Survival of geriatric patients after percutaneous endoscopic gastrostomy in Japan

Yutaka Suzuki, Seryna Tamez, Akihiko Murakami, Akihiko Taira, Akihiro Mizuhara, Akira Horiuchi, Chie Mihara, Eiji Ako, Hirohito Muramatsu, Hitoshi Okano, Hitoshi Suenaga, Kazuaki Jomoto, Junya Kobayashi, Katsunari Takifuji, Kazuhiro Akiyama, Koh Tahara, Koji Onishi, Makoto Shimazaki, Masami Matsumoto, Masashi Ijima, Masato Nakahori, Michiaki Kudo, Mikio Maruyama, Naohiro Washizawa, Nao Hiro Washizawa, Shinji Nishiwaki, Shinji Ono, Shigeki Ono, Shunichi Kitahara, Tohru Hikichi, Tatsuya Mikami, Tatsumi Yamamoto, Tomoyuki Ohta, Toshifumi Matsumoto, Toshio Iwase, Toshiyoshi Tsuji, Yukio Nishiguchi, Mitsuyoshi Urashima

Yutaka Suzuki,
Department of Surgery, International University of Health and Welfare Hospital, 537-3 Iguchi, Nasushiobara-shi, Tochigi 329-2763, Japan

Seryna Tamez,
Department of Molecular Epidemiology, Jikei University School of Medicine, 3-25-8 Nishi-shimbashi, Minato-ku, Tokyo 105-8461, Japan

Akihiko Murakami,
Endoscopy Unit, Iwate prefectural Central Hospital, 1-4-1 Ueda, Morioka-shi, Iwate 020-0066, Japan

Akihiko Taira,
Department of Internal Medicine, Tsuyama Chuo Hospital, 1756 Kawasaki, Tsuyama-shi, Okayama 708-0841, Japan

Akihiro Mizuhara,
Department of Surgery, Higashi Washinomiyahospital, 3-9-3 Sakurada, kuki-shi, Saitama 340-0203, Japan

Akira Horiuchi,
Digestive Disease Center, Showa Inan General Hospital, 3230 Akaho, Komagane-shi, Nagano 399-417, Japan

Chie Mihara,
Department of Neurology, Ebina Medical Support Center, 1519 Kawaguchi, Ebina-shi, Kanagawa 243-0433, Japan

Eiji Ako,
Department of Surgery, Sumitomo Hospital, 5-3-20 Nakano-shima, Kita-ku, Osaka-shi, Osaka 530-0005, Japan

Hirohito Muramatsu,
Department of Gastroenterology, Kiyoto Hospital, 1-1-1-1 Shin-ji, Kiyoto-ku, Sapporo-shi, Hokkaido 004-0831, Japan

Hitoshi Okano,
Department of Gastroenterology, Okano Clinic, 3 Higashishido-cho Jodoji, Sakyoku-ku, Kyoyo-shi, Kyoyo 606-8411, Japan

Hitoshi Suenaga,
Department of Geriatrics, Hitachihohospital, 3-4-22 Kujicho, Hitachi-shi, Ibaraki 319-1222, Japan

Kazuaki Jomoto,
Department of Internal Medicine, Jomoto Gastroenteric and Internal Medical Clinic, 5-8-9 Kuhonji, Kumamoto-shi, Kumamoto 862-0976, Japan

Junya Kobayashi,
Department of Surgery, Fujiyoshida Municipal Hospital, 6530 Kamiyoshida, Fujiyoshida-shi, Yamanashi 403-0005, Japan

Katsunari Takifuji,
2nd Department of Surgery, Wakayama Medical University Hospital, 811-1 Kimiidera, Wakayama-shi, Wakayama 641-8510, Japan

Kazuhiro Akiyama,
Department of Surgery, Tokatsu-clinic Hospital, 865-2 Hinokuchi, Matsudo-shi, Chiba 271-0067, Japan

Koh Tahara,
Department of Surgery, Kure Kyosai Hospital, 2-3-28 Nishi-chuo, Kure-shi, Hiroshima 737-8505, Japan

Koji Onishi,
Department of Internal Medicine, Matsue Seikyo General Hospital, 8-8-8 Nisshtutsu, Matsue-shi, Shimane 690-8522, Japan

Makoto Shimazaki,
Department of Gastroenterology, Hirano General Hospital, 176-5 Kurono, Gifu-shi, Gifu 501-1192, Japan

Masami Matsumoto,
Department of Internal Medicine, Nara Prefectural Gojo Hospital, 5-2-59 Noharanishi, Gojo-shi, Nara 637-8511, Japan

Masashi Ijima,
Department of Internal Medicine, Iseaki Municipal Hospital, 1-1-1 Tsunatorihomachi, Iseaki-shi, Gunma 372-0812, Japan

Masato Murakami,
Department of Internal Medicine, Murakami Memorial Hospital, 739 Omachi, Saijo-shi, Ehime 793-0030, Japan

Masato Nakahori,
Digestive Endoscopy Center, Sendai Kousei Hospital, 4-15 Hirose-machi, Aoba-ku, Sendai-shi, Miyagi 980-0873, Japan

Michiaki Kudo,
Department of Surgery, Onish Hospital, 139-1 Onishi, Fujioka-shi, Gunma 370-1401, Japan

Michio Maruyama,
Department of Surgery, Tokyo Metropolitan Ohkubo Hospital, 2-44-1 Kabuki-cho, Shinjuku-ku, Tokyo 160-8488, Japan

Mikako Takahashi,
Department of Internal Medicine, Tsuruoka Kyoritsu Hospital, 9-34 Humisono-cho, Tsuruoka-shi, Yamagata 97-0816, Japan

Nao Hiro Washizawa,
Nutritional Therapy Center, Toho University Omori Medical Center, 22-1-1 Omori-nishi, Ota-ku, Tokyo 143-8541, Japan
Abstract

AIM: To examine the long term survival of geriatric patients treated with percutaneous endoscopic gastrostomy (PEG) in Japan.

METHODS: We retrospectively included 46 Japanese community and tertiary hospitals to investigate 931 consecutive geriatric patients (≥ 65 years old) with swallowing difficulty and newly performed PEG between Jan 1st 2005 and Dec 31st 2008. We set death as an outcome and explored the associations among patient’s characteristics at PEG using log-rank tests and Cox proportional hazard models.

RESULTS: Nine hundred and thirty one patients were followed up for a median of 468 d. A total of 502 deaths were observed (mortality 53%). However, 99%, 95%, 88%, 75% and 66% of 931 patients survived more than 7, 30, 60 d, a half year and one year, respectively. In addition, 50% and 25% of the patients survived 753 and 1647 d, respectively. Eight deaths were considered as PEG-related, and were associated with lower serum albumin levels (P = 0.002). On the other hand, among 28 surviving patients (6.5%), PEG was removed. In a multivariate hazard model, older age [hazard ratio (HR), 1.02; 95% confidence interval (CI), 1.00-1.03; P = 0.009], higher C-reactive protein (HR, 1.04; 95% CI: 1.01-1.07; P = 0.005), and higher blood urea nitrogen (HR, 1.01; 95% CI: 1.00-1.02; P = 0.003) were significant poor prognostic factors, whereas higher albumin (HR, 0.67; 95% CI: 0.52-0.85; P = 0.001), female gender (HR, 0.60; 95% CI: 0.48-0.75; P < 0.001) and no previous history of ischemic heart disease (HR, 0.69; 95% CI: 0.54-0.88; P = 0.003) were markedly better prognostic factors.

CONCLUSION: These results suggest that more than half of geriatric patients with PEG may survive longer than 2 years. The analysis elucidated prognostic factors.

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Key words: Percutaneous endoscopic gastrostomy; Enteral nutrition; Comorbidity; Survival; Risk factor
Peer reviewer: Dr. Pankaj Garg, Consultant, Department of General Surgery, Fortis Super Speciality Hospital, Mohali, Punjab, Panchkula, 134112, India

Suzuki Y, Tamez S, Murakami A, Taira A, Mizuhara A, Horiuchi A, Mihara C, Ako E, Muramatsu H, Okano H, Suenaga H, Homoto K, Kobayashi J, Takifuiji K, Akiyama K, Tahara K, Onishi K, Shimagaki M, Matsumoto M, Iijima M, Murakami M, Nakahori M, Kudo M, Maruyama M, Takahashi M, Washizawa N, Onozawa S, Gosh S, Yamashita S, Ono S, Imazato S, Nishiwaki S, Kitahara S, Endo T, Iiri T, Nagahama T, Hikichi T, Mikami T, Yamamoto T, Ogawa T, Ogawa T, Ohita T, Matsumoto T, Kura T, Kikuchi T, Iwase T, Tsuj T, Nishiguchi Y, Urashima M. Survival of geriatric patients after percutaneous endoscopic gastrostomy in Japan. World J Gastroenterol 2010; 16(40): 5084-5091 Available from: URL: http://www.wjgnet.com/1007-9327/full/v16/i40/5084.htm DOI: http://dx.doi.org/10.3748/wjg.v16.i40.5084

INTRODUCTION

Percutaneous endoscopic gastrostomy (PEG) was initially developed as an enteral nutrition technique by Gauderer et al[1] and Ponsky et al[2] in 1980. Since then, PEG has been widely used for patients with swallowing difficulty, because of reduced laryngopharyngeal discomfort and a lower risk of aspiration pneumonia compared with a nasogastric tube[3,4]. However, PEG feeding was found to be associated with an absolute increase in risk of death compared with nasogastric feeding[5]. In spite of the evidence, PEG has been widely used especially for geriatric patients with the increasingly aging society. Despite the very large number of patients receiving this intervention, there is insufficient evidence to suggest that PEG is beneficial for patients with swallowing difficulty arising from dementia or other chronic diseases[6,7]. Therefore, we conducted retrospective studies in multiple community hospitals in Japan to examine the long-term survival of geriatric patients treated with PEG and to delineate the factors associated with their mortality.

MATERIALS AND METHODS

Study design and population

We conducted a retrospective cohort study of patients who underwent PEG between 2005 Jan 1st and 2008 Dec 31st at 46 community hospitals all over Japan, selected by the panel of 103 doctor-experts in PEG and the trustees of the PEG Doctors’ Network as a non-profit organization. The study was approved by the institutional review board of each hospital. Doctors in charge of PEG in the selected hospitals were asked to examine 20 consecutive patients on whom a new PEG was performed, after excluding patients (1) whose age was ≤ 64 years old; (2) who had previously had a gastrectomy; (3) who had cancer considered to affect the patient’s prognosis; and (4) who had gastrostomy performed for reasons other than nutritional support. The doctors were further asked to report the number of excluded cases as well as the number of patients who were considered as lost to follow-up.

Outcome measure

The primary outcome was set as death and the cut-off date was set at October 2009. In the case where the patient was alive, the doctor was further asked to state the status of the patient according to the following: (1) admission to this hospital, (2) admission in other hospital, (3) stay at nursing home, (4) stay at home, or (5) other. In case of loss to follow-up, the final date the patient was confirmed as alive was censored. Causes of death were selected from one from following: (1) primary diagnosis warranting PEG; (2) pneumonia; (3) cardiac failure; (4) cancer; (5) the PEG procedure; (6) other; and (7) unknown. The secondary endpoint was the removal of PEG because of improvement in the patient’s condition.

Variables

The following data were collected: (1) age; (2) gender; (3) height; (4) weight; (5) body temperature; (6) white blood cell (WBC)/μL; (7) hematocrit (Ht): %; (8) hemoglobin (Hb): g/dL; (9) aspartate aminotransferase (AST): IU/L; (10) alanine aminotransferase (ALT): IU/L; (11) blood urea nitrogen (BUN): mg/dL; (12) serum creatinine (Cr): mg/dL; (13) serum albumin: g/dL; (14) C-reactive protein (CRP): mg/dL; (15) previous history of pneumonia or ischemic heart disease; (16) comorbidity of dementia, diabetes, serious malnutrition judged by the doctor in charge; (17) starvation period before having PEG: none, within 1 wk, within 1 mo, more than 1 mo; and (18) primary diagnosis or underlying disease warranting PEG, selected from one from following: (1) Neurological disease: (a) Parkinson’s disease; (b) amyotrophic lateral sclerosis; (c) multiple system atrophy; or (d) other neurological disease; (II) Cerebrovascular disease: (a) cerebral infarction; (b) cerebral hemorrhage; (c) subarachnoid hemorrhage; or (d) other cerebrovascular disease; (III) Dementia: (a) severe; (b) mild; or (c) other type of dementia; and (IV) Other disease, at the time of the PEG procedure, obtained from medical charts.

Statistics analysis

The Student t-test and Mann-Whitney U test were performed for continuous variables with normal and not normal distribution, respectively. Overall survival curves were drawn using the Kaplan-Meier method and compared for each variable using log-rank tests. The Cox proportional hazard models were fitted for multivariate analysis using variables significant in the log-rank tests and other tests. Adjusted hazard ratios (AHR) and 95% confidence intervals (CI) were determined. All statistical analyses were performed using STATA 11.0 (STATA Corp., College Station, TX). P < 0.05 was considered statistically significant.

RESULTS

Of the 1168 patients who underwent PEG at the 46 se-
lected hospitals, 237 were excluded from further analyses, having met at least one of the exclusion criteria, and thus 931 patients were followed and the median duration was 468 d, ranging from 1 to 1668 d. Among 931 patients, 122 patients were censored due to loss to follow-up at a median of 71 d, ranging from 6 to 1582 d. Mean age was 81.4 years old, ranging from 65 to 99 years. Females were predominant (54%). The distribution of primary diagnosis warranting PEG is shown in Figure 1, where cerebrovascular diseases accounted for more than half of the study population. In the previous history, pneumonia and ischemic heart disease were reported in 63% and 19% of patients, respectively. In addition, diabetes comorbidity was 18%. In total, 502 deaths were observed (mortality 53%), of which 10 deaths (2.0%) occurred within 7 d, 49 (9.8%) within 30 d, 105 (21%) within 60 d, 216 (43%) within 6 mo, and 287 (57%) within 1 year. Causes of death classified by the doctors are shown in Figure 2, and pneumonia was the major cause of death. Eight deaths were considered as PEG-related deaths, according to the reports of the doctors. On the other hand, among 28 surviving patients (6.5%), PEG was removed.

Continuous variables of demographic and laboratory data at PEG installation were first compared between alive and dead patients (Table 1). Age, CRP, AST, BUN

| Variable                      | Total (n = 931) | Alive (n = 429) | Dead (n = 502) | P-value |
|-------------------------------|----------------|----------------|---------------|---------|
| Age (yr)                      | 81.4 ± 7.8     | 80.0 ± 7.9     | 82.6 ± 7.6    | < 0.0001† |
| Height (cm)                   | 153.0 ± 10.4   | 152.4 ± 10.5   | 153.5 ± 10.2  | 0.20†   |
| Weight (kg)                   | 44.7 ± 10.7    | 44.9 ± 10.8    | 44.6 ± 10.6   | 0.79†   |
| Body mass index (kg/m²)       | 19.3 ± 3.7     | 19.5 ± 4.0     | 19.1 ± 3.6    | 0.22†   |
| Body temperature (℃)          | 36.7 ± 0.5     | 36.7 ± 0.5     | 36.7 ± 0.5    | 0.82†   |
| White blood cell (/μL) 25/50/75 percentile | 5470/6770/8700 | 5500/6640/8570 | 5420/6800/8800 | 0.33‡   |
| C-reactive protein (mg/dL) 25/50/75 percentile | 0.4/1.2/2.8    | 0.4/1.0/2.4    | 0.4/1.2/3.2   | 0.016‡  |
| Hematocrit (%) 25/50/75 percentile | 29.8/33.5/37.1 | 30.9/34.2/37.7 | 29.2/32.8/36.6 | 0.0001‡ |
| Hemoglobin (g/dL) 25/50/75 percentile | 9.8/11.0/12.3  | 10.1/11.3/12.6 | 9.5/10.8/12.1 | 0.0001‡ |
| Aspartate aminotransferase (IU/L) 25/50/75 percentile | 18/24/35      | 18/23/31      | 18/24/39     | 0.019‡  |
| Alanine aminotransferase (IU/L) 25/50/75 percentile | 12/19/33      | 12/19/29      | 11/20/40    | 0.22‡   |
| Blood urea nitrogen (mg/dL) 25/50/75 percentile | 12.8/17.7/24.8 | 12.4/17.0/23.1 | 13.0/18.6/26.1 | 0.018‡  |
| Serum creatinine (mg/dL) 25/50/75 percentile | 0.42/0.59/0.80 | 0.40/0.56/0.76 | 0.44/0.60/0.81 | 0.0096‡ |
| Albumin (g/dL) 25/50/75 percentile | 2.6/3.0/3.3   | 2.7/3.0/3.4   | 2.6/2.9/3.2  | 0.0013‡ |

†The Student t-test was applied because the distribution was considered as normal; ‡The Mann-Whitney test was applied because the distribution was considered as not normal.

Figure 1 The distribution of primary diagnosis warranting percutaneous endoscopic gastrostomy. 1: Parkinson’s disease (7%); 2: Amyotrophic lateral sclerosis (2%); 3: Multiple system atrophy (2%); 4: Other neurological disease (2%); 5: Cerebral infarction (40%); 6: Cerebral hemorrhage (11%); 7: Subarachnoid hemorrhage (3%); 8: Other cerebrovascular disease (1%); 9: Severe dementia (15%); 10: Mild dementia (3%); 11: Other type of dementia (14%).

Figure 2 Causes of death classified by the doctors. 1: Pneumonia (59%); 2: Cardiac (14%); 3: Cancer (3%); 4: Other (22%); 5: Unknown (2%).

Figure 3 Kaplan-Meier survival curve of 931 patients. PEG: Percutaneous endoscopic gastrostomy.

as PEG-related deaths, according to the reports of the doctors. On the other hand, among 28 surviving patients (6.5%), PEG was removed.

Continuous variables of demographic and laboratory data at PEG installation were first compared between alive and dead patients (Table 1). Age, CRP, AST, BUN
Suzuki Y et al. PEG in Japan

A. Log-rank test: $P < 0.0001$

B. Log-rank test: $P = 0.0039$

C. Log-rank test: $P = 0.66$

D. Log-rank test: $P = 0.24$

E. Log-rank test: $P = 0.0002$

F. Log-rank test: $P = 0.0084$

G. Log-rank test: $P = 0.12$

H. Log-rank test: $P = 0.0058$

I. Log-rank test: $P = 0.96$
Figure 4  Kaplan-Meier survival curves compared. A: Gender; B: Previous history of pneumonia; C: Dementia; D: Previous history or comorbidity of diabetes; E: Previous history of ischemic heart disease; F: Presence of malnutrition as judged by the doctors; G: Starvation period before having percutaneous endoscopic gastrostomy: none, within 1 wk, within 30 d, more than 30 d; H: Cerebrovascular disease as an underlying disease; I: Neurological disease as an underlying disease. PEG: Percutaneous endoscopic gastrostomy.

Table 2  Cox proportional hazard models

| Variable | Single variable analyses | Multivariate analysis |
|----------|-------------------------|----------------------|
|          | Crude HR | 95% CI | P-value | AHR | 95% CI | P-value |
| Age (yr) | 1.03 | 1.01-1.04 | < 0.001 | 1.02 | 1.00-1.03 | 0.009 |
| C-reactive protein (mg/dL) | 1.07 | 1.05-1.10 | < 0.001 | 1.04 | 1.01-1.07 | 0.005 |
| Hemoglobin (g/dL) | 0.91 | 0.87-0.95 | < 0.001 | 0.98 | 0.92-1.05 | 0.530 |
| Alanine aminotransferase (IU/L) | 1.01 | 1.00-1.01 | < 0.001 | 1.00 | 1.01-1.00 | 0.170 |
| Blood urea nitrogen (mg/dL) | 1.01 | 1.01-1.02 | < 0.001 | 1.01 | 1.00-1.02 | 0.003 |
| Serum creatinine (mg/dL) | 0.99 | 0.95-1.03 | 0.640 | 0.94 | 0.83-1.05 | 0.280 |
| Albumin (g/dL) | 0.52 | 0.43-0.63 | < 0.001 | 0.67 | 0.52-0.85 | 0.001 |
| Female | 0.70 | 0.58-0.83 | < 0.001 | 0.60 | 0.48-0.73 | < 0.001 |
| No history of pneumonia | 0.76 | 0.63-0.92 | 0.004 | 0.99 | 0.79-1.24 | 0.950 |
| No history of ischemic heart disease | 0.66 | 0.53-0.82 | < 0.001 | 0.69 | 0.54-0.88 | 0.003 |
| No malnutrition | 0.76 | 0.63-0.93 | 0.009 | 1.09 | 0.85-1.39 | 0.490 |
| Cerebrovascular disease | 0.78 | 0.66-0.93 | 0.006 | 0.83 | 0.67-1.02 | 0.080 |

Adjusted for all the variables listed in the table. HR: Hazard ratio; CI: Confidence interval; AHR: Adjusted hazard ratio.

and Cr were significantly higher in patients who died than in those who survived. In contrast, Ht, Hb and albumin were significantly higher in patients who survived than in patients who died. Regarding PEG-related death, albumin levels were significantly lower (Mann-Whitney U test: \( P = 0.002 \)).

A Kaplan-Meier survival curve of the 931 patients was drawn (Figure 3): 99% survived more than 7 d; 95% survived more than 30 d; 88% survived more than 60 d; 75% survived more than 6 mo; 66% survived more than 1 year. Of the 931 patients, 50% and 25% survived 753 and 1647 d, respectively. Kaplan-Meier survival curves were then drawn for nominal or ordinal data (Figure 4). The prognosis of female patients was better than that of males (Figure 4A). Patients who had no history of pneumonia (Figure 4B) or ischemic heart disease (Figure 4E) survived longer than those with a history of the diseases. Patients who were considered as having malnutrition at the time of operation showed poorer survivals than those without malnutrition (Figure 4F). Patients whose comorbidity was cerebrovascular disease had a better outcome than patients with other comorbidities (Figure 4E). In contrast, the prognosis of patients with dementia (Figure 4C), diabetes (Figure 4D), or neurological disease (Figure 4I) were not different from those without the conditions. Duration of starvation before the PEG procedure had no significant impact on patient survival (Figure 4G).

Finally, using variables significant in the above analyses, Cox proportional hazard models were computed in single variable and multivariate analyses (Table 2). In single variable hazard models, patients with older age, and higher CRP, AST and BUN did show a significantly enhanced crude HR whereas higher Hb and albumin reduced the crude HR. In addition, no history of pneumonia or ischemic heart disease, no malnutrition, but a history of cerebrovascular disease significantly decreased crude HRs. However, in the multivariate hazard model, older age, higher CRP, higher BUN, lower albumin, male gender and a previous history of ischemic heart disease were significant risk factors of death after PEG insertion.

**DISCUSSION**

In this study, 502 deaths were observed (mortality 53%). However, 99%, 95%, 88%, 75% and 66% of 931 patients survived more than 7, 30, 60 d, 6 mo and 1 year, respectively. In addition, 50% and 25% of the patients survived 753 and 1647 d, respectively, suggesting that more than half of geriatric patients treated with PEG may survive more than 2 years. Although the situations of each study may not be the same, the overall survival rate of this study is superior\(^{[16-18]}\) or equivalent to previous reports\(^{[11-13]}\). Eight deaths out of 931 in the study population were reported as PEG-related, a rate almost equal to that in previous studies\(^{[16-18]}\). Although urinary tract infection and previous aspiration were predictive factors for death at 1 wk after PEG\(^{[16]}\) and CRP was found to be predictive of early mortality\(^{[17]}\), we also found that a lower albumin level was a significant risk factor for PEG-related death, which was a novel finding.

We also attempted to delineate prognostic factors for geriatric patients treated with PEG. In single variable analyses, older age, higher CRP, lower Ht/Hb, higher AST, higher BUN, lower albumin as well as male gender, previous history of pneumonia or ischemic heart disease, malnutrition, and non-cerebrovascular disease as an underlying disease at the PEG procedure were significantly associated with death. In a multivariate hazard model, older age, higher CRP and higher BUN were significant poor prognostic factors of death after PEG formation, where-
as higher albumin, female gender and no previous history of ischemic heart disease were markedly better prognostic factors. Thus, Hb, AST, previous history of pneumonia, malnutrition and cerebrovascular disease as an underlying disease were considered as confounders. Among prognostic factors significant in our study, older age, male sex, lower albumin levels and a previous history of pneumonia or aspiration were already recognized as poor prognostic factors\(^{18-24}\). In our single variable Cox hazard model, cerebrovascular disease as an underlying disease was a good prognostic factor, which was consistent with the previous evidence that patients with a previous diagnosis of stroke were more likely to be discharged home than others\(^{25}\). Thus, CRP, BUN and a previous history of ischemic heart disease were found as novel prognostic factors in our study.

The results of this study should be interpreted in the context of the study strengths and limitations. The study was performed in multiple community and tertiary hospitals spread over Japan, which enhanced its generalizability. To minimize selection bias, collaborating doctors were asked to choose 20 consecutive patients. The sample size was close to 1000 and the results of the Cox hazard models were considered relatively robust. On the other hand, because of the retrospective nature of the study, we could collect only basic clinical information that might result in recall bias in areas such as previous histories and diagnosis of underlying diseases.

In conclusion, these results suggest that more than half of geriatric patients treated with PEG may survive longer than 2 years in Japan. In the Cox proportional multivariate analysis, older age, higher CRP and higher BUN were significant poor prognostic factors of death after PEG, whereas higher albumin, female gender and no previous history of ischemic heart disease were markedly better prognostic factors.

**COMMENTS**

**Background**

Percutaneous endoscopic gastrostomy (PEG) has been widely used for patients with swallowing difficulty, because of reduced laryngopharyngeal discomfort and a lower risk of aspiration pneumonia compared with the nasogastric tube. However, PEG feeding was found to be associated with an absolute increase in mortality of underlying diseases. In spite of the evidence, PEG feeding was found to be associated with an absolute increase in risk of death compared with nasogastric feeding. In spite of the evidence, PEG has been widely used especially for geriatric patients with the increasingly aging society.

**Research frontiers**

Despite the very large number of patients receiving this intervention, there is insufficient evidence to suggest that PEG is beneficial for patients with swallowing difficulty due to dementia or other chronic diseases.

**Innovations and breakthroughs**

The patients were selected in a consecutive manner and followed up over a long time period.

**Applications**

In a Cox proportional multivariate analysis, older age, higher CRP and higher BUN were significant poor prognostic factors of death after PEG, whereas higher albumin, female gender and no previous history of ischemic heart disease were markedly better prognostic factors. The authors especially determined that a lower albumin level was a significant risk factor for PEG-related death, which was a novel finding.

**Peer review**

Good comprehensive effort, gives nice insight into PEG in elderly.

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