



# Paradoxical Lower BMI and Albumin Decrease as Predictors of Mild Hospital-Acquired Pressure Injury in Older Adult Patients

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## Abstract

**Aim:** To test the hypothesis that demographics, Pre-Pressure Injury (PI) nutrition care are associated with severe Hospital-Acquired PI (HAPI) in older adult patients.

**Methods:** The study was conducted under a retrospective observational design in all consecutive patients admitted to a single general hospital during 24 months between July 2014 and June 2016. The inclusion criterion was a new PI developed after admission. Exclusion criteria were: 1) no PI at admission or during hospitalization, 2) PI already present at admission, 3) hospitalization extending beyond the end of the study period, 4) missing data, 5) serum creatinine and/or total bilirubin >1.5 mg/dl, 6) death within 14 days after PI development. Data collection: 1) demographics-sex, age, body mass index (BMI), Charlson comorbidity index; 2) PI parameters-severity of PI scored by NPUAP and DESIGN-R score, 3) laboratory parameters -hemoglobin, serum albumin (Alb), C-reactive protein; 4) nutrition parameters- daily energy and protein intakes during the 7 days before PI development, 5) outcome parameters-mortality rate, length of stay in hospital. Then, all collected data were compared between two groups divided by the severity of PI: mild vs. severe.

**Results:** (1) HAPI prevalence and incidence were 1.73% and 1.20%, respectively. (2) Eighty percent of newly developed HAPI were mild. (3) The result showed a paradoxical association of lower BMI and albumin decrease after admission with mild HAPI development.

**Conclusion:** A paradoxical lower BMI and Alb decrease seems to be predictors of mild HAPI in older patients.

**Keywords:** Pressure injury; BMI; Serum Albumin; Old adult

## Abbreviations

Alb: Serum Albumin; BMI: Body Mass Index; CCI: Charlson comorbidity index; CRP: C-Reactive Protein; EPUAP: European Pressure Ulcer Advisory Panel; Hb: Hemoglobin; HAPI: Hospital-Acquired PI; NPUAP: National Pressure Ulcer Advisory Panel; PI: Pressure Injury; PNI: Prognostic Nutritional Index; TLC: Total Lymphocyte Count

## Introduction

Pressure Injury (PI), formerly known as a pressure ulcer [1], becomes a psycho-physical burden to inpatients and an economic burden to healthcare systems, especially in a super-aged society, where  $\geq 21\%$  of the population are older adults. The prevalence of PI in general hospitals was 2.94% in 2011, reduced to 1.99% in 2015 in a super-aging society [2,3]. This PI prevalence reduction is equivalent to 0.24% per year for four years. During this period, a novel PI severity scoring system, named the DESIGN-R scale, has been developed and spread to evaluate and standardize PI severity for the advancement of PI care [4]. In another systematic review conducted by the Cochrane library, however, PI was reported to affect as high as 10% of patients in hospitals [5]. Therefore, PI should be recognized as an important issue. Contrary to the prevalence issue, PI incidence has not been changed and maintained at a level of 1.60% during the same period. Besides efforts to

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reduce PI incidence, risk assessment tools to identify who is at risk of developing PI have been eagerly developed for more than 30 years, such as the Norton Scale developed in 1975 [6], the Water low scale in 1985 [7], and the Braden Scale in 1987 [8,9]. A systematic review stated that the risk assessment tools for development of PI are not sufficiently predictive mainly because of a lack of RCT evidence [10], but the tools continue to be recommended by the guidelines [11]. In addition, another systematic review conducted by Cochrane library also concluded that no PI risk assessment tools could be recommended because relevant RCT evidence is lacking [10]. In nutritional care for inpatients, NPUAP guidelines as European and US associations recommend for adults at risk of PI to be provided with 30 to 35 kcal/kg/day and 1.25 to 1.5 grams/kg body weight/day for energy and protein, respectively [2]. However, PI itself also contributes to worsened nutritional status, partly because nutrients and fluids are lost through exudates from PI wounds, and partly because appetite loss is accompanied with immobility, pain, and leads to malnutrition. In this context, therefore, we focused on Hospital-Acquired PI (HAPI) and nutritional care during pre-development of PI. To test our hypothesis that nutritional supports, mainly including energy and/or protein intakes 7 days before HAPI development, are associated with more severe HAPI development.

## Methods

The study was conducted as a retrospective observational design in all consecutive patients admitted to a single general hospital during 24 months between July 2014 and June 2016. The inclusion criterion was a new PI developed after admission. Exclusion criteria were: 1) no PI at admission or during hospitalization, 2) PI already present at admission, 3) hospitalization extending beyond the end of the study period, 4) missing data, 5) serum creatinine and/or total bilirubin >1.5 mg/dl for estimated liver or renal dysfunction, and 6) death within 14 days after PI development. Then, all collected data described below, including nutrition parameters, were compared between the two groups divided by their severity of PI: mild vs. severe (Figure). This study was approved by the ethics committee of the institute where all data were taken (Approval number: 2016-001). Given the nature of this study, the requirement for informed patient consent was considered not necessary.

### Data collection

Data were collected from the medical records at admission and during the study period. The collected data were as follows: 1) demographics, including sex, age at hospitalization, weight, Body Mass Index (BMI), and Charlson Comorbidity Index (CCI) as the severity indicator of comorbidities [12]; 2) PI parameters, including the severity of PI at occurrence as scored by the DESIGN-R score, NPUAP score, and risk of PI as described in "Management and Prevention of Pressure Ulcers" developed by the Japanese Ministry of Health, Labor and Welfare [13]. This score was evaluated by nursing staff in charge of PI. The DESIGN-R scoring system was developed to predict the clinical course of healing using the following six acronym-source components, namely depth (D), exudates (E), size (S), inflammation/infection (I), granulation tissue (G), and necrotic tissue (N). Pockets (P) is additionally added to the acronyms when an undermining pocket is identified during repeated weekly evaluations. All scores of E, S, I, G, N, and P, except D, were summed to indicate the severity of PI; 3) laboratory parameters, including Hemoglobin (Hb), Total Lymphocyte Count (TLC), Serum Albumin (Alb), C-Reactive Protein (CRP), and ONODERA's Prognostic Nutritional

Index (PNI) calculated by the equation  $[(10 \times \text{Alb}) + (0.005 \times \text{TLC})]$  [14]. At admission and during the treatment periods, these blood data were basically taken weekly; 4) nutrition parameters, including daily energy (kcal/kg of actual body weight/day) and protein (grams/kg of actual body weight/day) intakes during the 7 days before PI development, were calculated individually; 5) outcome parameters, including mortality rate and time-related outcomes - a) length of hospital stay (days), length of days between b) admission and PI development, c) PI development and discharge for the discharged subjects, and d) PI development and day of complete healing for the healed cases.

### Statistical analysis

Mann-Whitney's U test and Wilcoxon's rank sum test were used to compare continuous variables. The chi-square test and Fisher's exact test were used for comparisons between categories. Data were expressed as the median and inter quartile range in the case of continuous variables and as a numerical value and proportion in the case of category variables. Fourteen cases that had missing data on BMI were excluded. The significance level was set at  $P < 0.05$ . All analyses were conducted using SPSS Statistical Edition 23 (IBM, Armonk, NY, USA).

## Results

(1) A comparison among study subjects showed that HAPI prevalence and incidence among study subjects were 1.73% and 1.20%, respectively. (2) Eighty percent of newly developed HAPI subjects had mild (less severe) PI, equivalent to diagnosis stage I or II. (3) A comparison of all collected data between the two groups divided by their PI severity showed a significantly lower BMI and Alb decrease at HAPI occurrence in the mild group (16 vs. 20 kg/m<sup>2</sup>,  $P = 0.015$ ; 2.4 vs. 3.5 g/dl,  $P = 0.008$ , respectively), whereas daily energy and protein intakes during the 7 days before PI development did not differ (Table 1).

## Discussion

### Prevalence and incidence of hospital-acquired pressure injury

In the present study, we have highlighted HAPI as the study subject. PI incidence varied from 1.60% in the national survey to 2.06% in the present study. One of the reasons for the difference might be the observational methods: the national survey was point-observation and ours was interval-based. Moreover, the incidence of PI on a single day might have varied by the season and age of the observed population. To the contrary, observations on PI during a long period like the present study might be more reliable. To our knowledge, our study was the first to report the incidence of HAPI observed in a 24-month period. Another reason to explain the difference between the national survey and ours might be due to a difference of subjects' age. For example, the median age was 81 years in our study and 75 years in the national survey [2]. This median age difference is important because the age of inpatients is increasing in a super-aging society and, therefore, PI incidence might also be increasing. To test this hypothesis, an age-matched national survey with a long observation period might be necessary.

### The ratio of mild to severe PI inpatients

The mild/severe ratio of HAPI patients in the present study was calculated as 80%. This figure is equivalent to the result previously reported [15] and suggests that the majority of HAPI cases are less

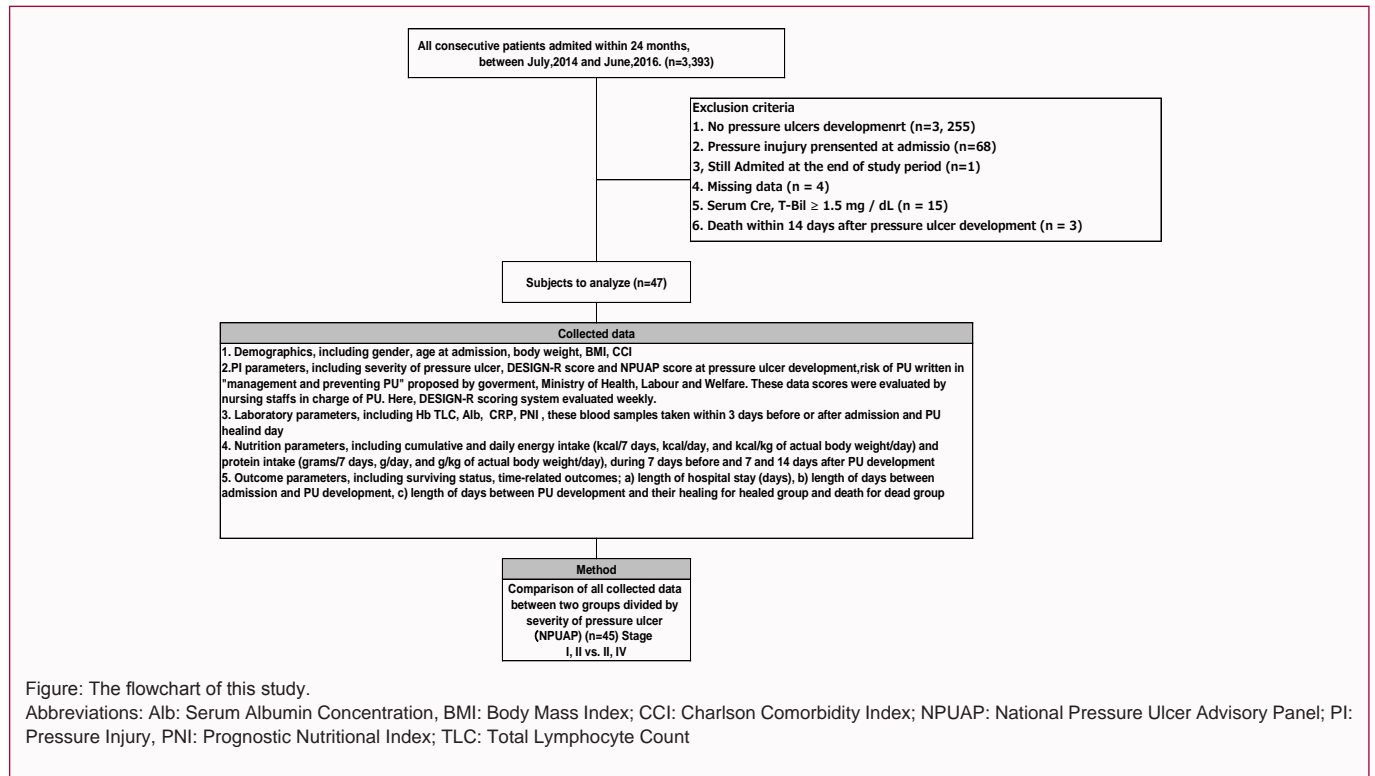


Figure: The flowchart of this study.

Abbreviations: Alb: Serum Albumin Concentration, BMI: Body Mass Index; CCI: Charlson Comorbidity Index; NPUAP: National Pressure Ulcer Advisory Panel; PI: Pressure Injury, PNI: Prognostic Nutritional Index; TLC: Total Lymphocyte Count

severe. This is one of the reasons why we focused on less severe, stage I and/or II, HAPI in adult patients over 80 years old.

### Paradoxical association of lower BMI with the less-severity of Hospital-acquired pressure injury in older adult patients

Before commencing our analysis, we predicted that smaller BMI as a nutritional indicator might be associated with more severe HAPI. This observation suggests that older adult in patients with a BMI  $<16$  kg/m<sup>2</sup> should be given more attention as being at risk of HAPI during the first month after admission. To the contrary, however, a review article stated that underweight patients with a BMI  $<19$  kg/m<sup>2</sup> did not have a significantly higher odds ratio for developing PI comparing to those with a normal BMI or an obese population [16]. To confirm whether older in patients with a BMI  $<16$  kg/m<sup>2</sup> area t greater risk of developing PI or not, further study is necessary. Another reason to explain the paradoxical associations mentioned above might be that older in patients with less severe HAPI had a tendency for more comorbidities and immobility estimated by CCI (3 vs. 2,  $P=0.677$ ). The immobility caused by being bed-ridden was observed more frequently in the mild group in the present study. This result was the same as the previously report [17]. However, the demographics of the subjects in that article were the presence of a critical illness and a median age of  $57 \pm 14.8$  years. In addition, another study focused on two different subjects: one group was evaluated at risk and another was not at risk before PI development. The median age was 57.9 years, and patients were admitted for surgery the following week [16]. In summary of the risk factors for HAPI, especially in adult inpatients older than 80 years, a BMI  $<16$  and  $\leq 18$  kg/m<sup>2</sup> might be paradoxically associated with development of mild and severe HAPI, respectively (Table 1). However, because the subjects' demographics and medical settings were different between the two above-mentioned articles and ours, a definitive conclusion cannot be drawn without further study.

### Decreasing Alb after admission to hospital seems a risk factor to develop HAPI

A lower Alb was observed for a mild PI occurrence, whereas Alb at admission in this group was not significantly lower. This result suggests that the larger decrease of Alb from admission to PI occurrence in the less severe PI group seems to reflect the larger inflammation shown as a higher CRP in this group (2.53 vs. 0.71 mg/dl,  $P=0.307$ ). In addition, comparing patients with Alb  $\leq 3.0$  g/dl at admission in the two groups, it was significantly larger in mild group than severe group (62% vs. 7%,  $p=0.017$ ).

These observations might be interpreted that patients in mild HAPI has tendency to have lower Alb and significantly lower Alb at HAPI occurrence. In other words, they could be at risk of HAPI as early as at admission and worsen their inflammatory response by the timing of PI occurrence at ages 80 years and older.

### Smaller energy intake during the 7 days before PI occurrence is associated with hospital-acquired PI development

The NPUAP guideline recommendations are to provide 30 to 35 kcal/kg/day for energy and 1.25 to 1.5 grams/kg body weight/day for protein to adults at risk of PI [2]. However, the daily energy and protein intakes during the 7 days before HAPI development in the less severe group were smaller than the above-mentioned recommendations (22.4 and 0.8 g/kg/day, respectively). These results might be related to patients developing HAPI earlier and a larger decrease of Alb from admission to PI development. From these observations, especially for older inpatients at risk of HAPI, at least 30 to 35 kcal/kg/day of energy and 1.25 to 1.5 g/kg/day of protein are suitable nutritional intakes, as the NPUAP guidelines recommend [18].

**Table 1:** Comparison of collected data between two groups divided by severity of pressure ulcer (NPUAP) in survivors: Mild (Stage I, II) vs. Severe (Stage III, IV).

		Total	Stage		P value*
			Mild (stage I, II)	Severe (stage III, IV)	
Number		45	36	9	
Data parameters					
Characteristics	Gender (male, n (%))	36/45 (80%)	17/36 (47%)	3/9 (33%)	0.358
	Age (years)	82 (77, 86)	83 (77, 88)	81 (72, 86)	0.560
	Weight (kg)	43 (37, 46)	41 (35, 46)	46 (42, 53)	0.037
	BMI (kg/m <sup>2</sup> )	17 (15, 20)	16 (15, 19)	20 (18, 23)	0.015
	CCI score at admission	3 (1, 5)	3 (1, 5)	2 (1, 4)	0.677
Primary diagnosis	neurology	14 (31%)	12 (27%)	2 (4%)	0.417
	lung diseases	11 (24%)	8 (18%)	3 (13%)	0.382
	heart diseases	5 (11%)	5 (11%)	0 (0%)	0.309
	orthopedics	5 (11%)	1 (2%)	4 (9%)	0.004
	UTI	3 (7%)	3 (7%)	0 (0%)	0.503
	dehydration	2 (4%)	2 (4%)	0 (0%)	0.636
	miscellaneous	5 (11%)	5 (11%)	0 (0%)	0.309
Laboratory parameters					
measured at admission	Hb, g/dL	11.5 (10.6, 12.6)	11.7 (10.9, 12.8)	10.7 (10.4, 11.6)	0.109
	Alb, g/dL	3.0 (2.6, 3.5)	3.0 (2.6, 3.5)	3.5 (2.4, 4.1)	0.195
	CRP, mg/dL	2.24 (0.68, 6.64)	2.53 (0.74, 7.01)	0.71 (0.35, 10.39)	0.307
	PNI	36.9 (32.6, 39.9)	36.9 (32.3, 38.9)	39.8 (30.2, 46.1)	0.106
measured at PI occurrence	Hb, g/dL	9.9 (8.9, 11.5)	9.9 (8.8, 11.1)	10.2 (9.4, 12.6)	0.274
	Alb, g/dL	2.6 (2.3, 3.1)	2.4 (2.2, 3.0)	3.5 (2.6, 3.8)	0.008
	Alb ≤ 3.0 g / dL, n (%)	31 (69%)	28 (62%)	3 (7%)	0.017
	CRP, mg/dL	2.00 (0.90, 4.25)	1.95 (1.15, 4.80)	2.30 (0.40, 3.20)	0.443
	PNI	33.2 (27.0, 39.1)	31.6 (26.3, 37.9)	39.8 (35.0, 43.4)	0.012
Δ value**	Hb, g/dL	-1.2 (-3.2, 0.2)	-1.6 (-3.3, 0.2)	0.0 (-2.2, 1.1)	0.097
	Alb, g/dL	-0.4 (-0.7, 0.1)	-0.4 (-0.9, -0.1)	0.0 (-0.6, 0.2)	0.114
	CRP, mg/dL	0.00 (-2.94, 2.01)	0.22 (-5.15, 1.94)	0.00 (-1.28, 2.28)	0.955
	PNI	-1.6 (-6.2, 1.0)	-1.8 (-7.1, 0.6)	0.0 (-4.4, 2.3)	0.294
Pressure injury parameters	Stage I, n (%)	0 (0)	0 (0)	0 (0)	1.000
	Stage II, n (%)	36 (80)	36 (80)	0 (0)	0.000
	Stage III, n (%)	9 (20)	0 (0)	9 (20)	0.000
	Stage IV, n (%)	0 (0)	0 (0)	0 (0)	1.000
	DESIGN-R score at PI occurrence	7 (5, 9)	7 (5, 8)	11 (6, 14)	0.024
PI risk factors, n (%)	Appetite loss	23 (51%)	21 (47%)	2 (4%)	0.058
	Bed-ridden (unable to change position)	33 (73%)	29 (64%)	4 (9%)	0.043
	Bony prominent	26 (58%)	22 (49%)	4 (9%)	0.297
	Chair bound (unable to leave chair without assistance)	32 (71%)	27 (60%)	5 (11%)	0.225
	Joint contracture	20 (44%)	16 (36%)	4 (9%)	0.648
	Localized edema	19 (42%)	16 (36%)	3 (13%)	0.416
	Moistured skin	29 (64%)	23 (51%)	6 (13%)	0.600
Nutrition parameters development: during 7 days before PI	Daily energy intake, kcal/kg	24.2 (16.4, 29.4)	22.4 (15.3, 30.5)	28.1 (24.2, 29.4)	0.328
	Daily protein intake, g/kg	0.9 (0.6, 1.3)	0.8 (0.5, 1.2)	1.1 (0.9, 1.4)	0.157
	NPC/N ratio, kcal/g	131.5 (115.0, 162.6)	133.9 (117.2, 162.7)	120.9 (109.7, 161.2)	0.407
Outcome parameters	Length of stay in hospital, days	109 (66, 132)	111 (65, 131)	94 (59, 149)	0.898
	Length of days between admission and PI occurrence, days	35 (17, 63)	32 (15, 56)	45 (17, 69)	0.660
	Length of days between PI occurrence and discharge, days	53 (32, 85)	56 (38, 96)	53 (31, 74)	0.854
	Mortality rate, non-survivors/ total subjects, n (%)	5 (11%)	4 (11%)	1 (11%)	0.742

All data are expressed in medium (25 % tile, 75 % tile).

\*P-value of comparison results between mild (stage II) vs. severe (stage III) group.

\*\* Δ value: difference between data measured at PI occurrence and at admission.

## Using a non-protein calorie: nitrogen (NPC/N) ratio as an indicator of nitrogen balance in pressure injury settings

The non-protein calorie: nitrogen (NPC/N) ratio has been reported as a relevant indicator of nitrogen balance in patients under various stress circumstances [19]. Given the previous review [19], setting the NPC/N ratio at 100 kcal/g could lead patients under stress to achieve a positive nitrogen balance, such as for HAPI patients. The NPC/N ratio of 133.9 in the mild group (Table 1) seems smaller than the 100 kcal/g required achieving a positive nitrogen balance. In this context, the energy and NPC/N should be set at 30 kcal/kg/day and 100 kcal/g respectively, and the amount of protein administered to prevent hospital-acquired PI is automatically calculated to be 1.5 g/kg/day. From this result, during the 7 days before PI development, not only energy intake but also the NPC/N ratio should be considered for patients at risk of HAPI. In clinical practices, when 1.5 g/kg/day of protein is provided or a smaller NPC/N ratio is set at 100 kcal/g as a protein loading strategy for adult patients older than 80 years old, like in the present study, careful attention must be paid to prevent renal functional impairment.

From these results, inpatients associated with BMI <16 kg/m<sup>2</sup> and Alb decrease <3.0 g/dl after admission seems be risk factors to develop HAPI and be candidate to treat with nutritional care of 30 kcal/kg/day and NPC/N setting at 100 kcal/g as optimal nutritional care. In other words, our hypothesis that nutritional support might be related to HAPI development seemed incorrect.

## Limitations of the Study

There were several limitations to the present study. First, the number of subjects was too small to draw definitive conclusions. Further, a larger population study is necessary to resolve this limitation. Second, given that some patients developed PI 30 days after admission, it is unclear whether the length of analysis seven-day period study for energy and protein provision might be proper or not. A longer period for analysis might help to clarify whether nutrition support is one of the leading factors for HAPI or not. Third, because this was a retrospective single facility study, the two groups differed in CCI scores. It was not examined whether or not patients with BMI <16 kg/m<sup>2</sup> and larger Alb decrease really develop HAPI. To assure this, a multi-center analysis could resolve these tendencies of biasing severity of comorbidities. Fourth, we proposed to set NPC/N at 100 to prevent HAPI. However, this proposal has not yet been examined to be proved. It must be validated to be correct or not to be able to prevent HAPI in older adult patients with NPC/N at 100 kcal/g.

## Conclusion

From the observation of the study during 24 consecutive months in a single institute, (1) PI prevalence and incidence were 1.73% and 1.20%, respectively. (2) Eighty percent of newly hospital-acquired PI cases were mild severity, diagnosed as stage I or II. (3) A comparison of all collected data between the two groups according to the severity of PI showed a BMI <16 kg/m<sup>2</sup> and Alb decreasing to below 3.0 g/dl at HAPI occurrence were paradoxically associated with the mild severity of PI occurrence. For older patients at risk of HAPI development, in addition to the recommended amounts of energy and protein (30 to 35 kcal/kg/day, 1.25 to 1.5 g/kg/day, respectively), an NPC/N ratio set at 100(kcal/g) might to be the key to nutrition care to prevent PI development. In summary, we would conclude that inpatients associated with BMI <16 kg/m<sup>2</sup> seems to be paradoxically associated with developing mild HAPI and to treat with nutritional care of 30

kcal/kg/day and NPC/N setting at 100 kcal/g.

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