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Research article

Clinical utility of resected pancreatic volume ratio calculation for predicting postoperative new-onset diabetes mellitus after distal pancreatectomy-a propensity-matched analysis

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ABSTRACT

Background: Limited literature is available on new-onset diabetes mellitus (NODM) after distal pancreatectomy. This study aimed to investigate the correlation between surgery-related factors and the incidence of NODM after distal pancreatectomy.
Methods: Patients were divided into the NODM-positive or NODM-negative group according to the diagnosis of NODM. After propensity score matching, the correlation between operation-related factors and the incidence of NODM was analyzed. The diagnostic threshold for predicting NODM was determined using the receiver operating characteristic (ROC) curve and the Youden index.
Results: No significant correlation was observed between the NODM incidence after distal pancreatectomy and operative blood loss, spleen preservation, surgical method (open or laparoscopy), postoperative ALB and HB (first day after surgery), and postoperative pathology. However, a significant correlation was found between the NODM incidence and the postoperative pancreatic volume or the resected pancreatic volume ratio. Resected pancreatic volume ratio was identified as a predictive risk factor for NODM. Youden index of the ROC curve was 0.548, with a cut off value of 32.05% for resected pancreatic volume ratio. The sensitivity and specificity of the cut off values were 0.952 and 0.595, respectively.
Conclusions: This study demonstrated that the volume ratio of pancreatic resection is a risk factor for the incidence of NODM after distal pancreatectomy. This can be used to predict the incidence of NODM and may have further clinical applications.

1. Introduction

Distal pancreatectomy is often performed for benign and malignant tumors located in the pancreatic body and tail of the pancreas [1,2]. The resection of a large amount of pancreatic tissue may greatly affect pancreatic endocrine and exocrine functions [3–5]. The incidence of diabetes mellitus (DM) after distal pancreatectomy was reported to reach a proportion of 5–42% [6]. Surgeons have developed various pancreatectomy procedures including local tumour resection and midsection pancreatectomy to preserve a more

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Abbreviations

NODM	new-onset diabetes mellitus
DM	diabetes mellitus
FBG	fasting blood glucose
IFG	impaired fasting glucose
ALB	Albumin
HB	hemochrome
BMI	body mass index
OR	Odds ratio
CI	confidence interval
SD	standard deviations

normal pancreatic volume for benign or low-grade pancreatic tumors [7–9].

Many studies have focused on the association between pancreatic volume and diabetes. Some studies have found that the pancreas is small and irregularly shaped in patients with type 2 diabetes [10]. The pancreatic volume also decreases in patients within the first year of being diagnosed with type 1 diabetes [11,12]. Several studies have suggested a positive relationship between diabetes and pancreatic volume reduction.

For distal pancreatectomy, the resected pancreatic volume ratio depends on the location and size of the tumour and the surgeon's grasp of the cutting line during surgery. A previous study found that above 44% resected pancreatic volume after distal pancreatectomy was an independent risk factor for new-onset DM (NODM) but the cutoff value of resected pancreatic volume to predict NODM was not assessed [13]. Therefore, we performed a propensity-matched analysis to study the correlation between operation-related factors and the incidence of NODM, and further indentify the cut-off value of resected pancreatic volume ratio to predict NODM after distal pancreatectomy.

2. Methods

2.1. Ethical compliance

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Sir Run Run Shaw Hospital committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This

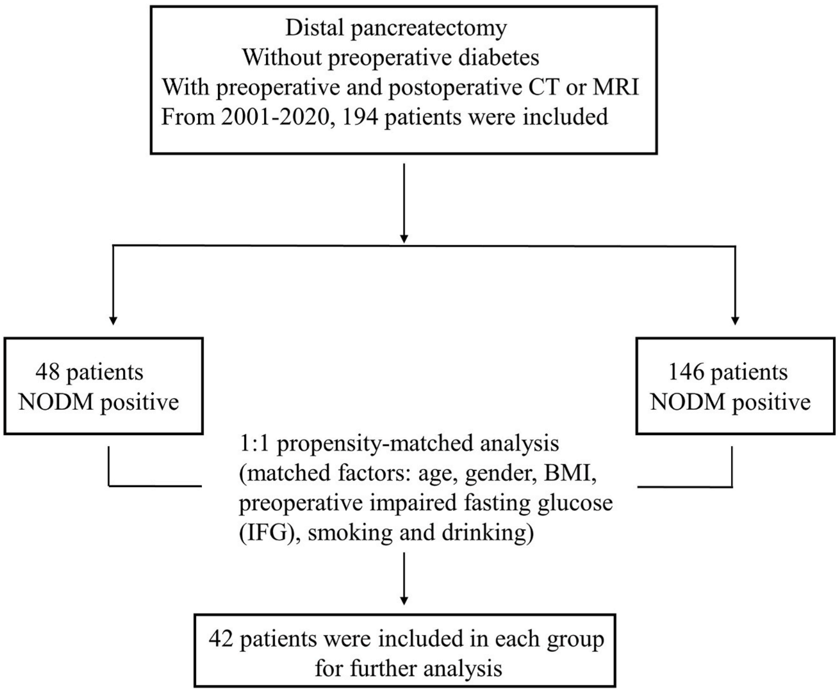

Fig. 1. Flow chart of patient selection.

study was also approved by the Sir Run Run Shaw Hospital Committee (2022-459-01).

2.2. Endocrine function evaluation

The endocrine function was evaluated by measuring fasting blood glucose (FBG) or serum HbA1c levels, according to the American Diabetes Association guidelines. Patients with FBG $\geq$ 7.0 or HbA1c $\geq$ 6.5% were diagnosed as NODM positive. FBG measurements were performed on the 1st, 3rd, 5th and 14th day after surgery. Patients with elevated FBG levels may require HbA1c measurement. The diagnosis time was also included in the follow-up period from 2 weeks to 12 months after surgery.

2.3. Patients and propensity matching

A total of 194 patients without DM who underwent distal pancreatectomy at the Run Run Shaw Hospital between 2001 and 2020 were enrolled. Of these, 48 patients were diagnosed as NODM positive and 146 patients were diagnosed as NODM negative. Baseline demographic characteristics including age, sex, body mass index (BMI), preoperative impaired fasting glucose (IFG), smoking and drinking were collected. Surgery-related factors included operative blood loss, preservation of the spleen, surgical method (open or laparoscopy), postoperative ALB and HB (first day after surgery), postoperative pathology and postoperative pancreatic volume and the resected pancreatic volume ratio. Major factors in demographic characteristics were used to match 1:1 as many patients in these two groups as possible. These factors included age, sex, BMI, IFG, smoking status, and drinking status. Further, 42 patients were included in each group (Fig. 1).

2.4. Pancreatic volume evaluation

1.25-mm-thick or 2-mm-thick computed tomography (CT) images were obtained preoperatively in 1 month and postoperatively in 3 months from each patient. The boundary of the pancreas excluding the vessels and tumors in each CT image was discussed and drawn by two professional doctors. After finishing the definition of the pancreatic boundary for all CT images from one patient (Fig. S1a), 3D reconstruction of the pancreas was automatically formed by the reconstruction software-United Imaging (Fig. S1b). The resected pancreatic volume ratio was calculated as [(preoperative pancreatic volume − postoperative pancreatic volume)/preoperative pancreatic volume]*100 (%).

2.5. Statistical analysis

Matchlt packages in R programming language was used for propensity-matching with detailed parameters: “nearest, ratio = 1, caliper = 0.2”, replace = FALSE. Chi-square or Fisher’s exact test were used to compare proportions between groups. Continuous data were analyzed using T-tests for means. Binary logistic regression models were used to assess the associations and risk factors for postoperative NODM development. Odds ratios (ORs) and 95% confidence intervals (CIs) were also determined. The diagnostic threshold was determined by the ROC curve and Youden index. Data are presented as means and standard deviations (SD), medians and ranges, or numbers and percentages (%). All statistical tests were two-sided with significance set at $P < 0.050$.

3. Results

3.1. Baseline demographic characteristics

The NODM-positive and NODM-negative groups had 48 and 146 patients, respectively. No significant difference was observed in the proportion of male patients between NODM positive group and NODM negative groups (43.8% vs. 37.0%, $P = 0.404$), Further, no significant difference was also observed in the proportion of smokers (12.5% vs. 15.8%, $P = 0.583$) and drinkers (12.5 vs. 8.2%, $P = 0.375$). The age (58.0 ± 12.9 years vs. 51.9 ± 15.2 years, $P = 0.013$), BMI (24.5 ± 3.6 kg/m^2 vs. 22.7 ± 3.0 kg/m^2, $P = 0.001$) and proportion of IFG (43.8% vs. 15.8%, $P < 0.001$) were significantly higher in the NODM positive group compared with those in the NODM negative group (Table 1). Furthermore, 42 patients were included in each group during propensity score matching. The general

Table 1
Baseline demographic characteristics.

Group	0	1	*P*-value
Number	146	48	
Gender = Male (%)	54 (37.0)	21 (43.8)	0.404
Age (mean (SD))	51.9 (15.2)	58.0 (12.9)	**0.013**
BMI (mean (SD))	22.7 (3.0)	24.5 (3.6)	**0.001**
IFG = N (%)	23 (15.8)	21 (43.8)	**<0.001**
Smoking = + (%)	23(15.8)	6 (12.5)	0.583
Drinking = + (%)	12 (8.2)	6 (12.5)	0.375

Group (1: NODM positive; 0: NODM negative); NODM: new-onset diabetes mellitus; IFG: impaired fasting glucose (Continuous data were analyzed using T-tests for means and Chi-square test were used to compare proportions).

characteristics of the two matched groups are presented in Table 2.

3.2. Comparison of operation-related factors in NODM-positive and NODM-negative groups

Comparisons of surgery-related factors between the two groups are presented in Table 3. There were no significant differences in operative blood loss, spleen preservation, surgical methods (open or laparoscopy), postoperative ALB and HB levels (first day after surgery) and postoperative pathology. Although no significant difference was observed in the preoperative pancreatic volume between the two groups (69.1 ml ± 24.1 ml vs. 63.0 ml ± 21.9 ml, $P = 0.227$), but the postoperative pancreatic volume in the NODM positive group was significantly less than that in the NODM negative group (33.5 ml ± 15.5 ml vs. 45.4 ± 19.5, $P = 0.003$). Furthermore, the proportion of pancreatic resection in the NODM positive group was significantly higher than that in the NODM negative group (52.1% ± 13.8% vs. 27.6% ± 17.3%, $P < 0.001$).

The distribution of the resected pancreatic volume ratios is shown in Fig. S2a. The comparison between the average resected pancreatic volume ratios of the NODM positive group and the NODM negative group is depicted in Fig. S2b. Preoperative pancreatic volume distribution and postoperative pancreatic volume distribution are shown in Fig. S3a and Fig. S3c. The comparison between the average preoperative pancreatic volume of the NODM positive group and the NODM negative group is shown in Fig. S2b. The comparison between the average postoperative pancreatic volume of the NODM positive group and the NODM negative group is shown in Fig. S2d.

3.3. Relationship between resected pancreatic volume ratio and NODM after distal pancreatectomy

All operation-related indicators, preoperative volume and resected pancreatic volume ratios were included in the binary logistic regression models. Postoperative pancreatic volume and resected pancreatic volume ratio were strongly correlated, and hence we only included resected pancreatic volume ratio in the analysis, potentially eliminating the individual differences of absolute value. The relationship between these factors and the risk of NODM is shown in Table 4. The results suggested that the resected pancreatic volume ratio and the risk of NODM were significantly related ($P < 0.0001$), whereas other factors were not significantly correlated. Further, the OR value of NODM after distal pancreatectomy was 1.112 when the resected pancreatic volume ratio increased by 1%.

The sensitivity and specificity of application of the resected pancreatic volume ratio in the diagnosis of NODM after distal pancreatectomy were analyzed using ROC curves (Fig. 2). Youden index was 0.548 with a cut-off value of 32.05% for resected pancreatic volume ratio. The sensitivity and specificity for NODM after distal pancreatectomy was 0.952 and 0.595, respectively.

3.4. Clinical application of the research finding

For tumors located in the body of the pancreas, surgeons have proposed a midsection pancreatectomy instead of a distal pancreatectomy to preserve the normal pancreatic volume as much as possible, however the possibility of complications may increase. Creating a screening method to select patients with high risk of postoperative NODM for distal pancreatectomy and a low risk of postoperative NODM for mid-section pancreatectomy is meaningful. Based on our research results, we proposed a promising screening method according to our research results. It also relies on 3D reconstruction and simulated resection using a computer-based analysis before the surgery (Fig. 3). It may be applicable to the resection of benign pancreatic lesions. For malignant tumors, a formal distal pancreatectomy, with splenectomy and a correct lymphadenectomy is still necessary.

4. Discussion

4.1. Operation-related factors and NODM

The incidence of NODM following distal pancreatectomy was reported to range from 5 to 42% [6], the incidence in the present study was 24.7% (48/194). The time to NODM development may range from the immediate postoperative period to up to 5 years postoperatively [14]. DM remains one of the main long-term complications of distal pancreatectomy [15,16]. In this study, we collected and matched the basic demographic characteristics of these patients to determine the correlation between operation-related

Table 2
Baseline demographic characteristics after 1:1 propensity-matched analysis.

Group	0	1	*P*-value
Number	42	42	
Gender = Male (%)	19 (45.2)	18 (42.9)	0.826
Age (mean (SD))	59.33 (13.19)	57.29 (13.29)	0.480
BMI (mean (SD))	23.56 (2.82)	23.95 (3.50)	0.575
IFG = N (%)	15 (35.7)	15 (35.7)	1
Smoking = + (%)	6 (14.3)	5 (11.9)	0.746
Drinking = + (%)	6 (14.3)	4 (9.5)	0.736

Group (1: NODM positive; 0: NODM negative); NODM: new-onset diabetes mellitus; IFG: impaired fasting glucose (Continuous data were analyzed using T-tests for means and Chi-square test were used to compare proportions).

Table 3
Comparisons of operation-related factors in the two groups.

Group	0	1	*P*-value
Number	42	42	
PV-pre (mean (SD))	63.0 (21.9)	69.1 (24.1)	0.227
PV-post (mean (SD))	45.4 (19.5)	33.5 (15.5)	**0.003**
PV resected- rate % (mean (SD))	27.6 (17.3)	52.1 (13.8)	**<0.001**
ALB (mean (SD), g/L)	33.0 (3.3)	33.1 (4.0)	0.95
HB (mean (SD), g/L)	114 (15)	118 (16)	0.278
Blood loss (mean (SD))	290.0 (334.8)	224.4 (194.8)	0.29
Splenectomy = + (%)	29 (69.1)	28 (66.7)	0.815
Open = + (%)	7 (16.7)	6 (14.3)	0.763
Pathology = Malignant (%)	19 (45.2)	18 (42.9)	0.826

Group (1: NODM positive; 0: NODM negative); NODM: new-onset diabetes mellitus.
PV: pancreas volume (Continuous data were analyzed using T-tests for means and Chi-square test were used to compare proportions).

Table 4
Result of binary logistic regression for risk factor analysis in NODM.

	OR	OR(95%CI)	*P*-value
PV-pre (1 ml)	1.025	1.025(0.993, 1.057)	0.124
PV resected- rate (1%)	1.112	1.112(1.061, 1.165)	**<0.0001**
Pathology (malignant)	0.984	0.984(0.24, 4.041)	0.982
HB (10 g/L)	1.094	1.094(0.65, 1.841)	0.736
ALB (1 g/L)	1.023	1.023(0.836, 1.252)	0.824
Blood loss (1 ml)	0.998	0.998(0.995, 1.001)	0.111
Splenectomy (positive)	0.351	0.351(0.068, 1.8)	0.209
surgical method (open)	0.882	0.882(0.121, 6.422)	0.901

NODM: new-onset diabetes mellitus; PV: pancreas volume; OR: Odd Ratio.

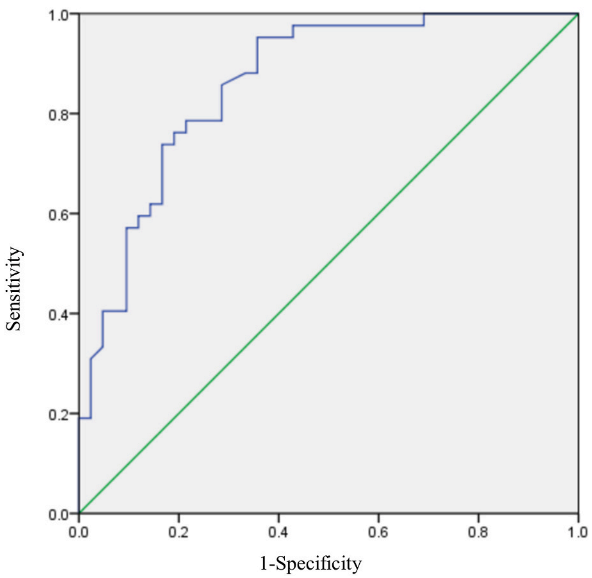

Fig. 2. The receiver operating characteristic curve of resected pancreatic volume ratio. The cut-off value of resected pancreatic volume ratio was 32.05% with a sensitivity of 95.2% and a specificity of 59.5%.

factors and NODM. A previous study reported that surgical blood loss and splenectomy were independent risk factors for NODM [17]. In our study we found that operation-related factors such as operative blood loss, preservation of the spleen, surgical method (open or laparoscopic), postoperative ALB and HB (first day after surgery) and postoperative pathology were not correlated with NODM. However, postoperative pancreatic volume and resected pancreatic volume ratio were significantly correlated with NODM. The multivariate regression analysis revealed that the resected pancreatic volume ratio could better predict the risk of NODM.

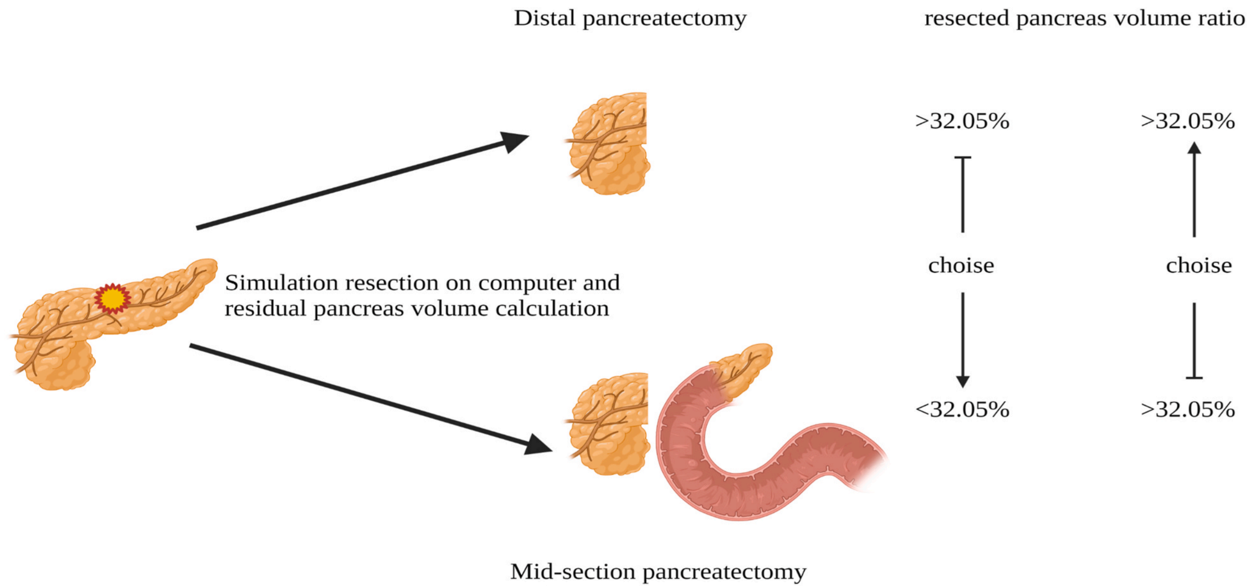

Fig. 3. Preoperative surgical choice based on the preoperative simulated resection for patients.

4.2. Resected pancreatic volume ratio and the risk of NODM

Owing to the development of three-dimensional reconstruction technology, the process and results of some surgical resections can be well simulated on a computer [18–21]. Through 3D computer reconstruction, the volume and proportion of the removed pancreas can be calculated preoperatively using a predetermined simulated resection. According to the present study, when the resection ratio was 32.05%, both the sensitivity and specificity of postoperative NODM can reached a relatively high level. Therefore, we used a simulated resection volume ratio exceeding 32.05% as the critical value to predict a high risk of postoperative diabetes. Using the resected pancreatic volume ratio to predict the possibility of postoperative diabetes would be valuable for clinical applications. Besides, the results also showed that the resected pancreatic volume ratio increased by 1%, and the OR value of NODM after distal pancreatectomy was 1.112. This reinforces the importance of preserving normal pancreatic tissue as much as possible.

In some cases of distal pancreatectomy, lesions are located in the body of the pancreas, and they may not be large, however, distal pancreatectomy may remove the body and tail of the pancreas simultaneously, resulting in a large loss of pancreatic tissue. Therefore, middle pancreatic resection has been proposed to better preserve some normal tissues of the distal pancreas. Considering that mid-section pancreatectomy may be more complex and may cause more complications [7,22–24], there is no standard method to distinguish whether a patient will benefit from midsection pancreatectomy over distal pancreatectomy. The conclusions of the present study can be applied as standards for NODM risk evaluation. Preoperative simulation resection is commonly used in hepatectomy to calculate the residual liver volume [25,26]. The ratio of the resected pancreas can also be calculated based on preoperative simulated resection on a computer. For the pre-resection of the mid-pancreatic tumour on the computer, the tangent line of the tumor resection was set to at least 1 cm. If the resected volume ratio of mid-section pancreatectomy is significantly less than 32.05% but the resected volume ratio of distal resection is significantly greater than 32.05%, it is considered that these patients will benefit from mid-pancreatic surgery in decreasing the risk of NODM. However, if the resected volume ratio is greater than 32.05% in both mid-section resection and distal resection, we believe that mid-pancreatic resection will not bring significant long-term benefits to the patient, at least for NODM incidence, but it may increase the risk of short-term complications. Hence, we believe that distal pancreatectomy is more suitable for these patients. It may be applicable to the resection of benign pancreatic lesions. For malignant tumors, a formal distal pancreatectomy, with splenectomy and a correct lymphadenectomy is still necessary. This also needs to be verified in further studies.

5. Limitations

This study has some limitations. First, our research object only included patients who underwent distal pancreatectomy but lacked patients who underwent pancreaticoduodenectomy. Resection of different parts of the pancreas may have different effects on post-operative blood glucose levels, therefore our conclusions apply only to patients undergoing distal pancreatectomy. Second, the sample size was not large enough. The results will be more convincing if more cases can be collected or a multicenter study can be conducted. Third, There may be other influential factors related to NODM that have not been identified. Postoperative complications are not among the postoperative factors analyzed, and we would investigate the impact of postoperative complications such as acute pancreatitis of the pancreatic remnant, pancreatic fistula, delayed gastric emptying and infection on NODM in future studies. Finally, utilizing the resected pancreatic volume ratio calculated by the simulation resection to select different surgical methods may only be applicable to the resection of benign pancreatic lesions. Additionally, there was a difference between the preoperatively, radiologically identified resection line and the actual intraoperative surgical resection line. The predicted pancreatic volume ratio may still differ from the actual ratio. This clinical application should be verified in future studies.

6. Conclusion

This study demonstrated that the resected pancreatic volume ratio is a risk factor for the incidence of NODM after distal pancreatectomy. The ROC curve and Youden index may be used to predict the incidence of NODM after distal pancreatectomy. These findings may have further clinical applications in the future.

Author contribution statement

Mingyu Chen and Hong Yu conceived and designed the experiments;

Jiliang Shen performed the experiments; analyzed and interpreted the data; contributed reagents, materials, analysis tools or data and wrote the paper

Jiasheng Cao performed the experiments; analyzed and interpreted the data; contributed reagents, materials, analysis tools or data;

Jie He performed the experiments; analyzed and interpreted the data.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15998.

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