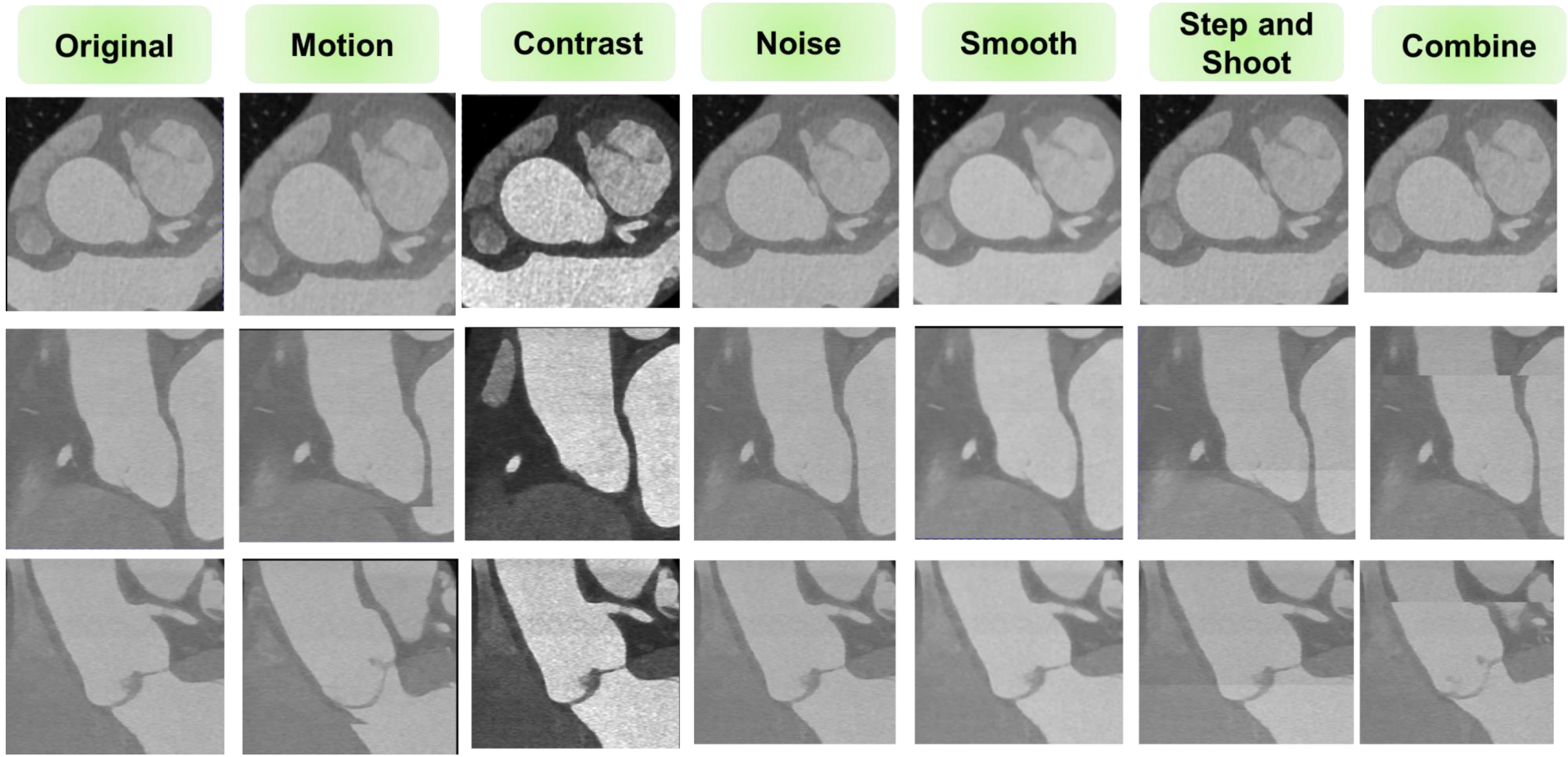
Supplemental Figure 23: Confusion matrices of ensemble model in Anomaly Detection in strategy 2 for external testing datasetat different cut-off points. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



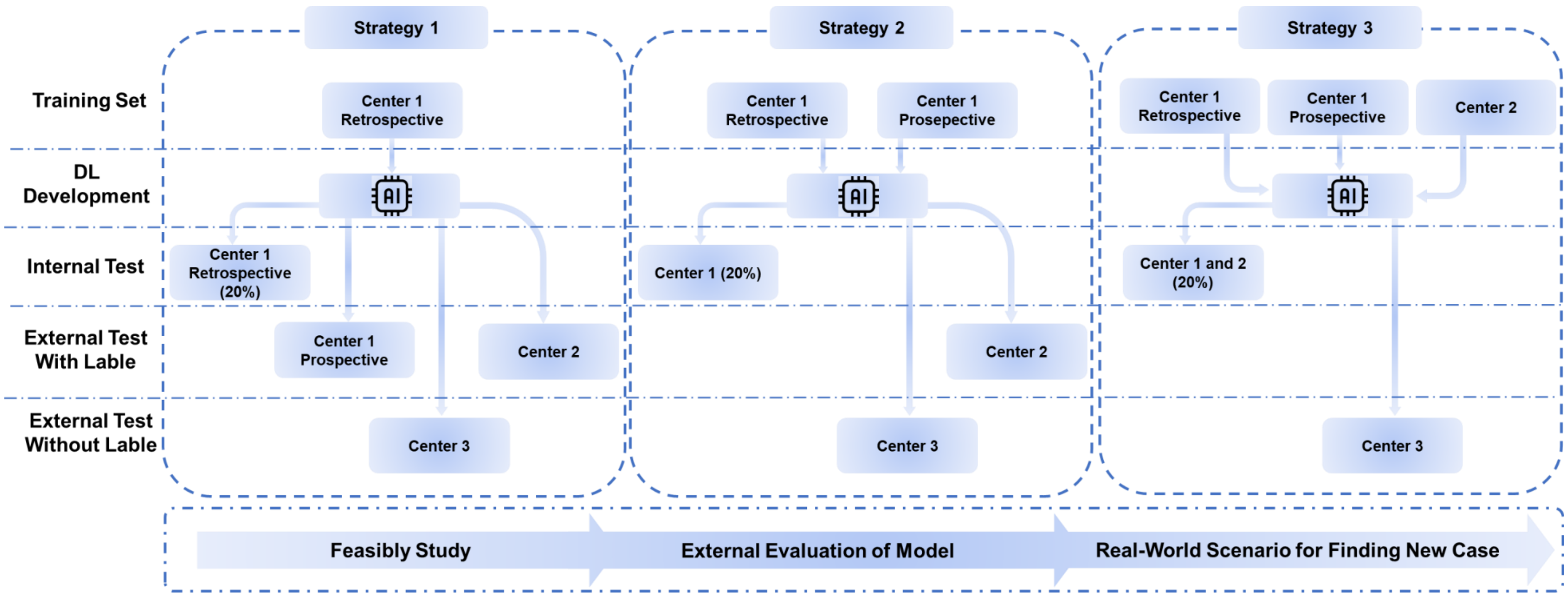
Supplemental Figure 24: Confusion matrices of ensemble model in Anomaly Detection in strategy 2 for external testing dataset at different cut-off points for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



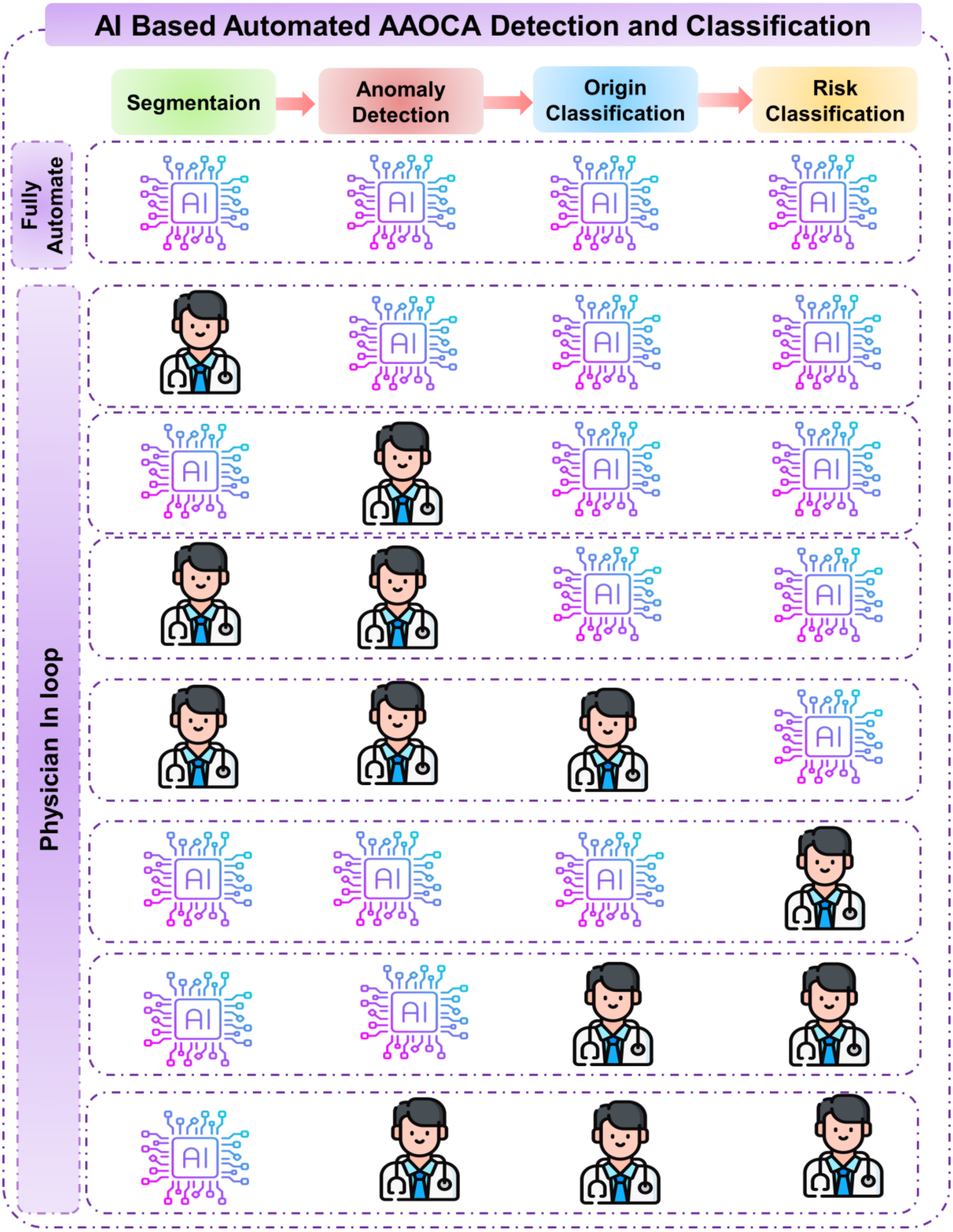
Supplemental Figure 25: Confusion matrices of ensemble model in Anomaly Detection in strategy 2 for external testing dataset at different cut-off points for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. Source data are provided as a Source Data file.



Supplemental Figure 26: Original image and different augmentations applied to the image in different views.



Supplemental Figure 27: Different possible strategies implemented to develop a more generalizable model using all available labeled datasets. The whole study was performed using Strategy 1; however, with Strategies 2 and 3, we expect the model to be more generalizable in real clinical scenarios and external test sets as more datasets will be used in the training set. <u>Strategy 1:</u> Model development was performed on the training dataset; the models were evaluated on the internal and external testing dataset with labeled cases. The external clinical testing dataset was used to evaluate the true and false positives, as the labeling was not available for this dataset. <u>Strategy 2:</u> Model training was performed on the entire dataset from Bern University Hospital. The labeled dataset from Zurich University Hospital served as an external testing dataset. The unlabeled open-access CCTA dataset (Guangdong Provincial People's Hospital) was used for external clinical evaluation, similar to Strategy 1. <u>Strategy 3:</u> Model training was performed on the entire datasets with labels, including data from Bern and Zurich University Hospitals. Following the previous strategy, external model performance was evaluated in the unlabeled dataset (external clinical evaluation dataset). Center 1: Bern University Hospital, Center 2: Zurich University Hospital, Center 3: Guangdong Provincial People's Hospital



Supplemental Figure 28: Different possibilities for using the developed AI model in clinical scenarios include fully automated applications and physician-in-the-loop systems. Anomaly Detection: distinguishing between normal cases and those with AAOCA, Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA), Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk.

Supplemental Tables

Supplemental Table 1: Summary statistics of the number of patients and images in each dataset for different classification tasks. Anomaly Detection: distinguishing between normal cases and those with AAOCA; Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA); risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. Source data are provided as a Source Data file.

Anomaly Detection				
Dataset	**# All patients**	**# All images**	**#AAOCA patients**	**#AAOCA images**
Training dataset	536	1567	147	598
Internal testing dataset	359	1066	58	319
External testing dataset	483	497	130	139
External clinical evaluation dataset	998	998	Unknown	Unknown
Origin Classification				
	# All patients	**# All images**	**#L-AAOCA patients**	**# L-AAOCA images**
Training dataset	145	585	54	207
Internal testing dataset	57	309	15	48
External testing dataset	125	134	63	67
Risk Classification				
	# All patients	**# All images**	**#High-risk patients**	**# High risk-images**
Training dataset	144	582	107	465
Internal testing dataset	57	309	44	275
External testing dataset	125	134	74	80

Supplemental Table 2: Image-wise demographic information, scanner details, and image acquisition parameters across different datasets. This information was extracted from registry data and the DICOM headers of each image. Detailed information from the external clinical evaluation dataset is publicly available in[11]. Source data are provided as a Source Data file.

		Train dataset	Internal test dataset	External test dataset
No.		1567	1066	497
Age, median [Q1, Q3]		61.0 [54.0,67.0]	61.0 [54.0,68.0]	57.0 [50.0,64.0]
Sex, no. (%)	**Female**	559 (35.7)	349 (32.7)	172 (34.6)
	Male	1008 (64.3)	717 (67.3)	325 (65.4)
BMI, median [Q1, Q3]		25.6 [22.7,29.3]	25.6 [23.1,28.7]	25.9 [23.2,28.7]
Manufacturer, n (%)	**GE**	6 (0.4)		491 (98.8)
	Siemens	1521 (97.1)	1048 (98.3)	6 (1.2)
	Canon	10 (0.6)	3 (0.3)	
	Philips	19 (1.2)	13 (1.2)	
	Toshiba	11 (0.7)	2 (0.2)	
Manufacturer Model Name, no. (%)	**GE - Discovery CT750 HD**			21 (4.2)
	GE - LightSpeed VCT	1 (0.1)		20 (4.0)
	GE - Revolution CT	3 (0.2)		450 (90.5)
	Siemens - SOMATOM Definition Flash	1306 (83.3)	865 (81.1)	3 (0.6)
	Siemens - Sensation 16			1 (0.2)
	Siemens - Sensation 64			2 (0.4)
	Canon - Aquilion ONE	10 (0.6)	3 (0.3)	
	Philips - Brilliance 64	4 (0.3)	13 (1.2)	
	Siemens - NAEOTOM Alpha	180 (11.5)	170 (15.9)	
	Siemens - SOMATOM Definition Edge	17 (1.1)	5 (0.5)	
	Siemens - SOMATOM Drive		3 (0.3)	
	Siemens - SOMATOM Force		5 (0.5)	
	Toshiba - Aquilion ONE	11 (0.7)	2 (0.2)	
	GE - Revolution EVO	1 (0.1)		
	GE - Revolution Frontier	1 (0.1)		
	Philips - Incisive CT	5 (0.3)		
	Philips - Spectral CT	9 (0.6)		
	Philips - iCT 256	1 (0.1)		
	Siemens - Perspective	2 (0.1)		
	Siemens - SOMATOM Definition AS	10 (0.6)		
	Siemens - Sensation 64 Cardiac	6 (0.4)		
Peak voltage (kVp), no. (%)	**70**	2 (0.1)	4 (0.4)	
	80	33 (2.1)	30 (2.8)	23 (4.6)
	100	1051 (67.1)	591 (55.4)	368 (74.0)
	110	2 (0.1)		
	120	437 (27.9)	401 (37.6)	96 (19.3)
	140	42 (2.7)	40 (3.8)	10 (2.0)
Exposure (mAs), median [Q1, Q3]		196.1 [117.4,267.6]	209.0 [122.3,291.6]	84.0 [72.8,100.2]
X-Spacing, median [Q1, Q3]		0.4 [0.3,0.6]	0.4 [0.3,0.6]	0.5 [0.4,0.5]
Y-Spacing, median [Q1, Q3]		0.4 [0.3,0.6]	0.4 [0.3,0.6]	0.5 [0.4,0.5]
Z-Spacing, median [Q1, Q3]		0.7 [0.7,0.7]	0.7 [0.7,0.7]	0.6 [0.6,0.6]

The Bern dataset (used for training and internal testing) was collected between 2009 and 2024, while the Zurich dataset (used as an external test set) was collected between 2021 and 2023.

Supplemental Table 3: Patient-wise demographic information in different datasets**.** Detailed information from the external clinical evaluation dataset is publicly available in[11]. Source data are provided as a Source Data file.

		Train dataset	Internal test dataset	External test dataset
No.		536	359	483
Age, median [Q1, Q3]		61.0 [54.0,67.0]	62.0 [55.0,69.0]	57.0 [50.0,64.0]
Sex, n (%)	**Female**	200 (37.3)	126 (35.1)	165 (34.2)
	Male	336 (62.7)	233 (64.9)	318 (65.8)
BMI, median [Q1, Q3]		25.5 [23.0,28.7]	25.7 [23.4,29.1]	25.9 [23.2,28.7]

Supplemental Table 4: Summary of different classification metrics for the ensemble models for different test datasets in male population. Anomaly detection: distinguishing between normal cases and those with AAOCA; Origin classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA; Risk classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic means of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

	Anomaly detection		**Origin classification**		**Risk classification**	
	Test internal	**Test external**	**Test internal**	**Test external**	**Test internal**	**Test external**
ROC AUC	0.999	0.999	0.999	0.998	0.998	0.996
Sensitivity	0.988	0.952	0.889	0.979	0.986	0.983
Specificity	0.987	1	1	1	1	0.976
F1-score	0.981	0.975	0.941	0.989	0.993	0.983
PPV	0.975	1	1	1	1	0.983
AUPR	0.998	0.998	0.995	0.998	1	0.997
Accuracy	0.987	0.985	0.987	0.99	0.987	0.98

Supplemental Table 5: Summary of different classification metrics for the ensemble models for different test datasets in female population. Anomaly detection: distinguishing between normal cases and those with AAOCA; Origin classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA; Risk classification: scoring the AAOCA risk, classifying it as either low-risk or high-risk anatomy. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic means of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

	Anomaly detection		**Origin classification**		**Risk classification**	
	Test internal	**Test external**	**Test internal**	**Test external**	**Test internal**	**Test external**
ROC AUC	0.997	1	1	1	1	0.992
Sensitivity	0.987	0.971	1	0.9	1	0.9
Specificity	0.993	1	1	1	1	0.923
F1-score	0.981	0.986	1	0.947	1	0.923
PPV	0.975	1	1	1	1	0.947
AUPR	0.991	1	1	1	1	0.995
Accuracy	0.991	0.994	1	0.941	1	0.909

Supplemental Table 6: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomaly detection in different testing datasets. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.993	0.99	0.994	0.994	0.995	0.993	0.998
	Sensitivity	0.978	0.925	0.984	0.956	0.994	0.967	0.987
	Specificity	0.984	0.992	0.979	0.987	0.976	0.983	0.989
	F1-score	0.97	0.952	0.968	0.962	0.969	0.964	0.981
	PPV	0.963	0.98	0.952	0.968	0.946	0.962	0.975
	AUPR	0.971	0.984	0.982	0.982	0.978	0.979	0.996
	Accuracy	0.982	0.972	0.98	0.977	0.981	0.979	0.989
External Testing Dataset	**ROC AUC**	0.994	0.997	0.999	0.999	0.998	0.997	0.999
	Sensitivity	0.928	0.942	0.95	0.964	0.971	0.951	0.957
	Specificity	0.994	0.994	0.994	0.997	0.98	0.992	1
	F1-score	0.956	0.963	0.967	0.978	0.961	0.965	0.978
	PPV	0.985	0.985	0.985	0.993	0.951	0.98	1
	AUPR	0.992	0.994	0.997	0.997	0.994	0.995	0.999
	Accuracy	0.976	0.98	0.982	0.988	0.978	0.981	0.988

Supplemental Table 7: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomaly detection in different testing datasets for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.995	0.988	0.998	0.996	0.996	0.995	0.999
	Sensitivity	0.979	0.905	0.983	0.946	0.996	0.962	0.988
	Specificity	0.979	0.992	0.981	0.985	0.966	0.981	0.987
	F1-score	0.969	0.942	0.973	0.958	0.966	0.962	0.981
	PPV	0.959	0.982	0.963	0.97	0.938	0.962	0.975
	AUPR	0.98	0.982	0.996	0.991	0.988	0.987	0.998
	Accuracy	0.979	0.962	0.982	0.972	0.976	0.974	0.987
External Testing Dataset	**ROC AUC**	0.992	0.996	0.999	0.998	0.998	0.996	0.999
	Sensitivity	0.923	0.933	0.952	0.952	0.981	0.948	0.952
	Specificity	0.991	0.995	0.991	0.995	0.977	0.99	1
	F1-score	0.95	0.96	0.966	0.971	0.967	0.963	0.975
	PPV	0.98	0.99	0.98	0.99	0.953	0.979	1
	AUPR	0.99	0.993	0.997	0.995	0.996	0.994	0.998
	Accuracy	0.969	0.975	0.978	0.982	0.978	0.977	0.985

Supplemental Table 8: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomaly detection in different testing datasets for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.989	0.991	0.985	0.991	0.993	0.99	0.997
	Sensitivity	0.974	0.987	0.987	0.987	0.987	0.985	0.987
	Specificity	0.993	0.993	0.974	0.989	0.993	0.988	0.993
	F1-score	0.974	0.981	0.951	0.975	0.981	0.972	0.981
	PPV	0.974	0.975	0.917	0.962	0.975	0.961	0.975
	AUPR	0.934	0.99	0.931	0.933	0.945	0.947	0.991
	Accuracy	0.989	0.991	0.977	0.989	0.991	0.987	0.991
External Testing Dataset	**ROC AUC**	1	1	0.999	1	0.997	0.999	1
	Sensitivity	0.943	0.971	0.943	1	0.943	0.96	0.971
	Specificity	1	0.993	1	1	0.985	0.996	1
	F1-score	0.971	0.971	0.971	1	0.943	0.971	0.986
	PPV	1	0.971	1	1	0.943	0.983	1
	AUPR	1	0.999	0.998	1	0.989	0.997	1
	Accuracy	0.988	0.988	0.988	1	0.977	0.988	0.994

Supplemental Table 9: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	1	0.994	0.997	0.999	0.999	0.998	0.999
	Sensitivity	0.938	0.875	0.958	0.938	0.938	0.929	0.938
	Specificity	1	0.989	0.996	1	1	0.997	1
	F1-score	0.968	0.903	0.968	0.968	0.968	0.955	0.968
	PPV	1	0.933	0.979	1	1	0.982	1
	AUPR	0.999	0.976	0.988	0.996	0.995	0.991	0.997
	Accuracy	0.99	0.971	0.99	0.99	0.99	0.986	0.99
External Testing Dataset	**ROC AUC**	0.99	0.988	0.997	0.978	0.997	0.99	0.999
	Sensitivity	0.97	0.955	0.94	0.94	0.985	0.958	0.955
	Specificity	1	0.985	1	0.97	0.985	0.988	1
	F1-score	0.985	0.97	0.969	0.955	0.985	0.973	0.977
	PPV	1	0.985	1	0.969	0.985	0.988	1
	AUPR	0.994	0.992	0.997	0.984	0.997	0.993	0.999
	Accuracy	0.985	0.97	0.97	0.955	0.985	0.973	0.978

Supplemental Table 10: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets for the male population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.999	0.991	0.994	0.999	0.999	0.996	0.999
	Sensitivity	0.889	0.815	0.926	0.889	0.889	0.881	0.889
	Specificity	1	1	0.995	1	1	0.999	1
	F1-score	0.941	0.898	0.943	0.941	0.941	0.933	0.941
	PPV	1	1	0.962	1	1	0.992	1
	AUPR	0.996	0.956	0.972	0.992	0.99	0.981	0.995
	Accuracy	0.987	0.978	0.987	0.987	0.987	0.985	0.987
External Testing Dataset	**ROC AUC**	0.986	0.998	0.996	0.991	0.996	0.994	0.998
	Sensitivity	0.957	0.979	0.957	0.957	0.979	0.966	0.979
	Specificity	1	0.981	1	0.962	0.981	0.985	1
	F1-score	0.978	0.979	0.978	0.957	0.979	0.974	0.989
	PPV	1	0.979	1	0.957	0.979	0.983	1
	AUPR	0.991	0.998	0.997	0.991	0.996	0.994	0.998
	Accuracy	0.98	0.98	0.98	0.96	0.98	0.976	0.99

Supplemental Table 11: Summary of different classification metrics across different folds and mean and ensemble results from 5-fold in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets for the female population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	1	0.997	1	1	1	0.999	1
	Sensitivity	1	0.952	1	1	1	0.99	1
	Specificity	1	0.946	1	1	1	0.989	1
	F1-score	1	0.909	1	1	1	0.982	1
	PPV	1	0.87	1	1	1	0.974	1
	AUPR	1	0.994	1	1	1	0.999	1
	Accuracy	1	0.948	1	1	1	0.99	1
External Testing Dataset	**ROC AUC**	1	0.975	1	0.946	1	0.984	1
	Sensitivity	1	0.9	0.9	0.9	1	0.94	0.9
	Specificity	1	1	1	1	1	1	1
	F1-score	1	0.947	0.947	0.947	1	0.968	0.947
	PPV	1	1	1	1	1	1	1
	AUPR	1	0.987	1	0.973	1	0.992	1
	Accuracy	1	0.941	0.941	0.941	1	0.965	0.941

Supplemental Table 12: Summary of different classification metrics, including mean and ensemble results from 5-fold in risk classifying (high risk vs. low risk) in different testing datasets (Risk Classification). Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.994	0.984	1	1	1	0.996	0.999
	Sensitivity	0.982	0.902	0.996	0.967	0.978	0.965	0.989
	Specificity	1	1	1	1	1	1	1
	F1-score	0.991	0.948	0.998	0.983	0.989	0.982	0.995
	PPV	1	1	1	1	1	1	1
	AUPR	0.999	0.998	1	1	1	0.999	1
	Accuracy	0.984	0.913	0.997	0.971	0.981	0.969	0.99
External Testing Dataset	**ROC AUC**	0.989	0.98	0.999	0.998	0.997	0.993	0.996
	Sensitivity	0.975	0.875	0.975	0.95	0.975	0.95	0.962
	Specificity	0.963	0.944	0.981	0.963	0.963	0.963	0.963
	F1-score	0.975	0.915	0.981	0.962	0.975	0.962	0.969
	PPV	0.975	0.959	0.987	0.974	0.975	0.974	0.975
	AUPR	0.992	0.985	0.999	0.999	0.998	0.995	0.997
	Accuracy	0.97	0.903	0.978	0.955	0.97	0.955	0.963

Supplemental Table 13: Summary of different classification metrics, including mean and ensemble results from 5-fold in risk classifying (high risk vs. low risk) in different testing datasets (Risk Classification) for the male population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	0.993	0.969	1	0.999	1	0.992	0.998
	Sensitivity	0.977	0.883	0.995	0.958	0.972	0.957	0.986
	Specificity	1	1	1	1	1	1	1
	F1-score	0.988	0.938	0.998	0.979	0.986	0.978	0.993
	PPV	1	1	1	1	1	1	1
	AUPR	0.999	0.997	1	1	1	0.999	1
	Accuracy	0.978	0.892	0.996	0.961	0.974	0.96	0.987
External Testing Dataset	**ROC AUC**	0.997	0.98	0.999	0.999	0.997	0.994	0.996
	Sensitivity	0.983	0.867	0.983	0.95	0.983	0.953	0.983
	Specificity	0.976	0.951	0.976	0.976	0.976	0.971	0.976
	F1-score	0.983	0.912	0.983	0.966	0.983	0.966	0.983
	PPV	0.983	0.963	0.983	0.983	0.983	0.979	0.983
	AUPR	0.998	0.986	0.999	0.999	0.998	0.996	0.997
	Accuracy	0.98	0.901	0.98	0.96	0.98	0.96	0.98

Supplemental Table 14: Summary of different classification metrics, including mean and ensemble results from 5-fold in risk classifying (high risk vs. low risk) in different testing datasets (Risk Classification) for the female population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, ROC: Receiver Operating Characteristic, AUC: Area under the curve, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Metrics	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	Mean	Ensemble
Internal Testing Dataset	**ROC AUC**	1	1	1	1	1	1	1
	Sensitivity	1	0.967	1	1	1	0.993	1
	Specificity	1	1	1	1	1	1	1
	F1-score	1	0.983	1	1	1	0.997	1
	PPV	1	1	1	1	1	1	1
	AUPR	1	1	1	1	1	1	1
	Accuracy	1	0.974	1	1	1	0.995	1
External Testing Dataset	**ROC AUC**	0.946	0.988	1	0.996	0.996	0.985	0.992
	Sensitivity	0.95	0.9	0.95	0.95	0.95	0.94	0.9
	Specificity	0.923	0.923	1	0.923	0.923	0.938	0.923
	F1-score	0.95	0.923	0.974	0.95	0.95	0.949	0.923
	PPV	0.95	0.947	1	0.95	0.95	0.959	0.947
	AUPR	0.956	0.992	1	0.998	0.998	0.989	0.995
	Accuracy	0.939	0.909	0.97	0.939	0.939	0.939	0.909

Supplemental Table 15: Summary of various classification metrics for the ensemble model with different cut-offs in anomaly detection in different testing datasets. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	0.1	0.997	0.953	0.946	0.901	0.966
	0.2	0.997	0.973	0.968	0.941	0.98
	0.3	0.997	0.987	0.983	0.97	0.99
	0.4	0.987	0.988	0.98	0.972	0.988
	0.5	0.987	0.989	0.981	0.975	0.989
	0.6	0.966	0.991	0.972	0.978	0.983
	0.7	0.947	0.993	0.965	0.984	0.979
	0.8	0.915	0.996	0.951	0.99	0.972
	0.9	0.909	0.996	0.948	0.99	0.97
External Testing Dataset	0.1	0.993	0.975	0.965	0.939	0.98
	0.2	0.993	0.986	0.979	0.965	0.988
	0.3	0.986	0.986	0.975	0.965	0.986
	0.4	0.971	0.997	0.982	0.993	0.99
	0.5	0.957	1	0.978	1	0.988
	0.6	0.942	1	0.97	1	0.984
	0.7	0.928	1	0.963	1	0.98
	0.8	0.914	1	0.955	1	0.976
	0.9	0.899	1	0.947	1	0.972

Supplemental Table 16: Summary of various classification metrics for the ensemble model with different cut-offs in anomaly detection in different testing datasets for the male population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	1	0.943	0.947	0.899	0.962
	0.2	1	0.966	0.968	0.938	0.978
	0.3	1	0.983	0.984	0.968	0.989
	0.4	0.988	0.985	0.979	0.971	0.986
	0.5	0.988	0.987	0.981	0.975	0.987
	0.6	0.959	0.989	0.969	0.979	0.979
	0.7	0.934	0.994	0.959	0.987	0.974
	0.8	0.896	0.998	0.943	0.995	0.964
	0.9	0.888	0.998	0.939	0.995	0.961
External Testing Dataset	**0.1**	0.99	0.968	0.963	0.936	0.975
	0.2	0.99	0.982	0.976	0.963	0.985
	0.3	0.981	0.982	0.971	0.962	0.982
	0.4	0.971	0.995	0.981	0.99	0.988
	0.5	0.952	1	0.975	1	0.985
	0.6	0.933	1	0.965	1	0.978
	0.7	0.923	1	0.96	1	0.975
	0.8	0.913	1	0.955	1	0.972
	0.9	0.904	1	0.949	1	0.969

Supplemental Table 17: Summary of various classification metrics for the ensemble model with different cut-offs in anomaly detection in different testing datasets for the female population. Anomaly Detection: distinguishing between normal cases and those with AAOCA. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	0.987	0.97	0.945	0.906	0.974
	0.2	0.987	0.985	0.969	0.951	0.986
	0.3	0.987	0.993	0.981	0.975	0.991
	0.4	0.987	0.993	0.981	0.975	0.991
	0.5	0.987	0.993	0.981	0.975	0.991
	0.6	0.987	0.993	0.981	0.975	0.991
	0.7	0.987	0.993	0.981	0.975	0.991
	0.8	0.974	0.993	0.974	0.974	0.989
	0.9	0.974	0.993	0.974	0.974	0.989
External Testing Dataset	**0.1**	1	0.985	0.972	0.946	0.988
	0.2	1	0.993	0.986	0.972	0.994
	0.3	1	0.993	0.986	0.972	0.994
	0.4	0.971	1	0.986	1	0.994
	0.5	0.971	1	0.986	1	0.994
	0.6	0.971	1	0.986	1	0.994
	0.7	0.943	1	0.971	1	0.988
	0.8	0.914	1	0.955	1	0.983
	0.9	0.886	1	0.939	1	0.977

Supplemental Table 18: Summary of various classification metrics for the ensemble model with different cut-offs in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	0.979	0.985	0.949	0.922	0.984
	0.2	0.979	0.992	0.969	0.959	0.99
	0.3	0.958	1	0.979	1	0.994
	0.4	0.938	1	0.968	1	0.99
	0.5	0.938	1	0.968	1	0.99
	0.6	0.938	1	0.968	1	0.99
	0.7	0.917	1	0.957	1	0.987
	0.8	0.875	1	0.933	1	0.981
	0.9	0.875	1	0.933	1	0.981
External Testing Dataset	**0.1**	0.985	0.94	0.964	0.943	0.963
	0.2	0.985	0.955	0.971	0.957	0.97
	0.3	0.985	0.985	0.985	0.985	0.985
	0.4	0.97	1	0.985	1	0.985
	0.5	0.955	1	0.977	1	0.978
	0.6	0.955	1	0.977	1	0.978
	0.7	0.94	1	0.969	1	0.97
	0.8	0.925	1	0.961	1	0.963
	0.9	0.91	1	0.953	1	0.955

Supplemental Table 19: Summary of various classification metrics for the ensemble model with different cut-offs in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets for the male population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	0.963	0.995	0.963	0.963	0.991
	0.2	0.963	0.995	0.963	0.963	0.991
	0.3	0.926	1	0.962	1	0.991
	0.4	0.889	1	0.941	1	0.987
	0.5	0.889	1	0.941	1	0.987
	0.6	0.889	1	0.941	1	0.987
	0.7	0.852	1	0.92	1	0.983
	0.8	0.815	1	0.898	1	0.978
	0.9	0.815	1	0.898	1	0.978
External Testing Dataset	**0.1**	0.979	0.925	0.948	0.92	0.95
	0.2	0.979	0.943	0.958	0.939	0.96
	0.3	0.979	0.981	0.979	0.979	0.98
	0.4	0.979	1	0.989	1	0.99
	0.5	0.979	1	0.989	1	0.99
	0.6	0.979	1	0.989	1	0.99
	0.7	0.957	1	0.978	1	0.98
	0.8	0.936	1	0.967	1	0.97
	0.9	0.915	1	0.956	1	0.96

Supplemental Table 20: Summary of various classification metrics for the ensemble model with different cut-offs in anomalous coronary artery origin classification (R-AAOCA vs. L-AAOCA) in different testing datasets for the female population. Origin Classification: classifying the anomalous vessel into either the right (R-AAOCA) or left (L-AAOCA). AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	1	0.946	0.933	0.875	0.961
	0.2	1	0.982	0.977	0.955	0.987
	0.3	1	1	1	1	1
	0.4	1	1	1	1	1
	0.5	1	1	1	1	1
	0.6	1	1	1	1	1
	0.7	1	1	1	1	1
	0.8	0.952	1	0.976	1	0.987
	0.9	0.952	1	0.976	1	0.987
External Testing Dataset	**0.1**	1	1	1	1	1
	0.2	1	1	1	1	1
	0.3	1	1	1	1	1
	0.4	0.95	1	0.974	1	0.971
	0.5	0.9	1	0.947	1	0.941
	0.6	0.9	1	0.947	1	0.941
	0.7	0.9	1	0.947	1	0.941
	0.8	0.9	1	0.947	1	0.941
	0.9	0.9	1	0.947	1	0.941

Supplemental Table 21: Summary of various classification metrics for the ensemble model with different cut-offs in risk classification (high risk vs. low risk) in different testing datasets. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	0.996	1	0.998	1	0.997
	0.2	0.996	1	0.998	1	0.997
	0.3	0.996	1	0.998	1	0.997
	0.4	0.993	1	0.996	1	0.994
	0.5	0.989	1	0.995	1	0.99
	0.6	0.985	1	0.993	1	0.987
	0.7	0.949	1	0.974	1	0.955
	0.8	0.935	1	0.966	1	0.942
	0.9	0.898	1	0.946	1	0.909
External Testing Dataset	**0.1**	0.988	0.944	0.975	0.963	0.97
	0.2	0.988	0.963	0.981	0.975	0.978
	0.3	0.988	0.963	0.981	0.975	0.978
	0.4	0.988	0.963	0.981	0.975	0.978
	0.5	0.962	0.963	0.969	0.975	0.963
	0.6	0.962	0.963	0.969	0.975	0.963
	0.7	0.938	0.963	0.955	0.974	0.948
	0.8	0.925	0.981	0.955	0.987	0.948
	0.9	0.875	0.981	0.927	0.986	0.918

Supplemental Table 22: Summary of various classification metrics for the ensemble model with different cut-offs in risk classification (high risk vs. low risk) in different testing datasets for male population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	0.995	1	0.998	1	0.996
	0.2	0.995	1	0.998	1	0.996
	0.3	0.995	1	0.998	1	0.996
	0.4	0.991	1	0.995	1	0.991
	0.5	0.986	1	0.993	1	0.987
	0.6	0.981	1	0.991	1	0.983
	0.7	0.935	1	0.966	1	0.94
	0.8	0.916	1	0.956	1	0.922
	0.9	0.879	1	0.935	1	0.888
External Testing Dataset	**0.1**	0.983	0.951	0.975	0.967	0.97
	0.2	0.983	0.976	0.983	0.983	0.98
	0.3	0.983	0.976	0.983	0.983	0.98
	0.4	0.983	0.976	0.983	0.983	0.98
	0.5	0.983	0.976	0.983	0.983	0.98
	0.6	0.983	0.976	0.983	0.983	0.98
	0.7	0.95	0.976	0.966	0.983	0.96
	0.8	0.933	0.976	0.957	0.982	0.95
	0.9	0.867	0.976	0.92	0.981	0.911

Supplemental Table 23: Summary of various classification metrics for the ensemble model with different cut-offs in risk classification (high risk vs. low risk) in different testing datasets for female population. Risk Classification: classifying the AAOCA risk, classifying it as either low-risk or high-risk. AAOCA: Anomalous aortic origin of the coronary artery, F1-score: a measure of a test's accuracy, the harmonic mean of precision and recall, PPV: Positive predictive value, AUPR: Area under the precision-recall curve. The slight differences in ROC-AUC values between figures and tables are due to the use of different libraries for calculations and rounding discrepancies. All values are rounded to three decimal places, which may result in a value of 1 (e.g., an AUC of 1.000 even if sensitivity and specificity are not both exactly 1.000). Source data are provided as a Source Data file.

Datasets	Cut-off	Sensitivity	Specificity	F1-score	PPV	Accuracy
Internal Testing Dataset	**0.1**	1	1	1	1	1
	0.2	1	1	1	1	1
	0.3	1	1	1	1	1
	0.4	1	1	1	1	1
	0.5	1	1	1	1	1
	0.6	1	1	1	1	1
	0.7	1	1	1	1	1
	0.8	1	1	1	1	1
	0.9	0.967	1	0.983	1	0.974
External Testing Dataset	**0.1**	1	0.923	0.976	0.952	0.97
	0.2	1	0.923	0.976	0.952	0.97
	0.3	1	0.923	0.976	0.952	0.97
	0.4	1	0.923	0.976	0.952	0.97
	0.5	0.9	0.923	0.923	0.947	0.909
	0.6	0.9	0.923	0.923	0.947	0.909
	0.7	0.9	0.923	0.923	0.947	0.909
	0.8	0.9	1	0.947	1	0.939
	0.9	0.9	1	0.947	1	0.939

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