

# Major Aortopulmonary Collateral Arteries and Their Effects on Perioperative Parameters and Mortality of Children with Tetralogy of Fallot: A Case-control Study

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## What's Known

- Inadequate pulmonary blood flow in the tetralogy of Fallot (TOF) can lead to the development of major aortopulmonary collateral arteries (MAPCAs), interfering with surgical repair.
- Each center has its own treatment method to manage MAPCAs, including conservative management, transcatheter, and surgical ligation. Final decision-making is challenging, and any additional feedback can help the team to do their best.

## What's New

- Closing the medium-sized MPCA in tetralogy patients before surgery might be advantageous by utilizing interventional methods. This approach has the potential to decrease the occurrence of complications both during and after surgery.
- The open MAPCA group had considerably higher blood transfusion volume and ICU stay, which could impact survival and prognosis.

## Abstract

**Background:** Inadequate pulmonary blood flow in tetralogy of Fallot (TOF) can lead to the development of major aortopulmonary collateral arteries (MAPCA), which interferes with surgical repair. The present study evaluated the features of MAPCAs among patients with TOF and their treatment approaches. Besides, perioperative parameters and mortality rates of our TOF patients with and without MAPCA were compared.

**Methods:** This retrospective case-control study was conducted from 2011 to 2020 at Namazi and Shahid Faghihi Hospitals, affiliated with Shiraz University of Medical Sciences, Shiraz, Iran. The significant aspects of MAPCAs, including their quantity, the presence of dual or single supply lung segments, and the employed devices for closure were evaluated. The patients were divided into three groups: TOF patients without MAPCAs as the control group, those with preoperative percutaneous MAPCA closure (Closed MAPCA), and those with small MAPCAs deemed unsuitable for percutaneous closure (Open MAPCA). A comparative analysis, encompassing hospital and surgical data, such as the presence of MAPCA, blood transfusion volume, intubation time, ICU stay, and mortality rates during and post-surgery, was performed among the aforementioned groups. The Chi square, Mann-Whitney, and Kruskal-Wallis tests were used to analyze the data.

**Results:** 59 patients were enrolled, with a mean age of 27.98±24.19 months. The control group included 34 patients with no collaterals, the closed MAPCA group had 12 patients with occluded collaterals, and the open MAPCA group had 13 patients with small collaterals unsuitable for closure. Blood transfusion volume and intensive care unit (ICU) stay were significantly higher in the open MAPCA group than the control group (P=0.01 and P=0.04, respectively). The highest mortality rate was seen in the Iranian Journal of Medical Sciences group (P<0.001).

**Conclusion:** In TOF patients, percutaneous MAPCA closure prior to surgical repair was recommended. This approach could potentially decrease the occurrence of complications both during and post-surgery.

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**Keywords** • Tetralogy of Fallot • Pulmonary circulation • Cardiopulmonary bypass

## Introduction

Tetralogy of Fallot (TOF) is the most prevalent cyanotic congenital cardiac disease, with a wide range of clinical manifestations. In some patients, particularly those with inadequate pulmonary blood flow due to severe right ventricular outflow tract stenosis, patent ductus arteriosus or aortopulmonary, collaterals take blood to the right or left pulmonary arteries or exclusively to certain parts of the lungs to increase arterial saturation as a compensatory mechanism.<sup>1</sup> Delayed surgical repair and subsequent chronic hypoxia might contribute to the further development of collaterals.<sup>2,3</sup>

Major aortopulmonary arteries (MAPCAs) were seen in 3-5% of TOF patients.<sup>2</sup>

Each center follows its own treatment approach to manage MAPCAs, including conservative management, transcatheter, and surgical ligation.<sup>2,4,5</sup> Based on these cases, determining the optimal approach presents a considerable challenge. Understanding the potential post-surgical complications could be beneficial in making a more informed decision.

This study aimed to evaluate the characteristics of MAPCAs and their associated treatment approaches in our institution, as well as to conduct a comparative analysis of perioperative parameters and mortality rates among children diagnosed with TOF, both with and without accompanying MAPCAs, who underwent surgical correction.

## Patients and Methods

This retrospective case-control study was conducted on consecutive pediatric patients under the age of 9 years who underwent total surgical repair of TOF with the transannular patch method from April 2011 to March 2020, at Namazi and Shahid Faghihi Hospitals, affiliated with Shiraz University of Medical Sciences (Shiraz, Iran).

The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1398.301) and conformed to the ethical guidelines of the Declaration of Helsinki (1975) and its later amendments or comparable ethical standards. The procedure was explained to the patient's guardians, and written informed consent was obtained from them before their enrollment.

### *Inclusion and Exclusion Criteria*

TOF patients who were treated using the transannular patch method and had a McGoon ratio of more than 1.8 based on preoperative cardiac catheterization were included in this

study. Patients with preoperative arrhythmias and underlying disorders other than TOF, tetralogy patients with missing pulmonary valves or pulmonary atresia, and those who required unifocalization were excluded from the study.

According to our institution's protocol, all TOF patients underwent cardiac catheterization before surgery. The number of MAPCAs entering the lungs, dual or single supply lung segments, occluding devices used to close them, access points for the occlusion of MAPCAs, and the number of devices used to close MAPCAs were determined.

### *Patients' Groups*

The patients were divided into three groups: TOF patients without MAPCAs as the control group, those with preoperative percutaneous MAPCA closure (Closed MAPCA), and those with small MAPCAs unsuitable for percutaneous closure (Open MAPCA).

### *Control Group*

After selecting the cases, the clinical database of Shiraz University of Medical Sciences (SUMS Clinical Data Base: <https://ped.sums.ac.ir>) was searched for TOF patients to establish a control group based on age, weight, and other relevant factors that matched the case groups.

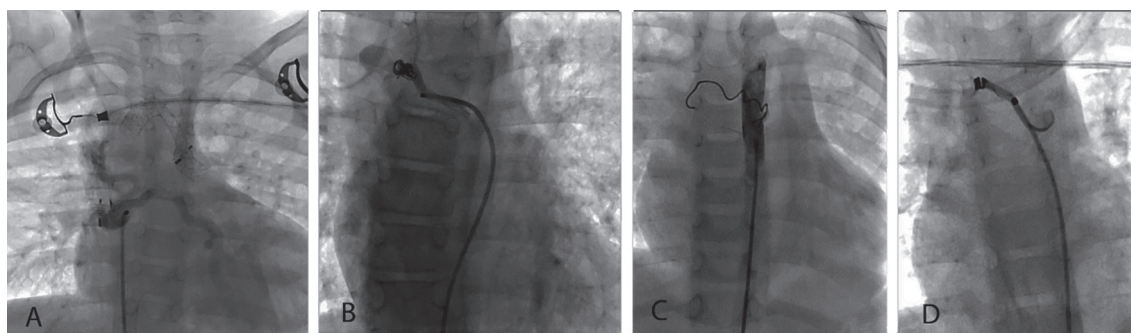
### *Data Gathering*

The three groups were compared based on hospital and surgical data, as well as mortality rates during and after the surgery. In addition, the influence of weight and age on major complications was investigated. The patients were divided into two groups based on their weight (cut-off: 10 Kg) and age (cut-off: 12 months). The data from these groups were compared without considering the MAPCA status. The necessary information regarding patients in the hospital, including data on cardiopulmonary bypass time, aortic cross-clamp time, blood transfusion volume, intubation time, and length of ICU and hospital stays, were systematically documented.

### *MAPCA Closure Strategy*

In the studied Centers, MAPCA closure was performed percutaneously using different types of ductus arteriosus closure coils, ductus arteriosus or ventricular septal defect Amplatzer, or vascular plugs (figure 1). If the diameter of the MAPCA was smaller than 4 mm, coils were used for closure; otherwise, other occluders were used.

If the lung segments had dual supply and if a catheter with a diameter of at least 5 French could be inserted into the MAPCAs, MAPCA



**Figure 1:** Four patients whose MAPCAs were closed using four different types of devices. A: MAPCA closure with perimembranous ventricular septal defect Amplatzer (Abbott Cardiovascular, MN, USA); B: MAPCA closure with Nit-Occlud PFM coil (PFM Medical, Cologne, Germany); C: MAPCA closure with Gianturco coil (William Cook, from Bjaeverskov, Denmark); D: MAPCA closure with MReye Flipper coil (Cook Medical, USA)

closure was performed. Otherwise, these small collaterals were avoided to be closed (figure 2). The femoral or axillary arteries served as the access point for MAPCA closure.

#### Statistical Analysis

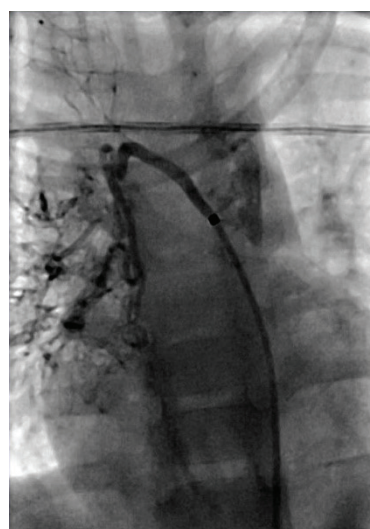
The data were analyzed using IBM SPSS software, version 21.0 (SPSS Inc., Chicago, IL, USA).

According to the Kolmogorov-Smirnov normality results, the Chi square, Mann-Whitney, and Kruskal-Wallis non-parametric tests were used. In addition, *post hoc* Bonferroni correction analysis was used to determine the differences between the groups. The descriptive results were expressed as mean±SD, median, and interquartile range.  $P < 0.05$  was considered statistically significant.

#### Results

This study enrolled 59 patients with a mean age of  $27.98 \pm 24.19$  months (5–110 months). According to the demographic findings, 57% of the patients were boys, and 43% were girls. The age of 18 patients (30.50%) were under the age of 12 months, and 41 patients (69.50%) were older than 12 months. The weight of 30 patients (50.87%) was less than 10 Kg, and the rest were  $> 10$  Kg.

The control group included 34 patients (57.50%), the second group included 12 patients (20.50%) who underwent MAPCA closure, and the third group included 13 patients (22%) who had small MAPCAs that were not eligible for closure. Different variables, including age, weight, blood transfusion volume, cardiopulmonary bypass time, aortic cross-clamp time, intubation time, and PICU stay among the surviving patients of the three groups were compared, and the results are presented in table 1. Patients who died in the hospital were excluded from the data presented table 1. Therefore, only hospital data were compared. There were no significant



**Figure 2:** The contrast was administered into the right lung through the MAPCA using the right Judkins. Following contrast injection, the size of the vessel and its arborization were assessed.

differences between the three groups in terms of weight, age, and other demographic variables.

Blood transfusion volume was significantly higher in the open MAPCA group ( $P = 0.01$ ; table 1). The duration of ICU stay was longer in the open MAPCA group than in the other two groups ( $P = 0.04$ ).

With regard to blood transfusion volume, the groups were compared using Bonferroni's corrected analysis, which revealed significant differences between the closed MAPCA group and the open MAPCA group ( $P = 0.03$ ), and also the control group and the open MAPCA group ( $P = 0.01$ ). Furthermore, this analysis was performed based on ICU stay days. There were significant differences between the control group and the closed MAPCA group, as well as the control group and the open MAPCA group ( $P = 0.04$  and  $P = 0.03$ , respectively).

Twelve patients in the closed MAPCA group had 17 MAPCAs occluded with the devices (14 MAPCAs with one device and three with two devices).

**Table 1:** Demographic and surgical data of surviving patients in three groups

Characteristics of the MAPCA groups	No MAPCA (n=32) Median (IQR)	Closed MAPCA (n=11) Median (IQR)	Open MAPCA (n=9) Median (IQR)	Total (n=52) Median (IQR)	P value
Age (months)	16.0 (19.5)	36.0 (24)	18.0 (16)	18.5 (22.5)	0.05
Weight (Kg)	10.0 (5.5)	11.5 (4)	10.0 (2.8)	10.0 (3.6)	0.16
Blood transfusion volume (cc/Kg)	25.0 (15.5)	17.5 (20.3)	43.2 (35)	25.0 (21)	0.01
Intubation time (hours)	14.5 (5.8)	17.0 (6)	19.5 (9.8)	15.0 (7)	0.43
ICU stay (days)	4.0 (2)	5.0 (2)	7.62 (2.5)	4.9 (2.1)	0.04
Cardio-pulmonary bypass time (min)	90.01 (34.3)	85.53 (45)	93.00 (42.5)	90.00 (32.8)	0.16
Aortic cross-clamp time (min)	54.75 (40.8)	51.50 (44)	70.00 (57.5)	59.00 (42.8)	0.23

ICU: Intensive care unit; IQR: Interquartile range; MAPCA: Major aortopulmonary collateral artery. P<0.05 was considered statistically significant. The Kruskal-Wallis test was used. Patients who died in the hospital were excluded. Therefore, the number of these patients is less than that in each group.

**Table 2:** Details on MAPCA anatomy and device closure in the second group of patients with 17 MAPCAs

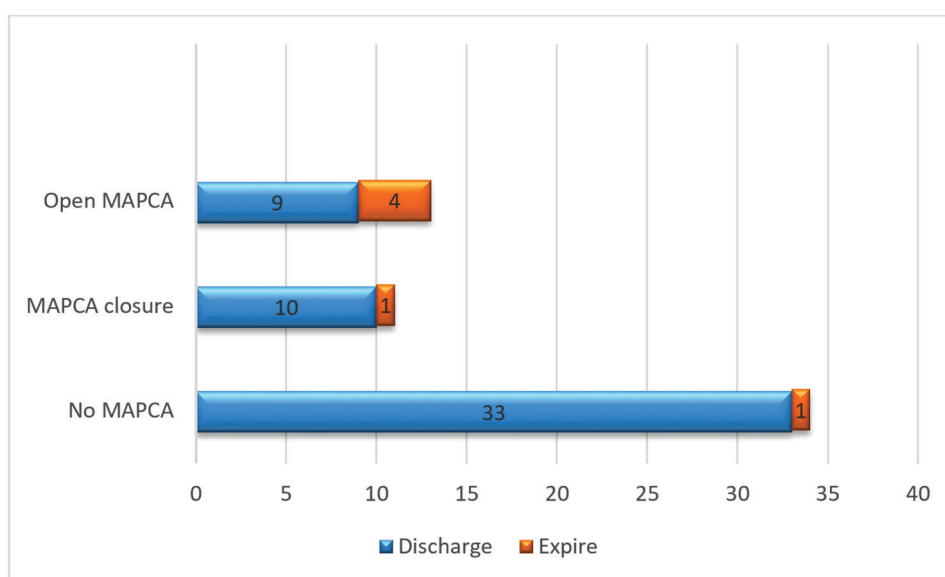
Variables	Type	N (%)
Connection of MAPCA to the Hilum and lung segments	No	6 (35.3%)
	Yes	10 (58.8%)
	Both	1 (5.9%)
Dual supply lung segments	No	3 (17.6%)
	Yes	14 (82.4%)
Number of devices to close MAPCA	1	14 (82.4%)
	2	3 (17.6%)
Access points	Axillary artery	4 (23.5%)
	Femoral artery	13 (76.4%)

MAPCA: Major aortopulmonary collateral arteries

The access points were selected based on axillary or femoral access points and according to MAPCA anatomy. Table 2 provides a detailed description of the MAPCAs in the closed MAPCA group.

The mortality rate of patients due to cardiac causes is presented in figure 3 and table 3. The third group (open MAPCA) had the highest mortality rate of 30.8% with a significant difference (P<0.001).

To assess the role of weight during heart cardiac surgery, the Mann-Whitney test was used to compare the perioperative data between two groups of children (below and above 10 Kg of weight). As indicated in table 4, there was a significant inverse relationship between lower weight and blood transfusion volume, duration of intubation, and ICU stay. The mean blood transfusion volume and intubation time in patients under 10 Kg were almost twice as much as in patients above 10 Kg.



**Figure 3:** This figure shows the comparison of the mortality rate between the three groups, which was more prevalent in the open MAPCA group (P<0.001).

**Table 3:** Characteristics of significant statistical data of each deceased patient in three groups

Groups	Control group	Closed MAPCA	Open MAPCA	P value
Number	1	1	1	<0.001
Blood transfusion volume during admission (cc/Kg)	20	10	0	25
ICU stay time (days)	12	0	0	0

ICU: Intensive care unit; MAPCA: Major aortopulmonary collateral artery; Chi-Square test was used; P<0.05 was considered statistically significant.

**Table 4:** Hospital data of patients based on weight (cut-off: 10 Kg) and age (cut-off: 12 months)

Characteristics	Weight	Mean±SD	P value	Age	Mean±SD	P value
Blood transfusion volume (cc/Kg)	<10 Kg	31.02±37.70	0.02	<12month	30.88±37.52	0.63
	≥10 Kg	15.88±12.86		≥12month	17.12±17.39	
Anesthesia time (hours)	<10 Kg	4.39±0.95	0.95	<12month	4.31±0.90	0.21
	≥10 Kg	4.45±0.52		≥12month	4.65±0.67	
Intubation time (hour)	<10 Kg	29.26±38.87	0.01	<12month	24.80±32.21	0.42
	≥10 Kg	13.04±4.86		≥12month	25.40±39.67	
ICU stay (days)	<10 Kg	6.08±4.15	0.07	<12month	5.58±4.00	0.78
	≥10 Kg	4.29±2.43		≥12month	5.67±3.51	
Pump time (minutes)	<10 Kg	90.14±29.50	0.88	<12month	89.79±28.00	0.27
	≥10 Kg	83.31±25.25		≥12month	84.59±29.79	
Aortic cross-clamp time (minutes)	<10 Kg	61.86±25.34	0.43	<12month	60.31±24.20	0.19
	≥10 Kg	56.88±25.50		≥12month	58.28±76.12	

The significance level was set at P<0.05, using the Mann-Whitney test.

In addition, the sample was divided into groups, including under 12 months and over 12 months, weighing less than 10 Kg and more than 10 Kg. The comparison of perioperative data indicated no significant difference between the groups, except for greater volume of blood transfusion and longer intubation time in patients weighing less than 10 Kg (table 4).

## Discussion

Due to low pulmonary blood flow, TOF patients develop compensatory mechanisms such as MAPCA to enhance oxygen saturation.

The findings of the present study indicated that TOF patients with open MAPCA had more complications and mortality rates during and after surgical correction, necessitating more advanced ICU care and a multidisciplinary approach. The blood transfusion volume, as a critical hemodynamic index, and ICU stay length were crucial factors in the studied patients.

High-flow vessels can exacerbate perioperative complications in patients with dual-supply lung segments due to pulmonary edema. Hence, the intraoperative complications and postoperative pulmonary edema could be avoided by making the right decision about MAPCA closure before surgery.<sup>6-8</sup>

MAPCAs cause complications during and after surgical repair. Blood flow in MAPCAs might be challenging during cardiopulmonary bypass, potentially leading to unpredictable

consequences. It might interfere with keeping the operative field clean and dry. Surgical closure of MAPCAs is performed before TOF surgery, while percutaneous closure is a suitable alternative.<sup>3</sup>

The surgical closure approach is demanding due to the difficulty of finding the exact location of MAPCAs, extensive surgery, tissue damage, excessive blood loss, and prolonged operation time. The percutaneous closure approach has limitations, such as the lack of access to MAPCAs, finding a suitable landing area for the devices, and the inability to insert the devices into the MAPCA. Additionally, occlusion might decrease oxygen saturation preoperatively in extremely cyanotic patients with large MAPCAs.<sup>2,4</sup>

Percutaneous closure of MAPCAs is now an acceptable alternative before surgical repair, and several Amplatzer, plugs, and coils can be utilized as off-label devices.<sup>1, 9</sup> However, determining whether to intervene is challenging due to the potential complications associated with the desaturation of the patients in the days before surgery. Sadiq and colleagues showed that patients after percutaneous MAPCA occlusion had a smooth surgical and postoperative recovery. However, two patients desaturated significantly after coiling and required urgent surgery.<sup>2</sup> Furthermore, some cases had multiple small collaterals unsuitable for closing, while their sum diameters were large enough to endanger the perioperative situation.

The present study focused on early postoperative mortality from cardiac causes,

which might be caused by etiologies, such as excessive blood return to the heart during surgery, which could obscure the surgical field and interfere with the surgeon's vision. Furthermore, postoperative pulmonary hemorrhage might pose a potential risk to the patients. The findings of the present study indicated that patients with collaterals who did not fulfill the criteria for closure (Open MAPCA group) had the highest mortality rate. Another study reported that MAPCA was a mortality risk factor after surgical correction of severe TOF.<sup>10</sup> Although that study evaluated other factors such as age, RV/LV size ratio, and ventricular septal defect size, the present study focused on hemodynamic parameters.

Several studies stated that the existence of MAPCAs during cardiopulmonary bypass surgery could cause blood loss, potentially leading to hypoperfusion of other organs.<sup>2, 11, 12</sup> Some studies showed that open MAPCA required more blood volumes of blood transfusion and longer ICU stays, which could be attributed to prolonged pump time, or lung hyperperfusion.<sup>12-14</sup> To evaluate this aspect in the present study, we focused on the volume of blood transfusion, which was the best quantitative factor. The open MAPCA group required more blood transfusion volume and was more exposed to blood transfusion complications. However, it was not possible to follow the hemodynamic sequence of organ hypoperfusion based on changes in GFR, serum creatinine, and liver function tests.

According to the findings of the present study, the patients with open MAPCAs had a significantly longer ICU stay and experienced more post-operative complications than the other two groups. These findings might indicate the negative effect of open MAPCAs on the hemodynamics status of tetralogy patients.

In some studies, the median time of postoperative mechanical ventilation after TOF total repair varied from 6 to 48 hours, with a median length of PICU stay of 3-6 days.<sup>14-16</sup> The median ICU stay among the patients of the present study was 5.5 days, and the median duration of mechanical ventilation was 17 hours. These findings were consistent with other studies on ICU care for complicated congenital heart surgery. However, no exact relationship was found between the prolongation of intubation time and the presence of open MAPCA. The PICU Man strategies for weaning of mechanical intubation were varied, and no definite protocol existed.

In other studies, weight was one of the factors influencing the incidence of major complications in tetralogy.<sup>13, 17</sup> The present study found that children weighing less than 10 Kg received almost twice as much blood transfusion volume

as children who weighed more and experienced longer intubation and ICU stays.

Another prominent factor influencing the incidence of major complications might be the patient's age at the time of surgery. There was no significant relationship between the two groups above and below 12 months in the entire sample with and without MAPCA, which contradicted the findings of other previous studies.<sup>13, 14</sup>

Previous studies revealed that most MAPCAs originate from descending aorta and subclavian arteries. However, they might also originate from the cervical vessels,<sup>18</sup> abdominal aorta, and coronary arteries, and differentiation of the MAPCAs might be mistaken for ductus arteriosus.<sup>13, 19</sup> Most TOF patients have normally arborized central pulmonary arteries, and none of the lung segments get blood supply exclusively from the MAPCAs; however, this is not always the case. Some arteries originate from MAPCAs, and some segments have dual supply. If some lung segments lack a dual blood supply and are supplied only by the MAPCA sources, the MAPCA should not be closed, and unifocalization should be performed.<sup>20-22</sup>

As a limitation of the present study, all hemodynamic aspects of MAPCAs, such as pulmonary overflow and pneumonia after operation among the three groups of patients were not evaluated. Moreover, this study was retrospective. Therefore, prospective studies with larger cohorts are recommended.

## Conclusion

If TOF patients have occluded MAPCAs, their lung segments will have a double blood supply, and the MAPCA's diameter will be large enough. In that case, it is recommended that all efforts be made to close the MAPCAs before performing TOF repair. This approach aimed to enhance the success and quality of the operation and reduce the patients' mortality rate.

Although the findings of the present study demonstrated some important surgical and hospital outcomes for TOF patients with and without MAPCA, doing meta-analysis studies in this field and comparing the results of several studies will improve the reliability of the data.

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### Authors' Contribution

M.E: Design and conception of the Study and writing the manuscript; A.N: Design the Study, Corresponding author, contributed to writing the manuscript; H.A: Analysis and interpretation of data, echocardiography of the patients; K.K: Data collection, Manuscript revision; N.M: Data collection, analysis, and interpretation of data, participation in writing and H.M: Data gathering, drafting the work, critical revision. All authors have reviewed and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Conflict of Interest:** None declared.

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