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Original article

Waist circumference and mortality: Impact of associated risk factors

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Abstract

Aim. – This study was designed to evaluate the risks of all-cause and cardiovascular mortality in subjects with large waist circumferences, with or without associated risk factors, and to determine whether or not waist circumference might identify high-risk subjects.

Methods. – The population included 55,800 men (aged 52.1 ± 8.2 years) and 28,937 women (aged 54.2 ± 9.1 years) who had undergone a health checkup at the Preventive and Clinical Investigations Centre between January 1999 and December 2004 with a mean follow-up of 4.7 ± 1.7 years. An increased waist circumference was defined as those in the last quintile of distribution. Mortality risk for each waist-circumference quintile, with or without associated risk factors (hypertension, diabetes, elevated LDL cholesterol), was evaluated using Cox's regression models, including age, gender, tobacco and alcohol consumption, and physical activity.

Results. – The percentage of subjects with hypertension, diabetes and raised LDL cholesterol levels increased from the first waist-circumference quintile to the last. After adjusting for variables, all-cause mortality risk did not increase significantly with large waist circumference only (HR: 1.19 [0.84–1.68]), but was significantly higher when an increased waist circumference was associated with at least one risk factor (HR = 1.58 [1.26–1.98]; 3.70 [2.05–6.68] for three risk factors). Similar results were observed for cardiovascular mortality (HR: 0.85 [0.19–3.68] with only large waist circumference and 3.56 [2.05–6.57] when waist circumference was associated with at least one risk factor).

Conclusion. – In a population with low-to-moderate mortality risk, waist circumference alone did not identify high-risk subjects, thus suggesting that a more global approach is necessary.

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Keywords: Epidemiology; Mortality; Risk factors; Waist circumference

Résumé

Tour de taille et mortalité : impact des facteurs de risque associés.

But. – Évaluer le risque de mortalité, toutes causes confondues des sujets ayant un tour de taille élevé, en présence ou non d'autres facteurs de risque, et déterminer si le tour de taille permet d'identifier les sujets à haut risque.

Méthodes. – La population était composée de 55 800 hommes (âge moyen : $52,1 \pm 8,2$ ans) et 28 937 femmes (âge moyen $54,2 \pm 9,1$ ans) qui ont eu un examen périodique de santé au centre d'investigations préventives et cliniques entre janvier 1999 et décembre 2004, suivi en moyenne $4,7 \pm 1,7$ ans. La limite pour un tour de taille élevé était le dernier quintile de la distribution. Les risques de mortalité dans chaque quintile de tour de taille en présence ou non d'autres facteurs de risque (hypertension, diabète, LDL-cholestérol élevé) ont été évalués à partir de modèles de Cox incluant l'âge, le sexe, la consommation de tabac et d'alcool et l'activité physique.

Résultats. – Le pourcentage de sujets avec une hypertension, un diabète ou un LDLc élevé, augmente de façon linéaire du premier au dernier quintile. Après prise en compte de nombreux facteurs, le risque de mortalité toute-cause n'augmente pas avec un tour de taille élevé (HR : 1,19 [0,84–1,68]). Le risque de mortalité augmente de façon significative quand le tour de taille élevé est associé à d'autres facteurs de risque (HR = 1,58 [1,26–1,98] pour un facteur de risque ; 3,70 [2,05–6,68] pour trois facteurs de risque). Des résultats similaires ont été trouvés avec la

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mortalité cardiovasculaire (HR = 0,85 [0,19–3,68] pour le tour de taille élevé uniquement et 3,56 [2,05–6,57] quand le tour de taille est associé à au moins un facteur de risque).

Conclusion. – Dans une population à risque de mortalité faible ou modérée, le tour de taille seul ne permet pas de détecter des sujets à haut risque ; une approche plus globale apparaît nécessaire.

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Mots clés : Épidémiologie ; Mortalité ; Facteurs de risque ; Tour de taille

1. Introduction

Excess weight is associated with an increased prevalence of common cardiovascular risk factors such as diabetes [1,2], hypertension [3] and dyslipidaemia [3]. However, the role of obesity as an independent risk factor for cardiovascular disease (CVD) and all-cause mortality remains unclear [2,4–5]. A previous report evaluated the relationship between overweight and cardiovascular mortality according to the presence or absence of associated risk factors (ARF) such as hypertension, hypercholesterolaemia and diabetes [6], and showed that, in a large European cohort of men and women, overweight was not associated with an increased risk of mortality in the absence of other ARF. One of the limitations of that study was that only body mass index (BMI), and not waist circumference (WC), was used to evaluate fat mass. However, a number of studies [7,8] have shown that WC may be a better predictor of mortality than BMI.

A study by Katzmarzyk et al. [9] found that, across WC categories, in men with at least two additional metabolic syndrome (MetS) components, the risk of CVD mortality increased. In another earlier report, the role of specific combinations of MetS components in all-cause mortality, according to recent definitions, was evaluated [10]. Among these specific combinations, it was found that a large WC together with elevated glucose, triglycerides or blood pressure (BP) were more strongly associated with all-cause mortality than other three-component combinations.

The aim of the present study was to evaluate the risks of all-cause and CVD mortality among subjects with an increased WC in the presence or absence of ARF, as defined in clinical practice, to determine whether or not WC in such a population is a relevant parameter for identifying high-risk subjects.

2. Methods

Subjects were examined at the IPC Center; (Centre d'Investigations Préventives et Cliniques), a medical centre subsidized by the French national healthcare system (sécurité sociale–CNAM) that offers all working and retired persons, and their families, free medical examinations every 5 years.

The present study population comprised all subjects aged 40 years and over who had undergone a health checkup between January 1999 and December 2004. The study population included 84,737 subjects: 55,800 men (age: 52.1 ± 8.2 years) and 28,937 women (age: 54.2 ± 9.1 years). Table 1 shows the main clinical characteristics of this population.

Supine BP was measured in the right arm using a manual mercury sphygmomanometer after a 10-min rest period. The first and fifth Korotkoff phases were used to define systolic and diastolic BP, respectively. Height and weight were recorded by a nurse. WC was measured in standing position, using an inelastic tape placed midway between the lowermost rib and iliac crest along the midaxillary line. Standard biological parameters (enzymatic method, using an Hitachi 917 automated analyzer) were measured under fasting conditions. Data on tobacco and alcohol consumption, physical activity, personal medical history and current medications were obtained by self-administered questionnaire. All clinical and biological evaluations, including electrocardiography (ECG), were performed on the same day. The IPC Centre received authorization from the Comité National d'Informatique et des Libertés (CNIL; the French Data Protection Agency) to conduct these analyses. All subjects gave their informed consent at the time of examination.

For each screened subject, vital statistics were obtained from the National Institute of Statistics and Economic Studies (INSEE; institut national de statistiques et d'études économiques, Paris, France). Causes of mortality, taken from death certificates, were provided by the Department of Mortality Studies at the National Institute of Health and Medical Research (Inserm; institut national de la santé et de la recherche médicale, Unit SC8). Causes of death were codified according to the International Classification of Disease (10th revision). Deaths prior to 2002 were recoded using the 10th revision, with CVD-related deaths coded according to Chapter IX (I10 to I82); validation of this procedure has been detailed elsewhere [10]. Based on the results of the validation, a follow-up date of June 2006 was accepted for completion of the entire study population. Subjects who died during the first year of follow-up were excluded. During the mean follow-up of 4.7 ± 1.7 years, a total of 936 deaths (701 men and 235 women) were recorded and, among them, 104 (76 men and 28 women) were due to CVD.

3. Statistical analysis

The characteristics of each WC quintile were compared using the Chi² test, and ARF were defined as follows: hypertension ≥ 140 mmHg and/or ≥ 90 mmHg and/or antihypertensive treatment; diabetes ≥ 1.26 g/L and/or antidiabetic treatment; and raised low-density lipoprotein (LDL) cholesterol ≥ 160 mg/dL [11]. An increased WC was defined as those in the last quintile of WC distribution. Quintiles were also calculated according to gender.

Mortality risk was compared across the following five groups: (1) no risk factors; (2) large WC only; (3) large WC plus one

Table 1
Main clinical and biological characteristics of the study population according to gender.

	Men	Women	All
<i>n</i>	55,800	28,937	84,737
Age (years)	52.1 (8.2)	54.2 (9.1)	52.8 (8.6)
Body mass index (kg/m ²)	25.9 (3.5)	24.5 (4.4)	25.4 (3.9)
Waist circumference (cm)	91.6 (9.9)	78.5 (11.0)	87.1 (10.3)
Cholesterol (g/L)	2.21 (0.4)	2.20 (0.39)	2.21 (0.39)
Glycaemia (g/L)	1.0 (0.02)	0.95 (0.01)	0.99 (0.02)
Triglycerides (g/L)	1.14 (0.7)	0.87 (0.44)	1.05 (0.63)
LDL cholesterol (g/L)	1.41 (0.35)	1.31 (0.35)	1.38 (0.35)
Hypertensives (% [n])	42.8 (23,861)	37.1 (10,748)	40.8 (34,609)
Diabetics (% [n])	4.0 (2256)	2.4 (688)	3.5 (2944)
Elevated LDL cholesterol (% [n])	28.1 (15,674)	19.5 (5629)	25.2 (21,303)
Physical activity (% [n])	46.8 (26,111)	45.3 (13,116)	46.3 (39,227)
Alcohol consumption (% [n]) ^a	19.4 (10,837)	9.4 (2719)	16.0 (13,556)
Tobacco consumption (% [n])	56.2 (31,221)	32.9 (9471)	48.2 (40,692)

Data are expressed as means (\pm SD) unless otherwise specified.

^a More than three glasses/day for men and more than two glasses/day for women.

ARF; (4) large WC plus two other ARF; and (5) large WC plus three other ARF. Those with ARF, but without an increased WC, were not included in the analyses.

As the relationship between WC and other risk factors did not differ between genders for either all-cause or CV mortality (data not shown), mortality analyses were carried out in the overall population. Survival curves were estimated using the Kaplan-Meier method and compared using the log-rank test. Mortality risks (for all-cause and CVD) in each quintile of WC were evaluated using Cox's regression models, including age, gender, tobacco and alcohol consumption, and reported physical activity. Assumption of proportional hazards was verified using Schoenfeld residual plots (data not shown). As all-cause and CVD mortality rates were higher in the first quintile compared

with the second quintile, the latter was used as the reference group. The same models were used to evaluate mortality risks in each WC and ARF group compared with the reference group (no increased WC and no associated risk factors).

Statistical analysis was performed using the SAS statistical software package (version 8.2).

4. Results

Table 1 presents the main characteristics of the study population according to gender, and Table 2 presents the means and distribution of WC and metabolic abnormalities according to WC quintiles. The percentage of subjects with hypertension, diabetes and elevated LDL cholesterol increased from the first WC

Table 2
Population characteristics according to waist-circumference (WC) quintiles.

WC	1st quintile	2nd quintile	3rd quintile	4th quintile	5th quintile
<i>n</i>	17,285	16,386	17,349	16,396	17,321
Men/women	11,234/6051	10,412/5974	12,073/5276	10,831/5565	11,250/6071
Age (years)	50.1 (7.9)	51.7 (8.3)	52.9 (8.4)	54.1 (8.6)	55.1 (8.8)
WC women (cm)	65.8 (2.8)	71.9 (1.5)	76.9 (1.4)	82.7 (2.0)	95.2 (7.6)
WC women (min–max)	40–69	70–74	75–79	80–86	87–136
WC men (cm)	78.5 (4.1)	86.1 (1.4)	90.9 (1.4)	96.2 (1.7)	106.0 (6.1)
WC men (min–max)	49–83	84–88	89–93	94–99	100–139
Hypertensives (% [n])	24.1 (4167)	30.7 (5024)	39.7 (6886)	47.4 (7769)	62.1 (10,763)
Diabetics (% [n])	1.1 (184)	1.5 (242)	2.5 (435)	4.0 (660)	8.2 (1423)
Elevated LDL (% [n])	17.1 (2936)	22.4 (3800)	25.6 (4013)	30.0 (5445)	30.5 (5109)
All-cause mortality (% [n])	0.93 (161)	0.90 (148)	0.97 (169)	1.11 (182)	1.59 (276)
CVD mortality (% [n])	0.12 (20)	0.04 (7)	0.09 (16)	0.15 (24)	0.21 (37)
HR ^a for all-cause mortality	1.17	1	0.92	0.94	1.29
95% CI	0.93–1.46		0.74–1.15	0.76–1.18	1.05–1.59
HR ^b for all-cause mortality	1.18	1	0.93	0.89	1.24
95% CI	0.89–1.55		0.70–1.22	0.67–1.18	0.95–1.62
HR ^a for CVD mortality	3.22	1	1.58	2.51	3.34
95% CI	1.36–7.63		0.64–3.88	1.07–5.86	1.47–7.60
HR ^b for CVD mortality	2.50	1	1.16	1.70	1.44
95% CI	1.09–5.73		0.48–2.82	0.78–3.73	0.66–3.15

Data are presented as means (SD) unless otherwise specified; CVD: cardiovascular disease; HR: hazard ratio.

^a Adjusted for age, gender, tobacco and alcohol consumption, and regular physical activity.

^b Adjusted for age, gender, tobacco and alcohol consumption, regular physical activity, BP, low-density lipoprotein (LDL) cholesterol and glycaemia.

Table 3
Percentage and number of deaths according to increased waist circumference (IWC) and other associated risk factors (ARF).

	No ARF	IWC	IWC + 1 ARF	IWC + 2 ARF	IWC + 3 ARF
<i>n</i>	33,536	4402	8339	3731	280
%	66.7	8.8	16.5	7.4	0.6
All-cause mortality (% [<i>n</i>])	0.53 (178)	0.85 (37)	1.30 (109)	1.50 (56)	4.28 (12)
CVD mortality (% [<i>n</i>])	0.05 (17)	0.05 (2)	0.26 (22)	0.21 (8)	0.71 (2)

CVD: cardiovascular disease.

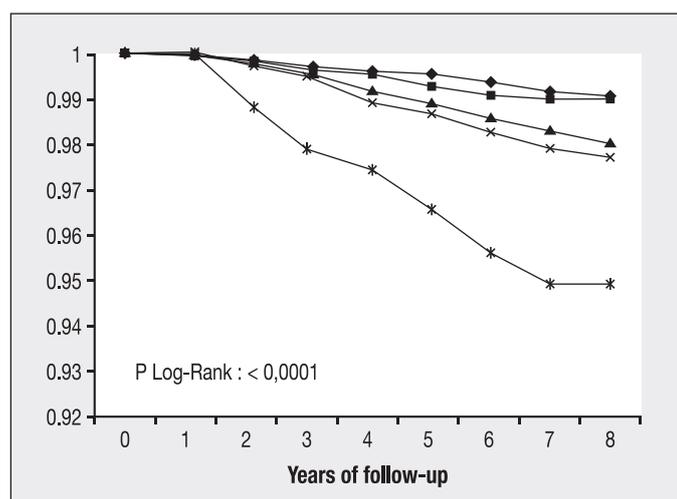


Fig. 1. Survival probability in each quintile of waist circumference (WC).
 —◆— No increased WC and no associated risk factors (ARF). —■— Increased WC, —▲— Increased WC + 1 ARF, —×— Increased WC + 2 ARF, —*— Increased WC + 3 ARF.

quintile to the last (24–62% [$P < 0.0001$], 1–8% [$P < 0.0001$] and 17–31% [$P < 0.0001$], respectively).

The percentage of all-cause mortality was higher in the fourth and fifth WC quintiles than in the first three quintiles. After adjusting for possible confounding factors (Section 2), the risk of all-cause mortality remained significantly higher for those in the last quintile of WC distribution. In addition, the risk of CVD mortality was significantly higher for those in the last two quintiles of WC distribution. Interestingly, the risk of CVD mortality was also significantly higher in the first quintile of WC distribution compared with the second quintile, which was the reference group. After adjusting for LDL, BP and diabetes, the risk of all-cause mortality was similar for each WC group. For CV mortality, excess mortality was observed only in the first group.

Table 3 shows the distribution of the study population in the different groups according to the presence or absence of an increased WC and other ARF. Overall, 20% of the population ($n = 17,321$) had a large WC. Of these, 26.3% had no ARF, 49.8% had one ARF, 22.3% had two ARF and 1.6% had three ARF. Mortality risk increased in each group compared with the reference group. However, when WC was not associated with another risk factor, mortality risk did not differ from the reference group, whereas the percentages of both all-cause and CVD mortality greatly increased in those with a large WC and at least one ARF.

Fig. 1 shows the survival curves for all-cause mortality in each group. Survival probability clearly decreased in the groups with larger WC compared with the reference group (log-rank $P = 0.0001$), and when WC was associated with at least one ARF.

As shown in Fig. 2A, after adjusting for age, gender, tobacco and alcohol consumption, and physical activity, all-cause mortality risk did not increase significantly when only WC increased (hazard ratio [HR]: 1.19 [0.84–1.68]). The risk of all-cause mortality was significantly higher when a large WC was associated with at least one ARF compared with no ARF (from HR = 1.58 [1.26–1.98] for one ARF to HR = 3.70 [2.05–6.68] when WC was associated with three ARF). Similar results were obtained when the waist-to-hip ratio and BMI were considered as anthropometric parameters instead of the WC (data not shown). The analysis also used raised triglycerides (≥ 1.50 g/L) instead of increased LDL cholesterol for lipid evaluations. Subjects with at least one ARF but no increased WC represented 49.5% of the

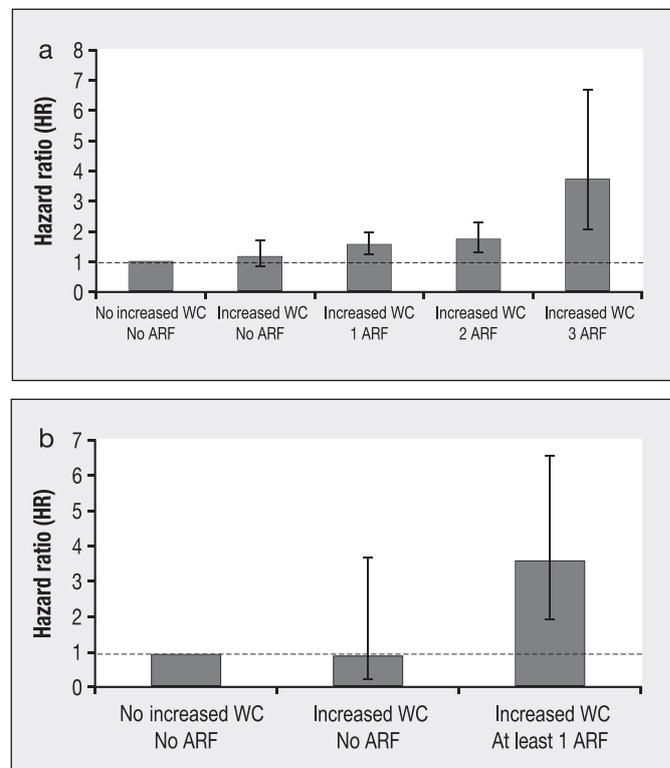


Fig. 2. A. hazard ratios (HR; and 95 CI) for all-cause mortality in each quintile. The reference group included those with no increased WC and no associated risk factors (ARF). B. HR (and 95 CI) for cardiovascular mortality in the first three quintiles. The reference group included subjects with no increased WC and no ARF.

population ($n=41,949$). The risk of all-cause mortality associated with ARF but no increase in WC was 1.36 (1.45–1.60).

Obesity, as determined by BMI, did not influence the relationship between WC and mortality. After adjusting for all risk factors, the risk of mortality associated with an increased WC was 1.35 (0.56–3.31) in the first BMI group ($\text{BMI} < 27 \text{ kg/m}^2$) and 0.75 (0.49–1.17) in the last BMI group ($\geq 27 \text{ kg/m}^2$). Interaction with BMI was not statistically significant.

The impact of ARF on WC and all-cause mortality was also tested using interaction terms in Cox's regression model, but the interaction was not significant (0.94 [0.77–1.15]).

Fig. 2B shows the CVD mortality risk in each group, with similar results. The risk of CVD mortality was no different in those with only an increased WC compared with the reference group (HR: 0.85 [0.19–3.68]). However, a significantly greater CVD mortality risk was observed among subjects with a large WC associated with at least one ARF (HR: 3.56 [2.05–6.57]).

5. Discussion

The present study assessed the role of ARF in the relationship between an increase in abdominal fat mass, as measured by WC, and mortality (both all-cause and CVD) in a large French population. To avoid an arbitrary threshold for an increased WC, the limits of the fifth quintile of WC distribution were chosen to define a large WC. Interestingly, the lower cut off level of the fifth quintile – 87 cm in women and 100 cm in men – did not differ from the thresholds usually considered to be a large WC according to MetS definitions [10]. In the present study, WC was clearly positively and linearly associated with all other ARF. According to this definition, one of the major findings of our study is that an isolated increased WC with no other ARF is not associated with increased mortality risk. These results were confirmed when WC was used as a continuous variable: the significant relationship between WC and mortality disappeared after taking into account all other risk factors. Indeed, this result failed to confirm the independent effect of WC on mortality observed in other populations [12–14]. In the present study population, of the subjects with a large WC, 26% had no ARF and represented 8% of the population. A similar prevalence has been observed in adults in the United States: 23.5% of normal-weight subjects had a cluster of cardiometabolic abnormalities, and 32% of obese subjects had no metabolic abnormalities [15]. This finding was consistent with previous studies [10] suggesting that, of the metabolic abnormalities constituting MetS with lower thresholds for BP and glucose abnormalities, some of the most deleterious effects were observed in the presence of increased WC associated with hyperglycaemia and hypertriglyceridaemia or high BP. However, a recent study by Hong et al. [16] found that WC did not belong to any of the high-risk combinations of MetS components.

Nevertheless, as suggested by a large number of studies, WC measurement is useful for prescreening high-risk subjects [17]. However, this point has not been clearly established. Various factors, such as ethnicity, can influence the observation. Among Asian populations, for example, the most predictive factor for screening high-risk subjects was BP and not WC [18]. Also, the

cutoff point for increased WC used in Caucasian populations is not applicable to Asian populations. In Southeast Asian populations, the degree of obesity was shown to increase the impact of metabolic abnormalities. For a given level of obesity, the prevalence of increased levels of BP, glucose and lipids was greater compared with Caucasian populations [19,20]. In the US population [14], a large WC ($> 102 \text{ cm}$ in men and $> 88 \text{ cm}$ in women) identified those at high risk of CVD. This means that the use of WC as a screening tool needs to take ethnicity into account to properly adjust cutoff points.

Age is another factor that needs to be considered when studying the relationship between WC and mortality. In the elderly, a high WC was associated with a lower mortality rate. According to the results obtained by Dolan et al. [21] in a cohort of women aged > 65 years, those with a BMI of 25–29.9 kg/m^2 had the lowest rates of mortality. In the present study population, due to the small numbers of subjects in this age category and, therefore, of their deaths, it was not possible to evaluate the role of age in the relationship between WC and mortality.

Another limitation of the present study was that ethnicity was not available in our data and could not be taken into account in our analyses. However, even if the threshold of WC were influenced by ethnicity, the relationship of ethnicity with other ARF is as yet unknown. Another factor is that the subjects who underwent a standard health checkup all lived in Paris or its suburbs and had similar lifestyles. Furthermore, the results may also have been influenced by variations in WC measurement despite its standardization. However, Ross et al. [22] have observed that the protocol for WC measurement has no influence on the association between WC and either all-cause or CV mortality.

In conclusion, fat-mass distribution as evaluated by WC is clearly and positively associated with mortality risk when associated with ARF. In a previous study with a longer follow-up (15 years) than in the present study, ARF were found to play a decisive role in the relationship between overweight, as assessed with BMI, and all-cause and CVD mortality [6]. The present study confirms that ARF are also determinants of the relationship between fat-mass distribution (as evaluated by WC) and all-cause and CVD mortality independently of overall fat mass. Thus, according to our study results, WC appears to be a robust parameter for prescreening subjects who are at high risk of diabetes, hypertension or dyslipidaemia. However, in a population with a low-to-moderate mortality risk and whose prevalence of obesity is not increased, the role of WC as a tool for detecting high-risk profiles is not sufficiently discriminating, thereby suggesting that a more global approach towards determining risk, one that includes WC, may be more appropriate.

Conflict of interest statement

No potential conflicts of interest relevant to this article were reported.

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