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Validation of the Ayurvedic construct, *Rasadhatudushti*, in adults at risk of cardiovascular diseases – A mixed-method studyRadhika Rani R K^{a,*}, M.A. Shajahan^b^a Department of Roganidana, Government Ayurveda College, Tripunithura, Ernakulam, Kerala, India^b Department of Dravyaguna, Government Ayurveda College, Thiruvananthapuram, Kerala, India

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ABSTRACT

Background: *Rasadhatudushti* (*RD*), the deranged state of *Rasadhatu*, is a construct in Ayurveda mentioned as the cause of diseases affecting the circulatory channels and the heart, collectively called cardiovascular diseases (CVD). It is a morbid condition generic to some other disorders, hence is non-specific to CVD. It was observed that *RD* was present in majority of acute coronary artery disease in a cross-sectional, descriptive study in 250 patients stabilized after an acute episode.

Objectives: To validate the available scale for assessing *RD* in the context of CVD risk.

To study the prevalence of *RD* in participants at risk of cardiovascular diseases.

Method: In the first part, validation of the scale for assessing *RD*, as mentioned in the texts, was done through standard steps for scale validation in the context of CVD risk. Psychometric analysis was done after administering the draft scale of 39 items in 218 participants above the age of 40 years who were not yet diagnosed with overt CVD conditions. Construct validation was done by comparing mean score of Framingham global risk score in high and low *RD* scores and comparing the reduction in CVD risk score assessed by Qrisk®2–2017 by life style modification and a conventional *RD* correction as add on. Second part was a cross sectional survey study to estimate the prevalence of *RD* in a specific population vulnerable to CVD. This was done in a sample of 160 sedentary government employees of Thiruvananthapuram District, Kerala, aged above 40, using the validated *RD* assessment scale.

Result: –The final scale to assess *RD*, 'RAS-RCVD', with 25 symptoms was found to have concurrent validity using WHO/ISH risk prediction as the reference standard. Framingham global risk score also showed significant but low positive correlation with eight as the cut off for *RD* score. The reduction in mean (SD) Qrisk score was 2.53 (3.22) in the trial group receiving *RD* correction drug and 0.30 (3.43) in the control with statistical significance ($p < 0.05$). The prevalence of *RD* as assessed by *RD* score above the cut off in the second part of the study was 49.4%. The prevalence of *RD* was significantly high in participants with moderate to high risk for CVD (61.3%).

Conclusion: – The construct *RD* was observed to be valid in pre-clinical states of CVD. There was a high prevalence of this morbid construct in moderate to high-risk individuals. Ayurvedic CVD prevention strategies need to target on correction of *RD* along with individual risk factor management.

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Abbreviations: *RD*, *Rasadhatudushti*; CVD, Cardiovascular disease; LSM, Life style modification; FGR, Framingham Global Risk.

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1. Introduction

Cardiovascular disease is responsible for approximately one-third of deaths worldwide. The burden of disease is increasing in recent decades in both developing and developed countries. Cardiovascular disease (CVD) is a broad term for a range of diseases affecting the heart and blood vessels, often resulting from atherosclerosis and/or high blood pressure, leading to life-threatening events [1]. Many studies have proven the fact that a diet low in

carbohydrates, fats and calories and regular physical activity reduces the risk of non-communicable disease, a group of lifestyle diseases including CVD. The report of the joint WHO/FAO expert consultation (Diet, nutrition and the prevention of chronic diseases, 2002), has come up with guidelines to reduce the burden of nutrition-related chronic diseases like obesity, diabetes, and cardiovascular disease. Nutritional research is now targeting dietary impacts in the primary as well as secondary prevention of CVD. *Rasadhatu* mentioned in Ayurvedic literature is a construct that regulates the constant supply of nutrients to the cells and tissues. Hence, it was logical to study this in the context of cardiovascular diseases.

Ailments related to the heart and other body channels have been considered in Ayurveda as caused by the vitiated state of *Rasadhatu*, one of the seven types of functionally distinct tissue elements in the human body [2]. *Rasadhatudushti (RD)* or vitiated *Rasadhatu* is one among many clinical constructs mentioned in Ayurveda that has to be inferred through observable clinical features. An observational study done in 2010, among 250 cases of acute coronary artery disease had revealed the prevalence of *RD* more than any other *Dhatus* (functionally distinct body elements) (Appendix 1). From the Ayurvedic perspective, it can be observed that CVD as well as the present-day lifestyle disorders are *Santarpnothavyadhis* (diseases caused by over-nutrition). Excess energy intake (*Atipurana*) along with sedentary life style (*Avyayama*) leads to deranged metabolism of the macronutrients, mainly carbohydrates, and fats. Such factors have been considered in Ayurveda as definite causes leading to *RD*. Though literary review provides a fair theoretical correlation, empirical evidence on the relation between *RD* and CVD was lacking. The study was an attempt to venture into this lesser-explored area to establish the significance of *RD*, if any, in people having the risk of developing CVD.

The deranged state of *Rasadhatu* is a construct that has to be inferred through observable clinical features. *Rasavidhi* (increase) and *Rasakshaya* (decrease) are the two states of perturbed *Rasadhatu*. *Rasapradosha* is the general term used to denote these deranged states, which is generic to a group of disorders ranging from febrile illnesses to infertility [3]. It seemed worth studying whether this symptom complex could be demonstrated in the participants having risk for developing CVD, and if so, to what extent. The objectives were aimed at exploring the relationship between the two. In the current Ayurvedic clinical practice, no practical guidelines are available for the prevention of CVD. If the above concept is found relevant, then Ayurveda can offer a comprehensive and cost-effective management strategy for the prevention of CVDs, much preventable morbidity of the present era.

2. Objectives

1. To validate the available scale for assessing *RD* in the context of CVD risk.
2. To study the prevalence of *RD* in participants at risk of cardiovascular diseases.

3. Materials and methods

The above objectives were studied in two parts. The first objective was intended to study if *RD* was identifiable or measurable in the context of risk for CVD. For this, the available scale of *RD* assessment *lakshanas* (clinical features) was studied through the standard psychometric steps for the development of a measuring scale. The second objective was achieved through a prevalence study in a sample of participants at risk for CVD.

3.1. Part I - Tool validation study

3.1.1. Design

Descriptive cross-sectional survey was adopted for the tool validation study. This part of the study was a theory-driven psychometric approach to obtain an instrument to objectively measure the clinical construct, *RD*. This involved application of standard steps of tool validation (Table 1) in the clinical features of *RD*, mentioned in classical texts, in the context of risk of cardiovascular disease.

3.1.2. Setting

Participants from Thiruvananthapuram and Ernakulam districts of Kerala were selected by conducting screening camps in the hospital OPD setting.

3.1.3. Study period

The scale development part of the study was conducted during June 2015 to November 2016.

3.1.4. Study population

General population above 40 years of age undiagnosed of any cardiovascular events.

- a . Inclusion criteria – Participants above the age of 40, who had not yet developed a cardiovascular event like myocardial infarction, stroke, or peripheral vascular occlusive diseases.
- b . Exclusion criteria – Participants having any overt clinical conditions other than diabetes were excluded because *lakshanas* (clinical features) of *RD* would be present in any active or acute disease conditions. Diabetics have a higher CVD risk; hence avoiding them would restrict their representativeness in the studied sample.

3.1.5. Sample size

For clinical purposes, Munro et al. recommend five participants per item in the draft tool. Another approach suggests a minimum of 200 as a fair sample size [4]. Hence, the draft tool was administered to 218 participants.

3.1.6. Sampling procedure

For scale development study, purposive sampling was done, to get all ranges of risk as assessed by the WHO/ISH risk prediction chart indicated for Indians [5]. Participants with a CVD risk of 10% and above were considered positive and those below 10% (green column) were negative cases. Objective risk score as per the Framingham Global Risk (FGR) scoring system for each subject was recorded.

3.1.7. Method

In literature, the symptoms related to *RD* are distributed under three domains - *Rasavridhi*, *Rasakshaya*, and *Rasapradosha*. There

Table 1
Steps in validating the scale for assessing *Rasadhatudushti* (Part I).

STEPS	ANALYSIS
Conceptualization, item generation, item selection	Content validation
Item wording with translation, sequencing, response formatting	
Pre-test, Pilot study	1. Reliability assessment 2. Construct and Criterion validity
Final administration	

is no clear reference as to which among these deranged states of *Rasadhatu* is involved in the pathogenesis of *Hridroga* (disease of the heart). Hence, the conceptualization of the scale was to include symptoms for assessing all the three morbid states related to *Rasadhatu*. Items of the scale were pooled from the available list of symptoms for the assessment of *RD* mentioned in Charaka Samhita [3], Sushruta Samhita [6], and Ashtanga Samgraha [7]. All these symptoms available were selected, avoiding repetitions in the process. Along with *Rasavridhi lakshanas*, symptoms of *Kaphavridhi* were also included, as mentioned in the texts. No items were excluded at this stage.

The meanings of the Sanskrit terms for symptoms in the draft tool were finalized as endorsed by five experts, including both clinicians and academicians through a structured open-ended questionnaire. *Sada*, a clinical feature coming under *Rasapradosa vikara* was excluded from the list as its meaning showed similarity with that of *Tandra* [8]. The word meaning of each symptom for *RD* assessment relevant to such a pre-clinical setting was finalized. *Murcha*, literally meaning loss of consciousness, was substituted with a trivial symptom namely dizziness, as endorsed by experts. *Srotorodha/lepa* (obstruction to body channels) being a nonspecific symptom was replaced with the symptom of constipation. The experts agreed to equal weightage to all the items of the tool. A logical sequencing was maintained. Symptoms having similar meaning were put with adequate spacing, with dissimilar ones in between.

For response formatting, experts had endorsed eliciting the frequency of the symptoms in the past three months, as the studied condition was a sub-clinical one. Response options were fixed as a three-point Likert and scoring was zero for very rarely, one for occasionally present, and two for frequently present. *Akalavali* (early onset of wrinkling of skin) was assessed by the observer and was scored as zero for mild, one for moderate, and two for severe. *Akalapalita* (early onset of graying of hair) was scored as zero for onset after 45 years of age, 1 for onset between 30 and 45 years, and 2 for onset before 30 years. *Sthoulya* (Obesity) was scored as per the BMI as 18.5–24.9 as zero, 25–29.9 as one, and ≥ 30 as two. The items were translated to simple English and then to vernacular words and included in the scale. The comprehensibility of the wordings used was pre-tested by giving the tool to a few respondents, who were the office staff within the institution. Experts and peers also reviewed the tool for comprehensibility.

A pilot test of the draft scale was administered in a sample of 20 government employees working in Public Offices, Thiruvananthapuram, to ensure the qualitative aspects of the tool like the acceptability of items and time required to administer the tool. Final administration of the draft tool with 39 symptoms was done in 218 participants. Smokers and those who had quit smoking within one year were considered current smokers. Standard wall-mount Stadiometer and platform type ISI labelled electronic weighing machine were used for measuring the height and weight respectively. The average of two seated blood pressure measurements was taken using calibrated standard Mercury Sphygmomanometers and Stethoscopes. A fully automated Analyser (Transasia EM360® and Coralyzer 200®) was used for serum biochemistry assay in the Institutions.

Data was analyzed by plotting an item-wise histogram and items that showed 100% skewness in either direction were removed. They were deleted after comparing their distribution in low risk and moderate to high-risk categories. Data related to the remaining symptoms were statistically analyzed using SPSS 24 (trial) version. Item analysis was used to clean up sub-scales to maximize reliability and validity. The process of identifying items

for potential deletion was iterative and initially based on the distribution of responses, inter-item correlation, and item-total correlation [9].

3.1.8. Reliability analysis

The reliability of the tool across time and raters were done during the final administration of the draft tool and statistically analyzed. The internal consistency reliability was done to know whether all items in the *RD* assessment tool were closely related to the entire construct. It was estimated using Cronbach's alpha coefficient. Internal consistency was repeated in the final tool on completion of the deletion process.

3.1.9. Validity analysis

Among the various validation procedures to ensure the psychometric properties of the tool, content validity, construct validity, and criterion validity were done as follows.

3.1.9.1 Content validity was ensured during the initial stages of the tool validation up to the pilot study. The meaning of Sanskrit terms from the literature relevant to the context of the study was included as per expert paneling. Review of translated draft tool done by experts and respondents during pre-test ensured the content validity of the tool. Face validity was ensured by formatting the response options and scoring.

3.1.9.2 Construct validity of the tool for *RD* assessment was evaluated after final administration using the standard factor analysis techniques.

Step 1 – The adequacy of the sample size was analyzed by Kaiser – Meyer – Olkin (KMO) measure and the factorisability of the items was ensured by the Bartlett's test of Sphericity.

Step 2 – Extraction of factors – Principal component analysis (PCA) was used to extract factors that ensure construct validity. Community of more than 0.4 was fixed as the criteria for retaining the items. As per Kaiser Criteria representing the amount of variability in the data expressed by a factor, factors with Eigen value of more than one were retained. The graphical representation of factors extracted from SPSS data using Scree plot was also done. Cumulative percent variance of the scale was also analyzed.

Step 3 – Promax rotation – Since the factors were found correlated, promax rotation was done on the retained factors to help better loading characteristics and to arrive at a more interpretable model. A factor loading of 0.4 and above was taken as the cutoff for deleting or retaining an item. The finalized model of the tool for assessing *RD* in participants at risk for CVD was named RAS-RCVD (*Rasadhatudushti* Assessment Scale in Risk for CVD)

3.1.9.3 Criterion validity – Criterion validity was done concurrently by comparing the score on the instrument taking the WHO/ISH risk prediction chart proposed for population-based screening as the reference standard to measure CVD risk. Participants having risk levels 10% or above were considered as positive cases and those below 10% as negative cases. Receiver Operating Characteristic (ROC) Analysis was used to obtain every possible cutoff point by plotting the sensitivity against 1-specificity. The area under the curve indicated the overall performance of the tool. After selecting a cutoff score with fair sensitivity and specificity, participants above the cutoff were considered positive and those equal to or below it as negative cases. Based on this categorization the diagnostic accuracy of the finalized tool, RAS-RCVD, was calculated.

3.1.9.4 Other measures of Construct validity –

- a. Convergent validity was analyzed by correlating the Framingham's Global risk score with that in the RAS-RCVD by finding the Spearman's rank correlation coefficient.

- b. Extreme group (discriminative) validity – The mean score of positive and negative cases of RD (above and below or equal to cut off score respectively) was analyzed by t test to study if they differ significantly, showing its ability to discriminate extreme groups.
- c. Hypothesis testing – It was verified if the chosen cut-off was good enough for distinguishing high-risk CVD participants from the low-risk. The alternate hypothesis proposed was the mean CVD risk score as per the FGR scoring method above the cut-off differed significantly from those below it. The second hypothesis was formulated on the logic that if the construct was related to CVD risk, then a drug indicated for RD but not known to prevent CVD would lower the risk score. The alternate hypothesis was that the risk reduction by such a drug along with lifestyle modification (LSM), recommended by WHO, differed from the risk reduction by LSM alone in participants below 30% of risk for CVD. Qrisk®2–2017, a more sensitive online CVD risk calculator for Indians was used to assess the risk reduction after 1 month of intervention in two small samples of 30 participants each.

3.2. Part II – PREVALENCE STUDY

3.2.1. Design

Cross-sectional survey in a specific population at risk for CVD.

3.2.2. Study setting

Employees of both central and state government offices with staff strength of minimum 50, within Thiruvananthapuram Corporation.

3.2.3. Study population

Studies have proven the strong association of sedentary lifestyles with increased CVD and all-cause mortality [10]. In a community survey conducted in Indians, sedentary lifestyle, obesity and low HDL-C were found as the most prevalent CV risk factors in subjects in the third and fourth decade of life [11]. Government employees (Class II and Class III) belong to the steady income group and low job-related stress, and share a common pattern of sedentary nature of the job, a pattern of low physical activity and food habits and timings; hence considered as more prone to CVD. Thus, the prevalence study was done in the said classes of government employees.

- a. Inclusion criteria – Both males and females above the age of 40 willing to participate were included.
- b. Exclusion criteria – Participants with established cardiovascular and renal diseases, those with any acute clinically overt diseases, and those without blood reports or failed to turn up for the blood check

3.2.4. Sampling technique

The cluster sampling technique was used after preparing a list of government offices both central and state, with staff strength of more than 50 within the Thiruvananthapuram corporation limit. From these, two clusters were randomly selected one each from central and the state government offices. A sampling frame of class II and III staff above the age of 40 was prepared in alphabetic order and 160 participants were selected by random number table method.

3.2.5. Sample size

The prevalence of RD in a pilot sample of 20 participants from the target population was 56%. The sample size was calculated based on the formula $n = ((Z1 - \alpha/2)^2 p (1 - p))/d^2$, where p was 56%.

The sample size observed was 78 with a relative precision of 20% and a confidence level of 95%. Then applying a design effect of two, the sample size was calculated and fixed as 160.

3.2.6. Method

For the prevalence study, the participants included in the study were interviewed for demographic data, presence of added risk factors like smoking history, family history of cardiovascular diseases, etc. Assessment of RD was done using the validated tool RAS-RCVD. Required clinical measures like BMI, blood pressure, and lipid profile were recorded as mentioned 3.1.7. CVD risk stratification was done using the WHO/ISH risk prediction chart. Advice for lifestyle modifications or referral for necessary pharmacological intervention, recommended for the specific risk level of each participant was provided as per the WHO guidelines [5].

3.2.7. Statistical analysis

The prevalence rate of RD was estimated by taking a score of more than eight (the cutoff score) as positive cases and others as negatives. The association of RD with various risk factors was analyzed using the Chi-square test. Simple numerical coding was used for categorical and ordinal variables. Continuous variables were presented as means and standard deviations, and categorical variables were presented as frequencies with percentages. The normality of the continuous variables was verified using Kolmogorov-Smirnov (K-S) test.

4. Results

4.1. Part I

Among the participants in which the scale was validated, 72% were within the age group 51–70 with almost equal distribution in age groups 51–60 and 61–70 (Table 2). 62.4% were males, while 37.6% were females.

Only 15.6% of participants were current smokers. 37.6% were hypertensive, 41.7% were diabetic and 39% were dyslipidaemic. 56% of participants were overweight or obese. 48.6% of participants had a family history of diabetes mellitus. Among the participants, 55.5% were having a moderate to high risk of developing a cardiovascular event in the next 10 years, as per the WHO/ISH risk prediction chart.

4.1.1. Reliability estimates

- i. Test-retest reliability – This was achieved by administering the draft tool twice over a gap of two weeks in a group of 15 participants. The Intra-class correlation coefficient calculated was 0.73 (95% CI of 0.50–0.89). This significant correlation was considered as a good agreement.
- ii. Interobserver reliability – The tool was administered to 18 participants by two different observers independently. The data showed an intra-class correlation coefficient of 0.83. Correlation above 0.75 is considered as a good range of reliability [12].
- iii. Internal consistency – Among the 39 items, three symptoms – *Asyavaiaasya*, *Arasajmata*, and *Akalavali* were deleted due to

Table 2
Distribution of age of participants.

Age group	Frequency	Percent
40–50	49	22.5
51–60	79	36.2
61–70	78	35.8
70 above	12	5.5
Total	218	100.0

100% skewness in the item-wise histogram. Cronbach's alpha (α) coefficient analyzed after the initial step of deletion of three items was 0.80. The final tool had α of 0.76. Many methodologists recommend a minimum α coefficient between 0.65 and 0.8. Being a subjective tool, the validated RD assessment tool had a fair degree of homogeneity as measured by Cronbach's alpha. Item-total correlation of the final tool did not show any negative values. Average inter-item correlations falling somewhere between 0.15 and 0.50 is acceptable [13]. Among the items *Svadudvesha*, *Sunyata* and *Anna-asraddha* had low item total correlation below 0.15.

4.1.2. Validity statistics—

Content validity – Content validity was ensured through the standard steps of conceptualization, item generation, item wording and sequencing, formatting and scoring of response, translation and back translation, and pre-test. Face validity of the tool was ensured by adopting proper response options and scoring methods. The format of structured multiple choices questions with 3 points Likert scale for response options was adopted so that interviewer bias could be reduced.

Construct validity – Following four steps of exploratory factor analysis protocol [14] and item reduction was followed.

- i. Suitability for factor analysis— The Kaiser-Meyer- Olkin (KMO) was 0.73, indicating an adequate sample size. A significant level of Bartlett's test of sphericity is required to check if the data is suitable for factor analysis. The study showed a good significance (p-value of <0.001).
- ii. Principal component analysis (PCA) was used to extract the factors. The number of factors based on Kaiser Criteria, communality of each item, percentage variance of each item, and the cumulative variance was derived from PCA. Items having communality less than 0.40 are eligible for deletion, as that item will struggle to load in any of the factors. In the

- present study, all the retained items had more than 0.5, indicating an ideal value of variance. The initial RD assessment tool with 36 items (after initial deletion of 3) had a cumulative variance of 62.29 with 14 factors. The scree plot demonstrated 10 factors having Eigen value of one and above. The cumulative variance after the deletion of 11 items was 62.18. The retained factor should account for at least 60% and preferably 75% of variance to be acceptable [15].
- iii. Rotation is a method to get better loading and as a thumb-rule factor loading of 0.40 is taken as the cutoff value for deletion of items. The items were carefully deleted one by one ensuring that either the total variance was improved or the number of factors was reduced. Different models were tried before arriving at the final tool. Eleven items namely *Praseka*, *Arochaka*, *Svaitya*, heartburn (included during the pilot study), *Srotorodha*, *Nidra*, *Hrddrava*, *Panđutva*, *Krsan-gata*, *Klaihya*, and *Akalapalita* were deleted to arrive at the final scale. Labeling of the 10 factors (Table 3) was not done as they were not theoretically explainable. The final tool was named 'RAS-RCVD' (*Rasadhatudushti* Assessment Scale in Risk for CVD) (Appendix 2).

Criterion Validity of RAS-RCVD was analyzed through concurrent validity using the WHO/ISH risk prediction chart indicated for population-based screening in Indians as the reference standard. The participants having a risk level of 10% or above were considered as positive cases and those below 10% as negative cases. Receiver Operating Characteristic (ROC) Analysis was used to obtain every possible cutoff point by plotting the sensitivity against 1-specificity. AUC of 0.5–0.7 has low accuracy and below 0.5 is not acceptable [16]. In the study, the area under the curve (AUC) was 0.55, with an insignificant Z score.

Being a screening tool, the point of cutoff was fixed at the maximum possible sensitivity without compromising the specificity too much. A cutoff score of more than eight was chosen which showed an acceptable level of sensitivity and a reasonable range of

Table 3
Result of exploratory factor analysis of RAS-RCVD.

Sl No	Name of Items	Factors									
		1	2	3	4	5	6	7	8	9	10
1	<i>Angmarda</i>	0.74									
2	<i>Alasya</i>	0.64									
3	<i>Tandra</i>	0.70									
4	<i>Svasa</i>		0.52								
5	<i>Anna-asraddha</i>		0.74								
6	<i>Agnisada</i>		0.78								
7	<i>Sabdasahatva</i>		0.44								
8	<i>Hrllasa</i>		0.49								
9	<i>Tamapravesa</i>			0.58							
10	<i>Saitya</i>			0.76							
11	<i>Murcha</i>			0.63							
12	<i>Spandana</i>				0.69						
13	<i>Ghattana</i>				0.50						
14	<i>Gaurava</i>				0.65						
15	<i>Kampa</i>					0.75					
16	<i>Sunyata</i>					0.67					
17	<i>Sosha</i>						0.50				
18	<i>Tarša</i>						0.79				
19	<i>Alpacheshtayasrama</i>							0.46			
20	<i>Sthoulya</i>							0.96			
21	<i>Kasa</i>								0.87		
22	<i>Jvara</i>								0.54		
23	<i>Sandhivisleša</i>									0.55	
24	<i>Svadudveša</i>									0.84	
25	<i>Sula</i>										0.88
Eigen value		3.94	1.68	1.51	1.49	1.39	1.24	1.16	1.12	1.02	1.01
Total % of variance		15.74	6.73	6.04	5.95	5.57	4.97	4.63	4.47	4.06	4.02
Cumulative % variance		15.74	22.47	28.51	34.46	40.02	44.99	49.63	54.10	58.16	62.18

Table 4
Number of high and low scores as per WHO and the validated tool.

RAS-RCVD score	Risk as per WHO		Total
	>/ = 10% (mod to high)	<10% (low)	
>8 (High)	71 (a)	41 (c)	112
</ = 8 (Low)	50 (b)	56 (d)	106
Total	121	97	218

specificity required for a subjective tool used for screening purposes. The number of high-risk and low-risk participants above and below this cutoff (Table 4).

Among the participants, 121 who had moderate to high risk for CVD (a + b) were considered positive cases. Among the positive cases, 71 were having an RD score of more than eight indicated as (a) (true positives). Thus, the sensitivity of the tool in identifying moderate to high-risk participants was 58.68% with a confidence interval of 49.37%–67.55%. 56 were identified as true negatives by the selected cutoff, as designated as (d), among 97 low-risk participants (c + d). Therefore, the specificity of the tool came out to be 57.73% with a confidence interval of 47.28%–67.70%. Various diagnostic values of the tool are summarized in Table 5. The upper limit of CI value for positive LR of around 2 indicates an increase in the probability of having moderate to high risk of CVD by around 15%, whereas the lower limit of CI value for negative LR of 0.5 indicates a decrease in the probability of not having moderate to high risk of CVD by around 15%. The diagnostic accuracy of this model of RD assessment tool in screening participants with CVD risk was 58.26% with a 95% confidence interval of 51.41%–64.88%.

Convergent Validity - The construct was analyzed for convergent validity by comparing the RAS-RCVD score with the score of CVD risk according to Framingham's Global Risk (FGR) scoring system. This risk assessment system is more objective with predetermined scores for variables like age, history of smoking, diabetes and hypertension, systolic blood pressure, total cholesterol, and HDL levels. Being nonparametric data, Spearman's correlation test was done which showed a low but significant correlation coefficient of 0.22 with a p-value <0.05.

Extreme group (Discriminative) Validity - The cutoff score was checked for discriminative validity by comparing the mean value of the RD score above and below the determined cutoff value. The mean score of RD in participants identified as negative cases and positives were respectively 4.88 and 13.75 with standard deviation 2.17 and 4.42. Comparing the means using the t-test for two independent samples showed a value of -18.66 with a p-value < 0.001. This shows that the cutoff score of above eight significantly discriminates the extremes values of RD.

Hypothesis Testing - The first hypothesis was to test if there exists a difference in the mean CVD risk scores in positive and negative RAS-RCVD scores. The test showed that the mean CVD risk score in high and low RD significantly differed (p < 0.01). The second hypothesis was tested by comparing the CVD risk in two groups after 1 month of intervention. The mean reduction in Qrisk@2-2017 score in RD correcting drug and the LSM

Table 5
Summary of diagnostic value of RAS-RCVD.

Statistic	Formula	Value (%)	95% CI (%)
Sensitivity	a/(a+b)	58.68	49.37–67.55
Specificity	d/(c + d)	57.73	47.28–67.70
Positive likelihood ratio	Sensitivity/(1- specificity)	1.39	1.05–1.83
Negative likelihood ratio	(1-sensitivity)/specificity	0.72	0.55–0.94
Positive predictive value	a/(a+c)	63.39	56.77–69.54
Negative predictive value	d/(b + d)	52.83	46.04–59.52
Diagnostic accuracy	(a+d)/(a+b + c + d)	58.26	51.41–64.88

(Mean = 2.53, SD = 3.22) group was higher than that in the LSM group (Mean = 0.30, SD = 3.43) which showed statistical significance (p < 0.05) in non-parametric testing of hypothesis. The Cliff's delta calculated showed a small effect size of 0.31, indicating a small clinical significance despite the statistical significance.

4.2. Part II

Among the 200 employees surveyed, 160 employees satisfying the inclusion and exclusion criteria were included in the study. Most of them (70%) were within the age group of 46–55 (Table 6).

Most of the participants in the study were females (66.9%). The percentage of current smokers were very low (6.3%) in the study. Regarding the CVD risk factors, 46.3% of participants were dyslipidaemic, 33.1% were hypertensive and 22.5% were diabetic. About half of the participants had high BMI; 40% were overweight and 11% had obesity. There was a high prevalence of family history of diabetes (70%), compared to hypertension (57%), heart disease (39%), and stroke (14%). The mean (SD) systolic blood pressure was 128.51 mmHg (16.92) with 133.25 (2.02) in males and 126.17 (1.69) in females. The mean (SD) serum total cholesterol was 221.71 (40.52) mg/dl with a slightly higher mean in males (222.36 (5.68)) when compared to females (221.39 (3.9)).

The WHO risk prediction chart categorized 46.9% of participants to have 10% and above risk to develop CVD in the next 10 years while the Framingham Global Risk (FGR) score predicted a higher number of 77.5% participants. The mean (SD) FGR scores were 11.51 (0.44) in males and 12.39 (0.65) in females. The prevalence of RD was estimated by taking a scores of above eight in the RAS-RCVD scale as a positive cases.

The prevalence of RD observed among the participants at risk for developing CVD was 49.4% with a 95% confidence interval of 41.4%–57.4% (Table 7). Among the participants with high RD prevalence, around 65% were females and 35% were males. The mean (SD) score of RD was 9.83 (0.84) in males and 9.81 (0.65) in females. Around 58% of participants with RD were above the age of 50.

On further analysis of the observations, it showed that 61.2% of participants with low CVD risk as per the WHO risk assessment had low RD (≤8) whereas 61.3% of participants belonging to moderate to high-risk individuals had higher RD which was statistically significant (p < 0.01). The prevalence of RD was significantly high in participants with BMI of more than 25 and in those with a history of heart attacks among the first-degree relatives.

5. Discussion

Any morbidity in the human body, according to the doctrines of Ayurveda, results from an imbalance of the metaphysical entities

Table 6
Age distribution of participants in the prevalence study.

Age group	Frequency	Percent
40–45	36	22.5
46–50	55	34.4
51–55	57	35.6
56–60	12	7.5
Total	160	100

Table 7
Prevalence of Rasadhatushti

Rasadhatushti	Frequency	Percent
Present (score >8)	79	49.4
Absent (score = /< 8)	81	50.6
Total	160	100.0

named *Doshas* and the derangement in the function and/or structure of the physical entities called the *Dhatus*. They are all constructs or abstracts that are inferred through their normal and abnormal functions in the body [17].

Vitiated *Rasadhatu* is a construct in Ayurveda mentioned to be the cause for diseases of the circulatory channels and the heart. Conceptually, the pathogenesis, as well as the current preventive measures of CVDs, can be explained well using this Ayurvedic construct. Empirical data of an observational study in CAD patients also suggested a higher percentage of vitiation of *Rasadhatu* than any other *Dhatus*. This was the preliminary evidence supporting the relevance of the construct RD in CVD. It was postulated that if derangement of *Rasadhatu* was related to and precedes CVD, it must be observable in participants at risk for developing cardiovascular diseases.

The validity of a construct needs to be enhanced by methodological triangulation using multiple research strategies. Hence, the initial part was designed to study the relevance of the concept with the help of various analyses ensuring the validity of the available theoretical scale. The next step was to estimate the prevalence of the said concept in a group of participants at risk of the condition. In the first part, the standard steps involved in scale development and validation were adopted to modify the available model of assessment of deranged *Rasadhatu* to a reliable scale that was relevant to participants who were at risk of CVD. The frequency of clinical features in the scale in the past three months might have invoked recall bias. This was an attempt to study the criterion validity of the scale with an acceptable screening method, the WHO/ISH risk prediction chart.

The low diagnostic values of RAS-RCVD may be attributed to its novelty, the subjectivity of items, and the possible recall bias. From the observation of correlation (although weak) established during convergent validation, a hypothesis was proposed that if the correlation is true, there could be a significant difference between the mean score of FGR above and below the cutoff score in the RAS-RCVD score. The mean FGR score above the cutoff in RAS-RCVD score was 13.91 ± 4.78 , $n = 65$, and below it was 12.24 ± 3.43 , $n = 153$. The above said hypothesis was accepted as an independent t-test showed a significant difference between the two means ($p < 0.01$). FGR score seems to be as most useful CVD risk assessment model in young Indian patients compared to ACC/AHA or 3rd JBS calculator [18]. Thus, the construct was further validated for its ability to distinguish moderate and higher risk participants from the lower risk.

Lack of evidence on the biological and clinical plausibility can be considered as the major drawback for the non-acceptance of Ayurvedic concepts and management strategies. A quasi-experimental research design helps to establish potential associations [19]. These designs can be stepping-stones to establish the rationale for subsequent, focused, RCTs. Qrisk®2–2017 is an online algorithm for predicting cardiovascular risk, incorporating more objective parameters than WHO/ISH risk chart. It estimates the risk of a person between 35 and 74 years for developing CVD over the next 10 years. Unlike Framingham score, this score based on UK data includes additional risk factors, such as ethnicity, deprivation (measured using the Townsend deprivation score, which is obtained from data associated with a person's postcode), body mass index, and blood pressure treatment [20]. It was observed that correction of RD reduces the risk for CVD; thus re-validating the construct. Participants were initially screened with WHO/ISH risk prediction chart to exclude participants at or above 30% risk for whom immediate pharmacological interventions were recommended. *Panchakolachurna* is the medicine of choice recommended

in conditions caused by RD and hence used to verify if its administration reduces the CVD risk over the risk reduction through the recommended LSM alone. As the intention of this part was not to study the effectiveness of the medicine, the effect of confounders and the comparability of groups were not analyzed. The observed results establish the relevance of the construct RD in CVD risk.

The validated tool could identify more moderate to high CVD risk participants (61.3%) than that expected from its sensitivity (58.7%) when applied in at-risk participants during the second part of the study. Estimation of higher prevalence of RD in moderate to high-risk scores in a sample of participants susceptible to CVD suggests that sedentary job is a common risk factor for both. A significant association between RD and BMI justifies this statement. The relatively high prevalence of RD (50.1%) observed in this group warrants the need for specific remedial measures. The significant association between the RD and CVD risk observed during this part of the study once again establishes the validity of the studied construct.

The validated scale RAS-RCVD can be used as a screening tool for identifying adults at >10% risk for CVD in limited resources settings. The utility of the scale, RAS-RCVD, as a screening tool for CVD is subject to further re-validation in geographically different population settings and also in larger samples. The presence of comorbidities other than diabetes was excluded in the scale validation process, which is a potential limitation of the scale. Above all, this tool was designed to assess RD in the context of CVD alone, and not in other conditions caused by RD. Though the intention of scale validation was not primarily to develop a screening tool, observations and analysis from the study triangulate the validity of the construct, RD in the context of CVD risk. Multipronged health benefits of specific Ayurvedic interventions to correct this morbid construct, if any, need to be studied through well-designed large sample clinical trials.

6. Conclusion

The mixed-method study provides a preliminary conclusion that the Ayurvedic construct, RD, is scientifically relevant to CVD risk. A significant proportion of RD was observed in participants with moderate to high-risk of CVD. It has been observed that the correction of vitiated *Rasadhatu* reduces the CVD risk; suggesting a possible causal association between the two. Diet, physical activity, mental stress, and even climatic variations directly influence the state of *Rasadhatu* through variations in the Agni. Therefore, advices on Ayurvedic healthy dietary habits, eating patterns, and lifestyle together with regular use of medicines correcting RD along with individual risk management would be beneficial to provide a comprehensive management strategy for reducing the CVD risk. The current work is a stepping-stone for future research on the possible association of the construct, *Rasadhatudushti* in CVD.

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Declaration of competing interest

None.

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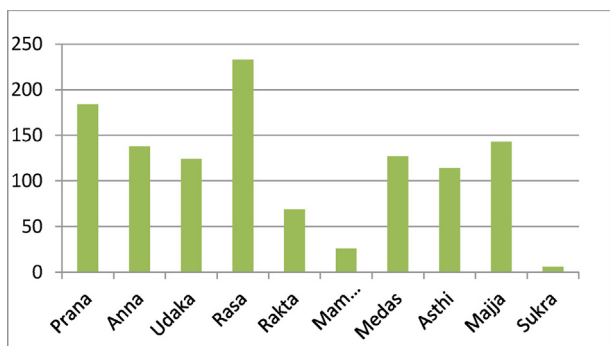
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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jaim.2022.100627>.

Appendices



Appendix 1. Chart showing prevalence of *Rasadhatu* vitiation compared to other *dhatus*; from an observational study on patients diagnosed of acute Coronary Artery Disease.

Appendix 2

The final validated scale for assessing *Rasadhatudushti* named 'RAS-RCVD' (*Rasadhatudushti* Assessment Scale in Risk for Cardiovascular Diseases).

Sl.No	Items	Meaning	Response rate		
			Very rare	Occasional	Frequent
1.	<i>Anna-āsraddha</i>	Lack of interest in food			
2.	<i>Hṛllāsa</i>	Nausea			
3.	<i>Gourava</i>	Heaviness of body			
4.	<i>Tandra</i>	Tiredness			
5.	<i>Angamarda</i>	Body ache			
6.	<i>Jvara</i>	Recurrent fever			
7.	<i>Agnināsa</i>	Reduced appetite			
8.	<i>Svādudveṣa</i>	Aversion to sweet taste			
9.	<i>Śaitya</i>	Feeling cold			
10.	<i>Ālasya</i>	Laziness			
11.	<i>Mūrccha</i>	Dizziness			
12.	<i>Śvāsa</i>	Dyspnoea on exertion			
13.	<i>Kasa</i>	Cough			
14.	<i>Sandhivīṣeṣa</i>	Laxity of joints			
15.	<i>Sabdhāsahatva</i>	Intolerance to noise			
16.	<i>Hṛdaya drava</i>	Palpitation			
17.	<i>Kampa</i>	Tremor			

Appendix 2 (continued)

Sl.No	Items	Meaning	Response rate		
			Very rare	Occasional	Frequent
18.	<i>Śoṣa</i>	Dryness of mouth			
19.	<i>Śūla</i>	Stomach pain			
20.	<i>Śūnyata</i>	Feeling of emptiness			
21.	<i>Spandana</i>	Twitching			
22.	<i>Ghattana</i>	Tightness of chest			
23.	<i>Alpapeṣṭayā śrama</i>	Easy fatigability			
24.	<i>Tarṣa</i>	Excessive thirst			
25.	<i>Sthoulya</i>	Obesity (BMI)	>25	25–29.9	≤/ <30

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