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Title: The Influence of Aerobic Exercise Training on the Double Product Break Point in Low-to-Moderate Risk Adults

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Abstract

The double product (DP) is the product of the heart rate (HR) and systolic blood pressure (SBP). The double product break point (DPBP) is a physiologic threshold that occurs at similar exercise intensities to that of the ventilatory threshold (VT). The influence of aerobic exercise training on the DPBP has not yet been examined. The purpose of this study was to examine whether aerobic exercise training (ET) increases the exercise intensity at which the DPBP occurs, and whether it increases in a similar fashion to the VT. Seven males and 11 females, all sedentary (mean \pm SD: age = 29.9 ± 10.5 yr) underwent supervised cardiopulmonary exercise testing using a cycle ergometer ramp protocol at baseline and after eight weeks of vigorous ET on a cycle ergometer. The VT was determined by gas analysis and the V-slope method. Experienced observers using standardized instructions visually determined the DPBP. Following ET, VO_{2peak} , maximal workload, and body composition variables all showed significant positive changes. The VO_2 at which the DPBP and VT occurred increased significantly from baseline to follow-up ($p < .001$). At baseline and at follow-up, the DPBP and VT did not differ. The DPBP and VT were significantly correlated to each other at both time points. Results suggest that the DPBP responds to ET in a similar fashion to that of the VT, and may be an easier and more useful marker of the VT for exercise training purposes.

Keywords: Exercise training, Double product break point, Ventilatory threshold, Cardiopulmonary exercise testing

Introduction

The double product (DP), also known as the rate pressure product, is the mathematical product of the heart rate (HR) and systolic blood pressure (SBP). The DP has long been used as a non-invasive measure of myocardial oxygen consumption during exercise (Gobel et al. 1978; Jorgensen et al. 1973; Kitamura et al. 1972). The DP has been a useful index in cardiac rehabilitation settings to identify specific workloads at which signs and symptoms of ischemia occur, and improvements in functional capacity relative to the onset of symptomatic ischemia (Arya et al. 2005; Durstine and American College of Sports Medicine. 2009).

Tanaka and colleagues were the first to identify that the DP increases more rapidly above the LT than below it, and were the first to identify a breakpoint in the double product (DPBP) with incremental exercise in healthy subjects (Tanaka et al. 1997; Tanaka and Shindo 1992). Several other studies have further examined the occurrence of the DPBP in healthy subjects as well as those with coronary artery disease (CAD), (Brubaker et al. 1997; Kim et al. 2003; Omiya et al. 2004; Riley et al. 1997), and have found that the DPBP occurs at similar exercise intensities to that of the lactate threshold (LT) and ventilatory threshold (VT). They conclude that the DPBP may be a useful non-invasive, and easier to obtain marker of the LT and VT in a wide range of individuals.

The LT and VT have long been used as markers of the anaerobic threshold (AT) (Svedahl and MacIntosh 2003). Use of the AT has ranged from assessing the exercise tolerance of cardiac patients (Wasserman et al. 1973), to predicting endurance performance in athletes, as well as for exercise prescription purposes (Davis et al. 1979; McConnell et al. 1993; Tanaka and Matsuura 1984; Tanaka et al. 1984). Numerous studies have shown that aerobic exercise training (ET) at or above the LT and VT results in a greater oxygen consumption ($\dot{V}O_2$) at which they occur. This has been noted both in healthy subjects and individuals with CAD (Jensen et al. 1996; Jones and Carter 2000; Poole and Gaesser 1985). Whether ET elicits a similar training response in the DPBP has not yet been investigated. Therefore, the primary purpose of this study was to determine if ET would result in an increase in the exercise intensity at which the DPBP occurs. The secondary purpose was to compare the DPBP and VT before and after ET, and to examine whether they occur at similar exercise intensities.

Methods

Subjects

The Institutional Review Board of Ball State University approved all methods and procedures. Sedentary subjects between the ages of 18 and 50 years old were recruited from the Ball State community and surrounding area. Individuals self reported their physical activity history. Individuals who reported no moderate intensity exercise ≥ 3 days per week for ≥ 30 minutes, vigorous intensity exercise ≥ 3 days per week for ≥ 20 minutes, or a combination of the two within the previous 6 months were considered “sedentary”. Individuals that were considered regular exercisers were excluded from study participation. Additionally, a predicted $VO_2\text{max}$ for each subject was calculated based on age, gender, BMI and physical activity history (Brubaker et al. 2002). Subjects with a predicted $VO_2\text{max}$ > the 50th percentile for their age and gender as indicated by the American College of Sports Medicine, were excluded (American College of Sports Medicine. et al. 2010). Additional exclusion criteria included: history of myocardial infarction or diagnosed with cardiovascular disease, diabetes mellitus, pulmonary disease, neurologic disorders (e.g. multiple sclerosis, cerebral palsy, etc.), hypertension, current pregnancy, or any orthopedic problem that would limit exercise ability. In addition, individuals taking any medications that would affect a normal exercise response of HR and SBP were excluded from participation.

Cardiopulmonary Exercise Testing

All subjects underwent maximal exercise testing on an electronically braked, cycle ergometer (SensorMedics, Ergometrics 800S, AG Bilthoven, The Netherlands) at baseline and after the ET training period. A standardized ramp protocol of 25 Watts per minute was utilized. Subjects were asked not to perform any vigorous physical activity or ingest any caffeine 24 hours prior to the exercise test. Heart rate and rhythm were monitored continuously via 12 lead electrocardiography (GE Case V6.5, GE Healthcare, Waukesha, WI). Ratings of perceived exertion (RPE) were assessed each minute utilizing the Borg 6 – 20 scale. Subjects were instructed to continue until they could no longer maintain 50 revolutions per minute or felt they could no longer continue. A maximal test was established by obtaining at least two of the following criteria: $RER \geq 1.1$, $RPE \geq 16$, or $\geq 85\%$ of age predicted maximal heart rate. If they did not achieve maximal exercise criteria, the data were excluded from analysis.

Systolic blood pressure (SBP) was measured by a reliable and validated automated blood pressure cuff (Tango +, Sun Tech Medical, Morrisville, NC) approximately every 15 to 20 seconds, which was

interfaced with the ECG system (Cameron et al. 2004; Furtado et al. 2009). The Tango + utilizes a microphone placed over the brachial artery and ECG input from the 12 lead ECG system. The DP was calculated by the Tango + unit. Gas exchange measurements were made via the Parvo Trueone 2400 Metabolic Measurement System (ParvoMedics, Sandy, Utah), which utilizes a high efficiency mixing chamber. Data was averaged to 20 second values. The measurements of VO_2 and carbon dioxide production (VCO_2) were used for determining VT and peak VO_2 .

Body Composition Measurements

Body mass index (BMI) in kg/m^2 was calculated from height and weight data, obtained through standardized procedures (American College of Sports Medicine. et al. 2010). Total body dual-energy X-ray absorptiometry DXA (Lunar Prodigy, software version 11.40.004, GE Medical Systems, Madison, WI) was used to measure percent body fat, fat mass, and fat free soft tissue mass. All DXA scans were completed by a single investigator who successfully completed a precision study. Quality control for soft tissue measurements was made daily.

DPBP/VT threshold determination

The DPBP and VT for all tests were determined visually by 2 experienced observers. If there was no agreement between the observers (within 10%), a third observer was utilized. The average of the 2 observers was used as the threshold. The V-slope method was used to determine the VT (Beaver et al. 1986). The DPBP was determined visually by two segment linear regression analysis, defined as the point at which a clear and sustained increase in the slope of the relationship of the DP and VO_2 commenced. The DPBP was defined as the VO_2 at which the first portion of nonlinear increase in the DP begins (Tanaka and Shindo 1992). If agreement was not reached with the third observer, then the data for that subject was excluded.

Aerobic Exercise Training

Subjects trained for an 8 week time period, with a 1 to 3 week ramp up period, as needed, to achieve the target training intensity. The goal was to train a minimum of 3 and a maximum of 4 sessions per week. Compliance was defined as attending > 85% of the sessions. The ramp up period began at 50% of maximum heart rate reserve (MHRR) for 30 minutes and increased to the target training stimulus of 75% of MHRR for 45 minutes in duration. Subjects exercised in a supervised facility and were continuously

monitored for HR to ensure the subject achieved and maintained the target exercise duration and intensity. All subjects trained on an upright, electronically braked, cycle ergometer.

Statistical Analysis

All analyses were performed using PASW (version 18.0, SPSS, Inc., Chicago, IL). Paired sample t-tests were used to evaluate differences in threshold, body composition, and exercise testing values at baseline and at follow-up testing. A p value of <0.05 was considered statistically significant.

Results

Eighteen subjects completed the training program. The DPBP could not be determined in 1 female who was eliminated from analysis. As a result, 17 subjects (7 males and 11 females, mean age 29.3 ± 10.5) were included in the analysis. All subjects achieved the target compliance level for ET, and all subjects were normotensive at baseline. Subject characteristics at baseline and after training are presented in Table 1. All subjects achieved maximal exercise criteria at both baseline and follow-up exercise tests (Table 1). Mean percent difference in DPBP threshold determination between observers was 7.6 and 8.0% for baseline and follow-up, respectively. Mean percent difference in VT threshold determination between observers was 8.5 and 4.4% for baseline and follow-up, respectively. The VO_2 at which the DPBP and VT occurred did not differ at baseline (Figure 1A). When expressed as a percentage of VO_{2peak} , the DPBP ($53.3\% \pm 17.4$) and VT ($59.2\% \pm 11.0$) still did not differ significantly.

At follow-up testing, VO_{2peak} , maximal workload achieved, percent body fat, fat mass, and fat free mass all showed significant positive changes (Table 1). The SBP at maximal exercise increased significantly from baseline to follow-up (Table 1), which may be a product of a greater maximal workload achieved after ET. The VO_2 at which the DPBP and VT occurred increased significantly following the ET (Figure 1A). When expressed as a percentage of VO_{2peak} , however, no significant change was noted for the DPBP ($p = 0.34$) or VT ($p = 0.66$), respectively (Figure 1B). Body weight, BMI, and maximal heart rate were unchanged after ET. After training, the DPBP and VT occurred at similar exercise intensities (Figure 1), expressed in $Liters\ min^{-1}$, or as a percentage of VO_{2peak} (60.8% and 61.6% for DPBP and VT, respectively). When the HR alone at the VT was examined before and after training, a 3.7% increase was noted, which was not significant (Figure 2). The Bland Altman plots for baseline and follow-up are shown in Figures 3 and 4, respectively. The DPBP and VT were significantly correlated at baseline ($r = 0.80$, p

<0.001) and at follow-up ($r = 0.74$, $p < 0.001$), and differences in VO_2 at the DPBP and VT against the mean value of VO_2 were mostly within ± 2 SD.

Discussion

To date, no previous study has examined the impact of aerobic exercise training on the DPBP. The primary finding of this study is that vigorous ET significantly increases the VO_2 ($\text{L}\cdot\text{min}^{-1}$) at which the DPBP occurs (Figure 1). When expressed as a percentage of $\text{VO}_{2\text{peak}}$, no change was noted. This finding is likely due to the higher fitness level achieved by the subjects as a result of the ET, reflected in the significantly higher $\text{VO}_{2\text{peak}}$ and peak workloads achieved following training. The secondary finding of this study is that the increase in DPBP seen with ET is coincident to that of the VT with ET.

While Tanaka and colleagues (Tanaka et al. 1997; Tanaka and Shindo 1992) were the first to identify that the slope of the DP was greater above the LT as well as the presence of the DPBP, it was Brubaker et al. (Brubaker et al. 1997) and Riley et al. (Riley et al. 1997) who were the first to compare the occurrence of the DPBP to the VT. Brubaker successfully identified the DPBP in cardiac patients during treadmill exercise testing. Mean VO_2 values at the DPBP and VT differed by 5%, which was similar to the current study (5.5% difference at baseline in $\text{L}\cdot\text{min}^{-1}$) (Brubaker et al. 1997). In addition, Brubaker et al. reports a significant correlation between the DPBP and VT ($r = 0.81$), which is similar to the findings of the current study.

Riley et al. (Riley et al. 1997) examined the relationship between the DPBP and VT in 10 healthy individuals and 10 patients with CAD undergoing cycle ergometer testing. They found the mean VO_2 value of the DPBP to be significantly higher than the VT (1.39 vs. 1.26 $\text{L}\cdot\text{min}^{-1}$ 10.3% difference). This difference may be a reflection of the two groups of subjects within this analysis, as significant CAD has been shown to decrease the VO_2 at which the AT can occur (Wasserman et al. 1973). Riley et al. further report that the DPBP and VT were correlated significantly ($r = 0.86$), which is also similar to the findings of the current study (Riley et al. 1997).

Omiya et al. in 2004 (Omiya et al. 2004) also studied the relationship between the DPBP and VT in 65 cardiac patients and found the mean workload at both thresholds to be similar, with a significant correlation between the two thresholds ($r = 0.76$, $p < 0.001$). Results from the current study confirm and extend these findings to an apparently healthy, yet previously inactive and overweight population.

The cause of the DPBP is not well understood, although it has been shown that catecholamine levels in the blood exhibit threshold phenomenon as well, with catecholamine levels significantly greater above the LT and/or VT (Mazzeo and Marshall 1989; Riley et al. 1997; Tanabe et al. 1994). This is suggesting that as exercise intensity and myocardial oxygen demand increases, a disproportionate increase in sympathetic activity occurs. During the initial onset of exercise, the HR increase seen is primarily through parasympathetic nervous system withdrawal. At higher exercise intensities however (after approximately 100 beats·min⁻¹), the HR increase to maintain cardiac output is primarily through sympathetic activity. With ET, sympathetic activity has been shown to decrease, reflected in decreased levels of plasma catecholamines during exercise (Winder et al. 1978). At a given cardiac output, the decrease in sympathetic activity results in a lower heart rate and therefore, lower DP. In the current study we can see that the HR at the VT remained unchanged (Figure 2), despite a significant increase in the VO₂ at which the VT and DPBP occurred (Figure 2). The resulting training effect allows an individual to exercise at a higher intensity prior to the occurrence of the DPBP, when sympathetic activity and myocardial oxygen demand increase significantly. This may be of particular interest in individuals with significant CAD, as ET may result in higher exercise intensities achieved prior to the onset of angina or ischemia symptoms. Given that the DP is a well established surrogate marker for myocardial oxygen consumption, and has been used in clinical rehabilitation settings previously, use of DPBP appears to be superior to the use of HR markers alone, as it is more closely associated to the exercise intensity at which the potential for adverse cardiovascular events increases. Furthermore, it allows for a higher energy expenditure during steady state exercise training, which is important for those desiring a reduction in excess body fat. Given the increase in VO₂ at the DPBP seen here (~ 0.28 L·min⁻¹), exercising at or just below the DPBP would equate to an approximate 1.5 kcal·min⁻¹ increase in energy expenditure (45 – 90 kcal for a 30 – 60 minute workout).

Limitations for the current study included the relatively small subject number. During the course of the study, several subjects dropped out due to inability to adhere to the training program. In addition, the inclusion of the non-exercising control group would have clarified the impact of the training stimulus alone on the results, and minimized any learning effect on the cycle ergometer exercise test that may have occurred in the study group.

In conclusion, results from the current study suggest that aerobic exercise training increases the VO_2 at which the DPBP occurs, and that the training effect is similar to the training effect seen with the VT. Results suggest that the DPBP may be a useful marker for the AT, and is easier to obtain than the VT or LT. The DPBP may have use in both healthy and clinical populations as an independent marker of exercise intensity. Yet to be explored is the minimum duration of DP measurement that will allow identification of the DPBP. We obtained DP values at 20-second intervals approximately. Examination whether measurements taken at slightly longer intervals (≥ 30 sec), yet still provide accurate DPBP determination, is needed. The current study employed a fairly vigorous ET program. Yet to be examined is whether lower intensity or volume of exercise would result in similar adaptations to the DPBP.

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Table 1 Subject characteristics (n = 17) before and after 8 weeks of aerobic exercise training

	Baseline	Follow-up
Weight (kg)	75.7 ± 17.0	75.1 ± 16.5
BMI (kg/m²)	25.8 ± 5.2	25.6 ± 5.1
Body fat (%)	34.4 ± 8.6	33.3 ± 8.9*
Fat mass (kg)	26.4 ± 10.2	25.5 ± 10.3*
Fat free mass (kg)	49.4 ± 11.8	50.3 ± 12.0*
VO_{2peak} (L·min⁻¹)	1.98 ± 0.69	2.29 ± 0.71*
VO_{2peak} (ml·kg⁻¹·min⁻¹)	26.1 ± 6.5	30.6 ± 7.2*
SBP_{peak} (mmHg)	200.4 ± 24.1	213.1 ± 21.9*
RER_{peak}	1.33 ± 0.11	1.26 ± 0.09
RPE_{peak}	17.7 ± 1.3	18.1 ± 1.2
Peak Workload (Watts)	182.5 ± 47.9	220.0 ± 56.9*

Data are given as mean ± standard deviation

BMI = Body Mass Index, HR_{peak} = Heart rate at peak exercise,

SBP_{peak} = systolic blood pressure at peak exercise, RER_{peak} = respiratory exchange ratio at peak exercise,

RPE_{peak} = rating of perceived exertion at peak exercise

* $p < 0.05$ baseline to follow-up

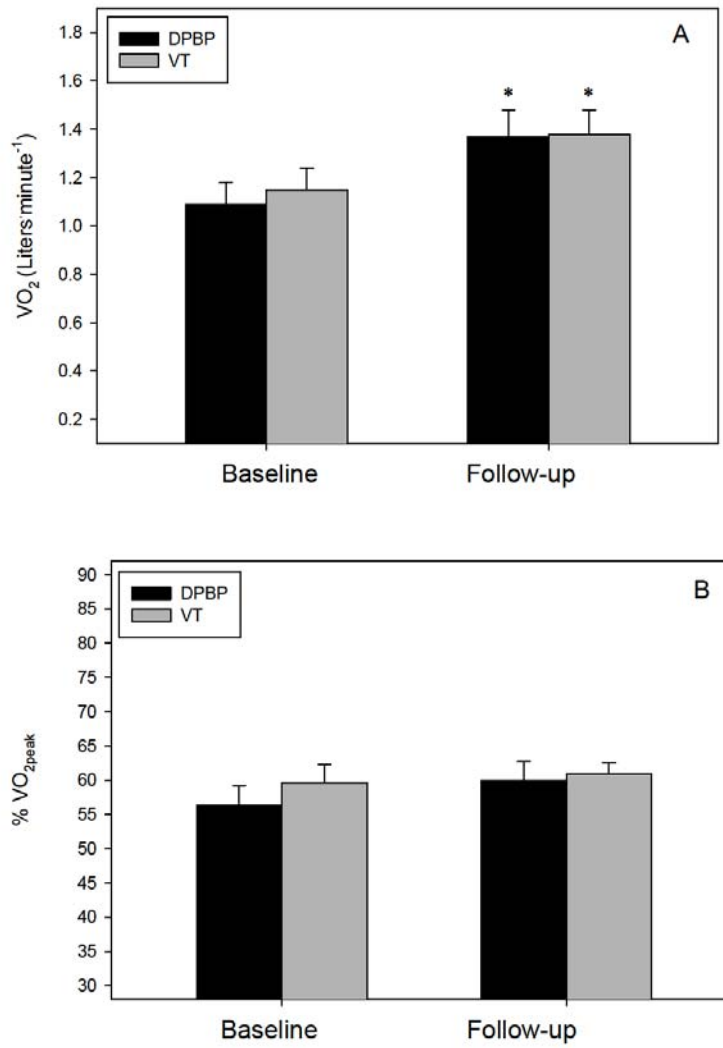


Fig. 1 Occurrence of the DPBP and VT before and after 8 weeks of aerobic exercise training in Liters·min⁻¹ (A) and % VO_{2peak} (B)

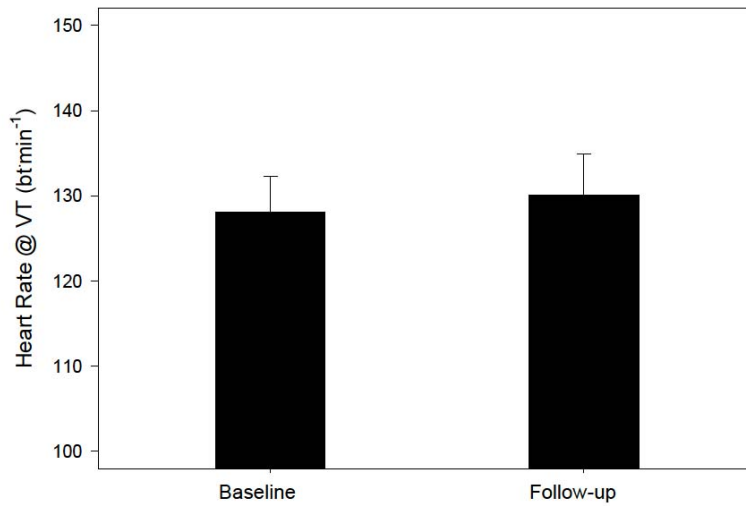


Fig. 2 Heart rate value at the VT before and after 8 weeks of aerobic exercise training

Difference (DPBP – VT) at baseline

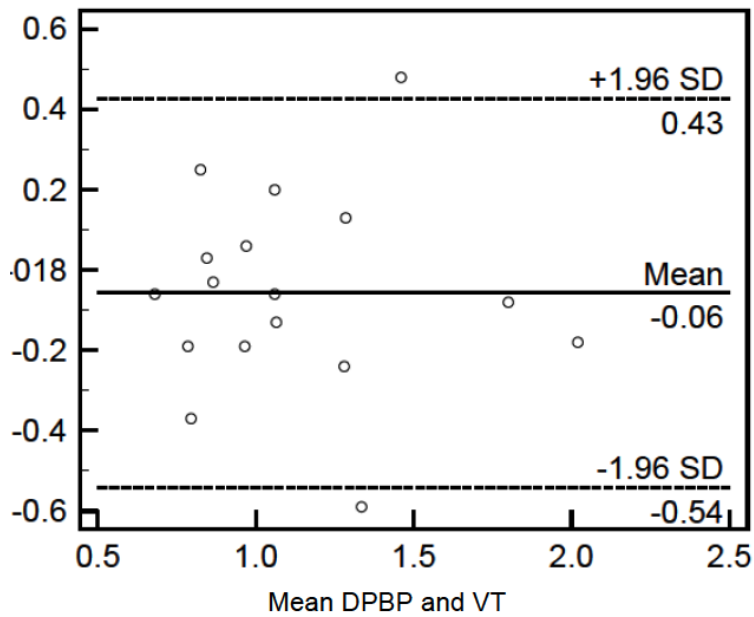


Fig. 3 Bland-Altman plot of the difference [ventilatory threshold (VT) – DPBP] against the mean VO_2 for DPBP and VT at baseline. The differences in VO_2 were within ± 2 SD of the mean VO_2 .

Difference (DPBP – VT) at follow-up

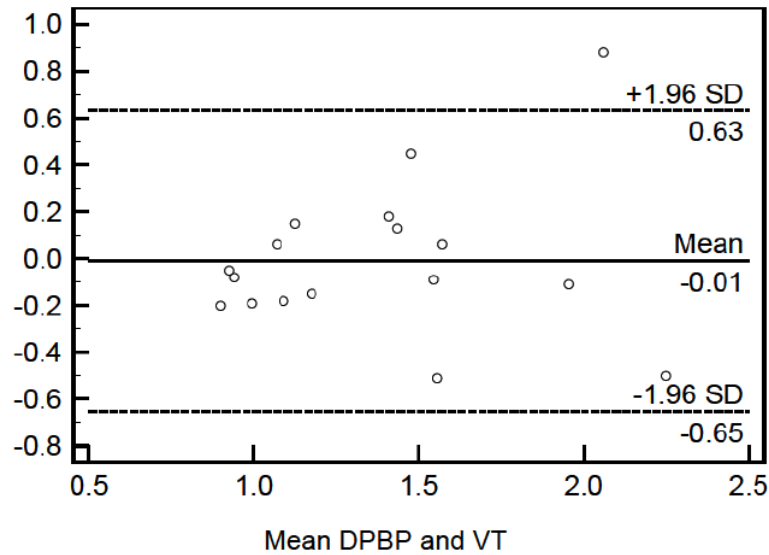


Fig. 4 Bland-Altman plot of the difference [ventilatory threshold (VT) – DPBP] against the mean VO_2 for DPBP and VT after 8 weeks of aerobic exercise training. The differences in VO_2 were almost within ± 2 SD of the mean VO_2 .