Structural equation modeling of qualification of pharmacists to improve subjected quality of life in cancer patients.

Shigeo Yamamura, Rieko Takehira, Keiko Kawada, Shirou Katayama, Kenji Nishizawa, Masaaki Hirano, Yasunori Momose

School of Pharmaceutical Sciences, Toho University, Funabashi, Chiba, Japan, Department of Pharmacy Service of the Nippon Medical School Hospital, Bunkyo-ku, Tokyo, Japan

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ABSTRACT. Purpose: To establish structural equation model (SEM) of subjected quality of life (QOL) in cancer patients taking into account qualification of pharmacists. **Method**: The SEM model was constructed from correlation matrix of the scores of answers of questions to both patients and pharmacists. Data were collected from 15 cancer patients who hospitalized and took opioid analgesics for pain control. The patients were asked 18 questions and pharmacists were asked seven questions. From the correlation matrix among scores of answers, a reasonable model was explored by SEM. **Results**: Health-related QOL (HRQOL) in cancer patients can be modeled by latent variables consist of contributions from physical, emotional and functional domains. The fitting between data and the model was acceptable by statistical goodness-of-fit (GOF) index. The modeled HRQOL by SEM was weakly correlated with subjected QOL in patients, indicating that subjected QOL in patients would be affected not only by above latent variables but other variables. The model taking into account qualification of pharmacists to improve subjected QOL in patients was also made by SEM. The model was reasonably explained and fitting between data and the model was acceptable from some statistical index. The final model suggests that pharmacist can raise subjected QOL in patients through restraining unpleasant side effects. **Conclusion**: The qualification of pharmacists to improve subjected QOL in patients can be modeled by SEM. The final model suggests that pharmacists with qualification to assess patients' pain status contribute to raise subjected quality of life in cancer patients.

Corresponding Author: Shigeo Yamamura, School of Pharmaceutical Sciences, Toho University, Miyama 2-2-1, Funabashi, Chiba, 274-8510, Japan, yamamura@phar.toho-u.ac.jp

INTRODUCTION

The role of pharmacists contributes to improve the quality of life (QOL) in patients through providing pharmaceutical care. There are many reports for intervention of pharmacists to improve patients' medical condition that is a part of patients' QOL and/or health-related QOL (HRQOL) [1, 2]. In palliative care, however most pharmacists had a basic knowledge of pain management, pharmacist documentation pertinent was reported to be poor [3]. Suh et al., also pointed out that there are sample size problems to determine directly the correlation between improvement of pharmacist knowledge and practice change [3]. Pharmacist intervention was reported to improve patients' pain relief [4]. Pain relief contributes to raise HRQOL in patients. Pain relief would take some part of HRQOL of patients, but not all. If pharmacist's qualification to improve HRQOL in patients can be modeled by multivariate analysis, a significance of intervention of pharmacist in palliative care setting would be revealed. HRQOL is known to consist of various elements, such as physical, emotional, social and functional domains. These elements are statistically categorized to be latent variables that are not directly observable or measured, as psychological variables like "intelligence". This means that multivariate analysis only using observed variables would be insufficient to model the relationship between HRQOL in patients and pharmacist qualification. Structural equation modeling (SEM) specifies the direct and indirect relationships among the latent variables and is used describe the amount of explained unexplained variance. SEM is a very general, chiefly linear, chiefly cross-sectional statistical modeling technique comprising traditional statistic analysis as factor analysis, path analysis and regression analysis [5, 6]. SEM is a largely confirmatory technique and can be used to determine whether a certain model is valid.

Table 1. Characterization of the 15 patients who involved in the study.

Patient (No.)	Gender	Age	Diagnose	Opioid
1	F	61	Condrosarcoma	Morphine
2	M	79	Lung	Morphine
3	M	70	Malignant lymphoma	Morphine
4	M	67	Multiple myeloma	Morphine
5	F	59	Esophageal	Fentanyl
6	M	67	Multiple myeloma	Morphine
7	F	66	Breast	Morphine
8	M	60	Multiple myeloma	Morphine
9	F	59	Rectal	Morphine
10	F	54	Breast	Fentanyl
11	M	63	Colon	Morphine
12	F	73	Esophageal	Fentanyl
13	F	55	Colon	Fentanyl
14	M	75	Lung	Morphine
15	F	63	Lung	Morphine

Because SEM can deal with abstraction of psychological effects as latent variable, it has been applied to measure the HRQOL of patients in nursing care [7-9]. In medical practice, SEM is also applied to assess the HRQOL of patients [10, 11]. In the field of pharmacy and pharmaceutical sciences, SEM has been applied to assess bioavailability and consumer satisfaction in pharmacy [12-14]. However, there have been little investigations to make reasonable statistical model of pharmacist qualification to improve subjected QOL in patients in pain care setting.

In this study, we examined the relationship among subjected QOL in patients, pharmacist qualification to improve HRQOL in patients and other related variables by SEM approach. The attempt was focused on what pharmacist's qualification improves subjected QOL in cancer patients.

METHOD

Participants

Patients: 18 patients diagnosed with cancer who hospitalized in Nippon Medical University Hospital (Sendagi, Tokyo Japan) were candidates for this study. All patients took opioid analgesics for pain control and a pain control team organized by physicians, pharmacists and nurses provided appropriate cares in the hospital. Patients were excluded if they started chemotherapy during this research or they did not complete the answer form due to their bad illness. 15 patients were enrolled in this study and agreed with answer the questions by signing. The background characteristics of 15 patients were summarized in Table 1. Answers by patients were collected by interviewing by pharmacist using a questionnaire four times every one week at bedside. Questions in a questionnaire are listed in Table 2.

Pharmacists: Eight pharmacists providing pharmaceutical care in a pain control team were involved in this study. Many of them have had an experience of pain management in a pain control team in the hospital, but did not receive particular training of pain management. Pharmacists scored simply, not structured, for patients' status by 7 questions themselves when they interviewed with patients. (Table 3).

Questionnaire

A questionnaire in this study to assess HRQOL of patients was developed by referring SF36, Functional Living Index-Cancer: (FLIC) and Functional Assessment of Cancer Therapy: General (FACT-G) for assessment of heath-related quality of life (HRQOL) [15, 16, 17].

According to a suggestion from a local research committee, the number of questions in questionnaire was limited to be 18 in order to avoid unnecessary burdens on patients. The questions in the questionnaire were mainly selected from 4 important domains of HRQOL (EWB: emotional well-being, FWB: functional well-being, SWB: social well-being and PWB: physical well-being).

Table 2. Questionnaire for patients and score (mean ± S. D.) for the questions.

No.	Question	Score	Mean ± S. D.
1	Did you have good sleeping?	Never (1 2 3 4 5) Very Much	4.15 ± 0.98
2	Do you have uneasiness about your pain and/or nausea?	Never (1 2 3 4 5) All the time	2.73 ± 1.38
3	Have felt uneasy?	Never (1 2 3 4 5) All the time	1.87 ± 1.04
4	Have felt depressed?	Never (1 2 3 4 5) All the time	2.31 ± 1.38
5	Have felt under concentration?	Never (1 2 3 4 5) All the time	3.23 ± 1.31
6	Did you feel nausea?	Never (1 2 3 4 5) Very Much	2.23 ± 1.51
7	Did you vomit?	Never (1 2 3 4 5) Very Much	1.63 ± 1.15
8	Did you have constipation?	Never (1 2 3 4 5) Very Much	2.78 ± 1.64
9	Did you have diarrhea?	Never (1 2 3 4 5) Very Much	1.44 ± 0.88
10	Rate of your pain?	No pain (0 1 2 3 4 5 6 7 8 9 10) Maximal pain ever experienced	3.20 ± 1.76
11	Were you able to move with no pain freely?	Never (1 2 3 4 5) Very Much	3.43 ± 1.24
12	Did you enjoy a book or radio or television program?	Never (1 2 3 4 5) Very Much	2.53 ± 1.38
13	Were you able to move to a rest room with no assistance freely?	Never (1 2 3 4 5) Very Much	2.75 ± 1.95
14	Were you able to tell your family about your mind?	Never (1 2 3 4 5) Very Much	4.60 ± 0.71
15	Do you need more explanation about effect and side effect of analgesics?	Never (1 2 3 4 5) Very Much	1.53 ± 1.08
16	Were you able to tell the pharmacist about your pain?	Never (1 2 3 4 5) Very Much	3.46 ± 1.74
17	Were you able to tell the nurse your pain?	Never (1 2 3 4 5) Very Much	4.90 ± 0.30
18	Rate of your overall quality of life?	Too bad (1 2 3 4 5) Very good	2.50 ± 0.82

Q1-Q5 belong EWB, Q6-Q10 belong PWB, Q11-Q13belong FWB, Q14 belong SWB. (17). Q15-Q18 was to explore the relationship among patients and other health professionals. Answers were made on scores ranging in 1 to 5 except for Q10. Answer of Q10 was made on score ranging 0 to 10.

Table 3. Questionnaire for pharmacists and score (mean ± S. D.) for the questions.

No.	Question	Score	Mean ± S. D.
1	Do you think that the patient understands for medication?	Never (1 2 3 4 5) Very much	3.33 ± 0.97
2	Do you think that the patient could communicate with physician for pain?	Never (1 2 3 4 5) Very much	3.85 ± 0.81
3	Do you think that the patient could communicate with nurse for pain?	Never (1 2 3 4 5) Very much	4.20 ± 0.76
4	Do you think that you grasp the patient's pain?	Never (1 2 3 4 5) Very much	3.68 ± 0.53
5	How would you rate overall QOL of the patient?	Too bad (1 2 3 4 5) Very good	3.03 ± 0.92
6	How would you rate pain-score of the patient?	No pain (0 1 2 3 4 5 6 7 8 9 10) maximal pain ever experienced	2.05 ± 1.11
7	How long have you experienced for pain control?	1:<1yr, 2:1-5yrs, 3:5-10yrs, 4:>10yrs	1.88 ± 0.61

All questions except for pain score were scored on a five-point score and some of them were reversed coded. The pain score was recorded on an eleven-point scale ranging 0 (no pain) to 10 (maximal pain ever experienced). Pharmacists evaluated the patients' status on a five-point scale or an eleven-point scale for pain.

Since some answer forms from patients or pharmacists did not completed, a number of paired (patient and pharmacist) form was 40 and they were used for SEM analysis. Mean scores and their standard deviations of each answer from the patients and pharmacists were summarized in Table 2 and 3.

The scores of answers can be candidates on parameter of the model.

This study design and questionnaire were reviewed by a local research committee.

Structural equation modeling (SEM)

Structural equation model (SEM) is a comprehensive statistical approach to test hypotheses about relation among latent and/or observed variables. Possible models including latent and observed variables were built with AMOS 5.0J (SPSS Japan, Tokyo, Japan). Each latent variable in the model was measured with more than two observed variables.

Table 4. Correlation matrix used in SEM for model 1 and model 2.

	Q1	Q2	Q5	Q6	Q7	Q10	Q12	Q13	Q18
Q1 (Sleep)	1.000								
Q2 (Uneasiness)	0.165	1.000							
Q5 (Concentration)	0.294	0.234	1.000						
Q6 (Nausea)	0.158	0.340	0.312	1.000					
Q7 (Vomit)	0.006	0.290	0.160	0.665	1.000				
Q10 (Pain)	0.042	-0.019	0.158	0.188	0.178	1.000			
Q12 (Enjoy Books/TV)	-0.175	-0.476	-0.451	-0.343	-0.359	-0.087	1.000		
Q13 (Move)	0.007	0.012	-0.259	-0.251	-0.273	-0.060	0.213	1.000	
Q18 (QOL)	-0.032	-0.171	-0.228	0.010	-0.068	-0.054	0.217	-0.081	1.000
S.D.	0.975	1.377	1.310	1.509	1.148	1.757	1.377	1.945	0.816

S.D. is standard deviation of answer of each question. Please refer questions in Table 1 and 2.

For the analysis, correlation matrix calculated with list-wise case deletion were used. Maximum likelihood method was used for the estimation of parameters.

We decide a possible model according to the following criteria: 1) The model can be reasonably explained, 2) The model fits the data by statistically as goodness-of-fit index (GFI) of 0.90 or greater, comparative goodness-of-fit index (CFI) of 0.90 or greater, root-mean square error of the approximation (RMSEA) less than 0.05, and a chi-square is not significant ($p>0.05$) [6]. Although standardized root mean square error (SRMSE) was also presented to demonstrate a multivariate normality, SEM is not so sensitive for multivariate normality rather than factor analysis. When two or more models were met above criteria, the final model was selected based on Akaike's information criterion (AIC), a statistic of goodness-of-fit adjusting number of estimated parameters. (See appendix).

RESULTS AND DISCUSSION

Structural Equation Modeling of HRQOL of Cancer Patients

Assuming that HRQOL of patients consists of four latent variables (EWB, FWB, SWB and PWB domains) as reported in the literature [17], an initial model was constructed by exploratory factor analysis. Then, the model was modified to make better fit between the model and data by trial and error approach.

Table 4 shows the correlation matrix of variables used in the final model. Because of little contribution to the model, other variables were removed during optimization of the model. The final model is shown in Fig. 1 with path diagram (model 1) in which circles (or ellipses) represent unobserved latent variables, squares (or rectangles) represent observed variables and single arrows represent the impact of one variable on another. e1 to e12 and d1 to d3 enclosed in a circle indicate error representing measurement error. The single-headed arrows represent linear dependencies. The numeric values located with single-arrows is an estimate of standardized regression weight (standardized maximum likelihood parameter). The estimates of standardized regression weight from errors to variables (e1 to e12 and d1 to d3) were removed in the path diagram in order to clear the relationship among variables.

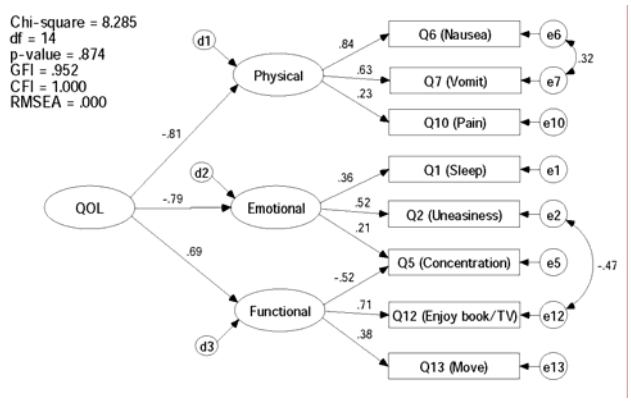

Figure 1. SEM model of HRQOL of cancer patients with standardized regression weights (model 1).

The final model suggests that HRQOL in cancer patients consists of three latent variables. From the observed variables in three latent variables, the latent variables were regarded to be physical, emotional and functional elements, respectively. Although there are a little conflict in signal of standardized regression weight among variables, overall, this model would be acceptable from empirically, and statistics of goodness-of-fit between the model and data were very good to be GFI=0.952, CFI=1.000, RMSEA=0.000, SRMSE=0.0615 and chi-square=8.285 (df=14, p=0.874).

This result positively supports the previous finding that the HRQOL of the patients consists of four ideal domains (EWB, FWB, SWB and PWB) reported the results by Ward et al., [17], even though lack of SWB domain in our model. This result also indicates that data collected in this study contain information explaining HRQOL of patients.

From the magnitude of estimates of standardized regression weight, physical and emotional domains were predominant elements in HRQOL of cancer patients rather than functional domain indicating that experiences of nausea and vomiting were mainly decreased HRQOL of patients. We further examined the model taking into account relationship between of HRQOL estimated by model 1 and subjected QOL in patients in Q.18. The final model is shown in Figure 2 (model 2). A double arrow between estimated HRQOL (latent variable) and subjected QOL (observed variable) represents the correlation coefficient between two variables.

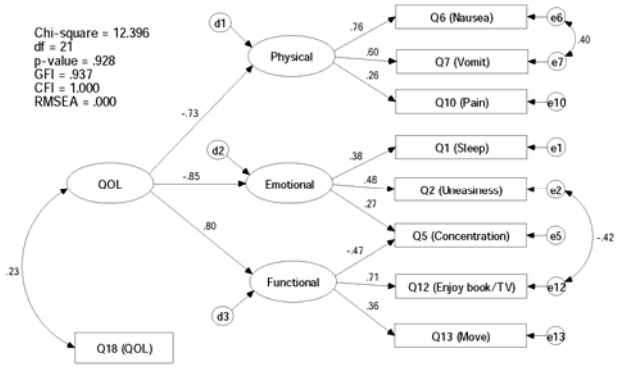

Figure 2. SEM Model of correlation between estimated HRQOL and subjected QOL in patients with standardized regression weights (model 2).

We did not further modify the relationship among the variables to improve the fit, because a purpose was to investigate the relation between estimated HRQOL in model 1 and subjected QOL answered by patients. Model 2 also satisfied all statistical criteria (GFI=0.937, CFI=1.000, RMSEA=0.000, SRMSE=0.0688 and chi-square=12.396 (df=21, p=0.928)).

As shown in Figure 2, a correlation coefficient between estimated HRQOL by model 1 and subjected QOL in patients was weak to be 0.23 (not significant). This would be result that since the patients in this study were in the hospital and received appropriate cares from pain care team; their pain was well controlled by taking appropriate amount of opioid analgestics. This result also suggest that a meaningful part of subjected QOL in patients would be influenced by other parameters (latent or observed variables), such as qualification and/or intervention of medical professionals.

SEM Modeling of subjected QOL in patients and qualification of pharmacists

We postulated that a weak correlation between modeled HRQOL and subjected QOL in patients would result that subjected QOL is influenced by qualification and/or intervention of other medical professionals. Then, the relationship between qualification of pharmacists and subjected QOL in patients was modeled by SEM.

The model was established on three hypothesis: 1) As described before, the estimated HRQOL was strongly related with the physical element such as nausea and vomiting, suggesting that severity of side effects of opioid would be one of predominant factors to describe HRQOL of patients; 2) If the “severity” of side effects is controlled to be low, this would lead comfortable life of patients in hospital and HRQOL score in patients would increase; 3) If pharmacists can restrain side effects of patients, subjected QOL in patients would increase.

We explored the reasonable model to express the relationship among subjected QOL in patients, qualification of pharmacists and severity of symptoms by SEM.

Table 5. Correlation matrix used in SEM for model 3.

	Pt-Q2	Pt-Q5	Pt-Q8	Pt-Q10	Pt-Q18	Ph-Q4	Ph-Q7	Difference
Pt-Q2 (Uneasiness)	1.000							
Pt-Q5 (Concentration)	0.234	1.000						
Pt-Q8 (Constipation)	0.222	0.203	1.000					
Pt-Q10 (Pain)	0.205	0.141	0.568	1.000				
Pt-Q18 (QOL)	-0.171	-0.228	-0.354	-0.137	1.000			
Ph-Q4 (Grasp the pain)	0.086	0.221	-0.087	-0.060	-0.090	1.000		
Ph-Q7 (Experience)	0.019	-0.028	-0.158	-0.006	0.233	-0.291	1.000	
Difference of pain score between by Pt and Ph	-0.116	-0.104	0.183	0.294	0.202	-0.107	0.310	1.000
S.D.	1.377	1.310	1.641	1.836	0.816	0.526	0.607	1.091

Pt and Ph indicate the questions for patients and pharmacist, respectively. S.D. is standard deviation of answer of each question. Please refer questions in Tables 1 and 2.

The final model and correlation matrix are shown in Figure 3 (model 3) and Table 5, respectively. In the model 3, one calculated parameter was introduced to make reasonable model, that is, absolute value of difference of pain scores answered by patients and assessed by pharmacists. This parameter would express a level of pharmacists' skill to assess pain level of patients, because when the parameter is 0, the pharmacist can assess the patients' pain exactly. The statistics of goodness-of-fit parameters of model 3 were all satisfactory to be GFI=0.907, CFI=0.958, RMSEA=0.039, SRMSE=0.1192 and chi-square=16.957 (df=22, p=0.388).

The final model consists of 4 latent variables, expressing "qualification of pharmacists", "skill of assessment" of pain level in patients, "severity" of side effect" and "comfort" level, respectively. From the magnitude of estimates of standardized regression weight between variables, the model can be explained as follows: when pharmacists have high ability with skill to assess patients' pain level, they can work to restrain unpleasant symptoms such as pain and constipation. If "severity" of side effects can be reduced by intervention by pharmacists, "comfort" level of patients would be increased with decreasing uneasiness and increasing of subjected QOL. Thus, subjected QOL in patients was considered to be one of factor describing "comfort" level of patients in the SEM model.

The "qualification of pharmacists" consists of skill to assess the pain level of patients and experience in pain control team. The former was found to be predominant factor in "qualification of pharmacists". When pharmacists who have excellent skill to assess the pain level of patients would intervene in pain control setting, they can restrain the unpleasant symptoms of patients as pain and constipation. As a result, subjected QOL in patients will be improved.

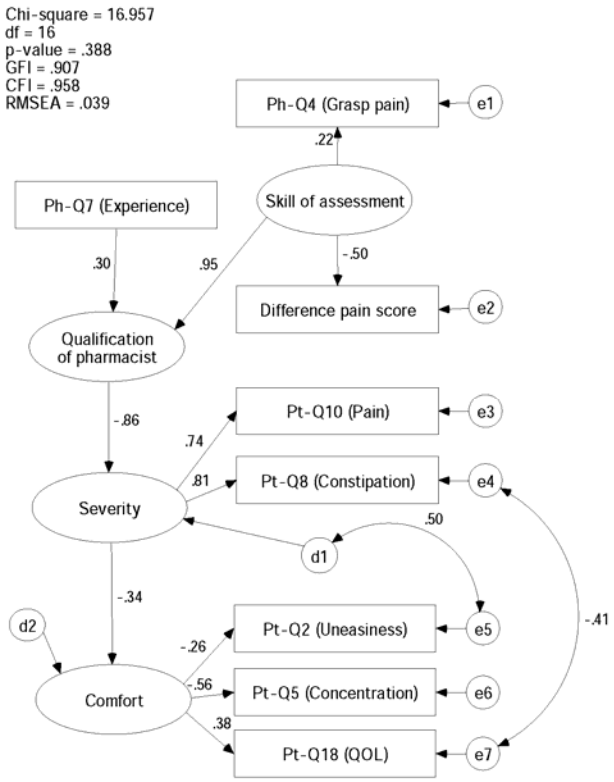

Figure 3 SEM model of subjected QOL in patients taking into account intervention of pharmacists with standardized regression weights (model 3).

Gammaitoni et al. reported that the palliative-trained pharmacist can play an important role in managing chronic pain [18]. On the other hand, Malone et al. indicated that clinical pharmacists had no significant impact on HRQOL as measured by SF-36 at high risk patients [19]. These reports suggest that a professional of pharmacists to improve QOL of cancer patients have not been evident. Our research indicates that pharmacists with good skills and qualification to assess patients' pain can improve QOL of patients.

This model is a quite simple model to express the relation between HRQOL of patients and qualification of pharmacists to evaluate pain of patients. Because the number of questions to patients was limited to be 18 according to the suggestion by a local research committee, items of questionnaire were not sufficient to make sophisticated model to evaluate HRQOL. Furthermore, sample size was also insufficient to make rigid model.

Using SEM modeling, the relationship between subjected QOL in patients and qualification of pharmacists can be expressed by path diagram being easy to understanding. SEM model would be a useful statistical technique to express the relationship between latent variable such as patients' QOL and intervention by health care stuffs.

We will investigate effective interventions of pharmacists to improve QOL of cancer patients by multi-institutional setting in future.

APPENDIX

Index of overall model fit used in SEM [5, 6]

Goodness-fit-index (GFI) indexes the relative amount of the observed variances and covariance's accounted for by a model. GFI varies from 0 to 1 and a model with GFI close to 1 indicates a very good fit.

Comparative goodness-of-fit index (CFI) indexes the relative reduction in lack of fit as estimated by non-central chi-square of a target model vs. a baseline model. CFI varies from 0 to 1. CFI close to 1 indicates a very good fit.

Root-mean square error of the approximation (RMSEA) residuals are the coefficients which result from taking the square root of the mean of the squared residuals, which are the amounts by which the sample variances and covariance's differ from the corresponding estimated variances and covariance's. The closer the RMR to 0 for a model being tested, the better the model fit.

Chi-square test is the statistical test of the lack of fit resulting from over-identifying restrictions placed on the model. If chi-square difference shows no significant difference between the unconstrained original model and the nested, constrained modified model, then the modification is accepted.

Akaike Information Criterion (AIC) is a goodness-of-fit measure that adjusts model chi-square to penalize for model complexity. AIC reflects the discrepancy between model-implied and observed covariance matrices. AIC close to zero reflects good fit and between two AIC measures, the lower one reflects the model with the better fit.

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