

[ORIGINAL ARTICLE]

Factors for Predicting Outcomes among Non-HIV Patients with Pulmonary Tuberculosis

Toshinori Tsukahara¹, Nobuyuki Horita¹, Ken Tashiro¹, Kenjiro Nagai¹, Masaharu Shinkai¹,
Masaki Yamamoto¹, Takashi Sato¹, Yu Hara¹, Hideyuki Nagakura¹, Yuji Shibata¹,
Hiroki Watanabe¹, Kentaro Nakashima¹, Ryota Ushio¹, Akimichi Nagashima¹,
Misako Ikeda¹, Atsuya Narita¹, Katsuhito Sasaki¹, Nobuaki Kobayashi²,
Makoto Kudo² and Takeshi Kaneko¹

Abstract:

Objective Onodera's Prognostic Nutritional Index (PNI), determined as "10× albumin (g/dL) + 0.005× lymphocyte count (/μL)," was originally designed to determine the risk of complications following gastrointestinal surgery. This single-center, retrospective observational study was designed to investigate whether or not the PNI can predict the treatment outcome.

Methods We consecutively reviewed HIV-negative pulmonary tuberculosis adults in an isolation ward. Most patients were being treated with standard three- or four-drug regimens. Patients were discharged after consecutive negative smears/cultures were confirmed. The risk of all-cause death was assessed using a multivariable Cox proportional hazard model and a log-rank trend test.

Results During the observation period, we observed 371 consecutive patients with a median age of 72 (interquartile range [IQR]: 54-82) years. In our cohort, 295 (79.5%) patients were discharged alive, and 76 (20.5%) died in-hospital. Patients who died in-hospital had a lower PNI [median 21.2 (IQR: 18.5-25.9)] than those who were discharged alive [median 35.1 (IQR: 28.0-43.3); $p < 0.001$]. The area under the receiver operating characteristic curve was 0.87. After dividing the patients based on the baseline PNI quartile, those patients with a lower PNI showed a poorer survival than those with a higher PNI (log-rank trend $p < 0.001$). After adjusting for other baseline variables, the baseline PNI was still associated with in-hospital death with a hazard ratio of 0.86 (95% confidence interval: 0.82-0.91, $p < 0.001$).

Conclusion Our results showed that a low PNI was clearly related to a poor survival prognosis in smear-positive HIV-negative pulmonary tuberculosis inpatients.

Key words: antibiotics, blood cell count, cohort study, nutrition, pulmonary tuberculosis

(Intern Med 56: 3277-3282, 2017)

(DOI: 10.2169/internalmedicine.9120-17)

Introduction

Mycobacterium tuberculosis (TB) is a pathogenic microorganism that is typically spread through the air when a patient with pulmonary TB coughs. Approximately nine million people newly develop TB every year, and one-third of the world's population is thought to be infected with TB (1).

TB bacilli often affect the malnourished, immunosuppressed, and elderly (2-4). According to World Health Organization reports, country-level socio-economical background is reflected in TB epidemiology (5). For example, TB in the South-East Asia and African regions has a high prevalence of HIV-coinfection and high mortality from TB. Furthermore, TB in some Western Pacific countries is characterized by occurring most frequently among the elderly. Currently,

¹Department of Pulmonology, Yokohama City University Graduate School of Medicine, Japan and ²Respiratory Disease Center, Yokohama City University Medical Center, Japan

Received: March 2, 2017; Accepted: April 20, 2017; Advance Publication by J-STAGE: October 11, 2017

Correspondence to Dr. Nobuyuki Horita, nobuyuki_horita@yahoo.co.jp

most TB patients can be cured if a combination antibiotic regimen is properly administered. In addition to antibiotics, support of the host's immune response by an adequate nutritional status plays an important role in TB care. Therefore, malnutrition and immunodeficiency negatively affect the prognosis of tuberculosis patients (6, 7).

The serum albumin level and total lymphocyte counts are commonly used measurements to determine a patient's nutritional status. Onodera's Prognostic Nutritional Index (PNI) is an indicator that was originally designed to predict the prognosis and risk of complications following gastrointestinal surgery (8, 9). PNI is additionally used to evaluate the preoperative condition of non-gastrointestinal cancer patients (9, 10). However, few studies have explored whether or not PNI can be a prognostic marker in patients with non-malignant, non-surgical backgrounds. Given the mutual interaction between nutritional status and immunity, it is reasonable to hypothesize that PNI can be a good indicator when evaluating pulmonary TB patients.

This single-center observational study was designed to investigate whether or not the lymphocyte count and serum albumin level can be used to predict the treatment outcome of smear-positive HIV-negative pulmonary tuberculosis inpatients with a primary focus on Onodera's PNI.

Materials and Methods

This retrospective observational study was carried out in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects published in 2015 by Ministry of Health, Labour and Welfare, Japan (11). In accordance with these guidelines, informed consent of the patients was waived because the study adopted a retrospective observational design. The Institutional Review Board of Yokohama City University approved the study protocol (Approved ID: B150701004).

Inclusion criteria

We retrospectively and consecutively obtained the data of patients who satisfied the following criteria: (i) Smear-positive HIV-negative pulmonary tuberculosis inpatients, (ii) admitted to the isolation ward of our university hospital from January 2007 to November 2015, (iii) ≥ 16 years of age, and (iv) antibiotics initiated on admission.

The diagnosis of TB was made based on one or more of the following: culture, polymerase chain reaction, or a loop-mediated isothermal amplification assay (4). The HIV status was checked for every patient on admission.

Antibiotics regimen

We initiated directly observed treatment in an isolation ward. The first-choice regimen is two months of combined isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) followed by four months of isoniazid and rifampicin (2, 12). The alternative regimen is two months of combined isoniazid, rifampicin, and ethambutol (HRE) followed by seven

months of isoniazid and rifampicin (2, 12). This alternative HRE regimen was mainly selected for patients who had a high risk of drug-induced liver injury. When neither HRZE nor HRE were appropriate, other regimens were administered. The isoniazid and rifampicin maintenance therapy was prolonged when a patient had a cavity lesion, miliary TB, immunosuppressant usage, or persistent smear positivity after two months of treatment. The dose of each antibiotic was as follows: isoniazid 5 mg/kg/day (maximum 300 mg/day), rifampicin 10 mg/kg/day (maximum 600 mg/day), pyrazinamide 25 mg/kg/day (maximum 1,500 mg/day), and ethambutol 15-20 mg/kg/day (maximum 750-1,000 mg/day) (12).

Assessment on admission

Onodera's PNI was determined as follows: $10 \times \text{albumin (g/dL)} + 0.005 \times \text{lymphocyte count (/}\mu\text{L)}$ (8, 9). According to the Onodera's report, a preoperative PNI >45 suggests that resection and anastomosis of the gastrointestinal tract can be safely practiced, PNI of 40-45 suggests that the procedure may be dangerous, and PNI <40 suggests that such an operation may be contraindicated (8).

Other baseline patient data on admission regarding X-ray, sputum exam, and blood tests were also obtained.

The smear grade indicating the pretreatment bacterial load was classified into four grades according to Japanese guidelines using Ziehl-Neelsen stain ($\times 1,000$): (\pm) ≥ 1 AFB/ 300 fields, (+) ≥ 1 AFB/ 100 fields, (2+) ≥ 1 AFB/ 10 fields, and (3+) ≥ 10 AFB/ field.

Outcomes

When a patient who was taking effective chemotherapy with clinical improvement was proven not to be infective, we discharged the patient. Non-infectiveness was confirmed based on three or more consecutive smear-negative or culture-negative sputum samples obtained on different days (13). Sputum samples were taken once a week. We used death certificates to determine the cause of death.

Statistical analyses

Continuous variables were presented as the median and interquartile range (IQR) unless otherwise specified. The correlation between PNI and other parameters was assessed using Spearman's rank correlation test, wherein, $|r| < 0.2$ indicates no meaningful correlation, $0.2 \leq |r| < 0.4$ indicates a weak correlation, $0.4 \leq |r| < 0.6$ indicates a moderate correlation, $0.6 \leq |r| < 0.8$ indicates a strong correlation, and $0.8 \leq |r|$ indicates a very strong correlation. The multivariable Cox proportional hazard model was used to estimate the hazard ratio (HR) adjusted by other variables. A log-rank trend test was used to compare the Kaplan-Meier survival curves. A Mann-Whitney test was used to compare non-parametric non-paired continuous variables.

All analyses were performed using the Excel Toukei 2012 (SSRI, Tokyo, Japan) or GraphPad Prism, version 6.0 (GraphPad Software, San Diego, USA) software programs.

Table 1. Background Patient Characteristics on Admission, Treat Regimen, and Outcomes.

N=371	
Age (years)	72 (54-82)
Sex (female)	146 (39.4%)
Cavity on X-ray	155(41.8%)
Bilateral infiltration on X-ray	273 (73.6%)
Smear on admission $\geq 2+$	206 (55.5%)
Previous history of TB treatment	41 (11.1%)
Concomitant extra-pulmonary TB	39 (10.5%)
Diabetes	101 (27.2%)
Immunosuppressant	45 (12.1%)
Chronic cardiac disease	54 (14.6%)
Chronic pulmonary disease	44 (11.9%)
Chronic liver disease	42 (11.3%)
Chronic renal disease	44 (11.9%)
Active malignancy	42 (11.3%)
Total protein (g/dL)	6.6 (5.85-7.2)
Hemoglobin (g/dL)	11.1 (9.7-12.6)
Aspartate aminotransferase (IU/dL)	25 (19-43)
Creatinine (mg/dL)	0.65 (0.51-0.90)
Albumin (g/dL)	2.8 (2.2-3.6)
Lymphocyte/leukocyte count (%)	11.9 (6.0-18.0)
Lymphocyte count (/ μ L)	803 (433-1,212)
Prognostic nutritional index	32.0 (24.7-41.1)
Treatment regimen	
HRZE	217 (58.5%)
HRE	124 (33.4%)
Other regimen	30 (8.1%)
Outcomes	
Discharged alive	295 (79.5%)
Died in-hospital	76 (20.5%)

HRZE: isoniazid, rifampicin, pyrazinamide, and ethambutol, HRE: isoniazid, rifampicin, and ethambutol, TB: tuberculosis
 Parentheses indicate the interquartile range or percentage, depending on the outcome.

Table 2. Spearman's Rank Correlation Coefficients (r) with the Prognostic Nutritional Index.

	r	p value
Age (years)	-0.45	<0.001
Sex (female)	-0.11	0.035
Cavity on X-ray	0.03	0.587
Bilateral infiltration on X-ray	-0.30	<0.001
Smear on admission $\geq 2+$	-0.08	0.102
Previous history of TB treatment	0.05	0.379
Concomitant extra-pulmonary TB	-0.08	0.141
Diabetes	-0.01	0.895
Immunosuppressant	-0.21	<0.001
Chronic cardiac disease	-0.17	0.001
Chronic pulmonary disease	0.02	0.727
Chronic liver disease	-0.22	<0.001
Chronic renal disease	-0.09	0.085
Active malignancy	-0.04	0.495
Total protein (g/dL)	0.73	<0.001
Hemoglobin (g/dL)	0.60	<0.001
Aspartate aminotransferase (IU/dL)	-0.47	<0.001
Creatinine (mg/dL)	0.13	0.013

TB: tuberculosis

All data were evaluated on admission.

A low PNI was observed for patients with older age ($r=-0.45$, $p<0.001$), bilateral infiltration on X-ray ($r=-0.30$, $p<0.001$), immunosuppressant ($r=-0.21$, $p<0.001$), chronic liver disease ($r=-0.22$, $p<0.001$), and high aspartate aminotransferase ($r=-0.47$, $p<0.001$). The total protein ($r=0.73$, $p<0.001$) and hemoglobin ($r=0.60$, $p<0.001$) levels positively correlated with the PNI (Table 2).

A comparison of the surviving and dead patients

In our cohort, 295 (79.5%) patients were discharged alive, and 76 (20.5%) patients died in-hospital. The cause of death was tuberculosis for 63 patients and non-tuberculosis for 13. One patient each died from pneumonia, lung cancer, acute myocardial infarction, heart failure, brain bleeding, brain infarction, hepatocellular carcinoma, liver cirrhosis, chronic hepatitis C, autoimmune hepatitis, pan peritonitis, renal failure, and sepsis. The median durations of hospitalization were 67 days (IQR: 42.5-97.5) for patients who were discharged alive and 26 days (IQR: 12-58.5) for those who died in-hospital. The lymphocyte count [median 872/ μ L (IQR: 532-1,307) for surviving patients; median 356/ μ L (IQR: 147-658) for non-surviving patients; $Z=7.1$; $p<0.001$] and serum albumin level [median 3.1 g/dL (IQR: 2.5-3.8) for surviving patients; median 2.0 g/dL (IQR: 1.7-2.3) for non-surviving patients; $Z=9.9$; $p<0.001$] were significantly lower for the patients who died in-hospital than for patients who were discharged alive (Fig. 1A, B).

PNI and the prognosis

Patients who died in-hospital had a lower PNI [median 21.2 (IQR: 18.5-25.9)] than those who were discharged alive [median 35.1 (IQR: 28.0-43.3); $Z=10.0$; $p<0.001$] (Fig. 1C).

Results

Patients' background characteristics

During the observation period, 371 consecutive patients satisfied the inclusion criteria. Our cohort consisted of 225 men (60.6%) and 146 women (39.4%) with a median age of 72 (IQR: 54-82) years.

Among the 371 patients in our cohort, 155 (41.8%) had one or more pulmonary cavities on X-ray, and bilateral infiltration on X-ray was observed for 273 (73.6%) patients (Table 1). The medians of the total white blood cell count, lymphocyte percentage, and absolute lymphocyte count were 7,100/ μ L (IQR: 5,500-9,400), 11.9% (IQR: 6.0-18.05), and 803/ μ L (IQR: 433-1,212), respectively.

In our cohorts, 217 (58.5%), 124 (33.4%), and 30 (8.1%) patients were treated with HRZE, HRE, and other regimens, respectively.

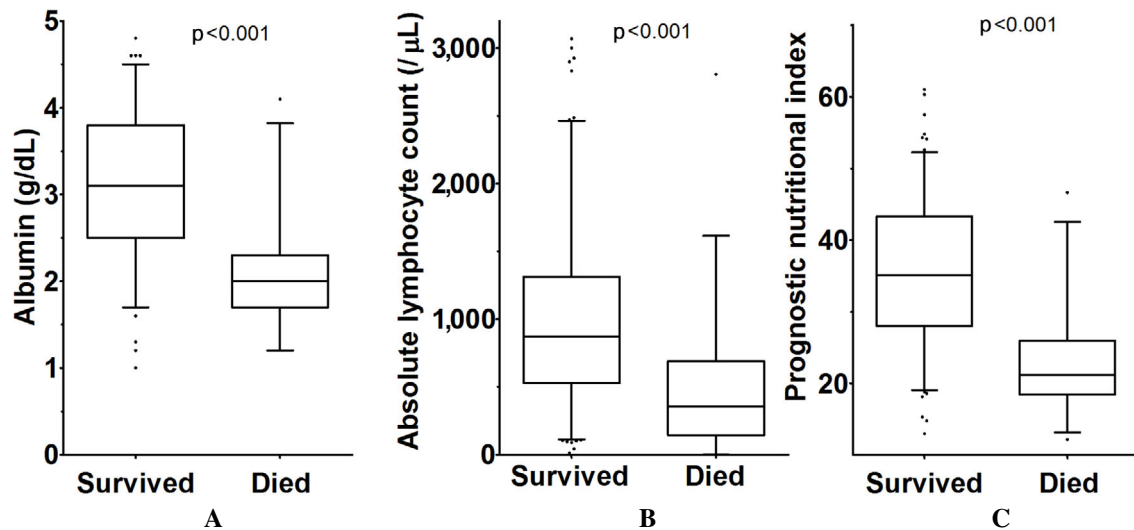


Figure 1. Comparisons of the albumin level, lymphocyte count, and the prognostic nutritional index. The central bar indicates the median. The bottom and top of the box indicate the 25th and 75th percentiles, respectively. The whiskers indicate the 2.5th and 97.5th percentiles. *p* is for the Mann-Whitney test. Survived: patients who were discharged alive. Died: patients who died in-hospital

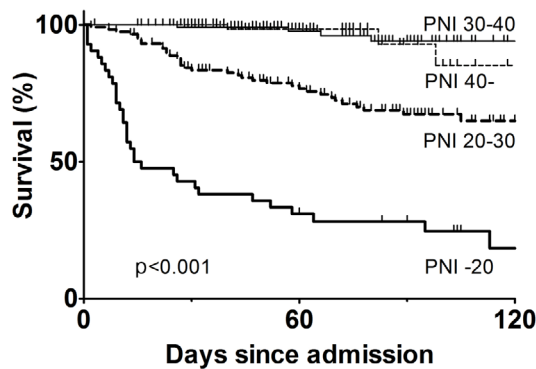


Figure 2. Kaplan Meier survival curve. PNI: prognostic nutritional index. Patients discharged alive were censored.

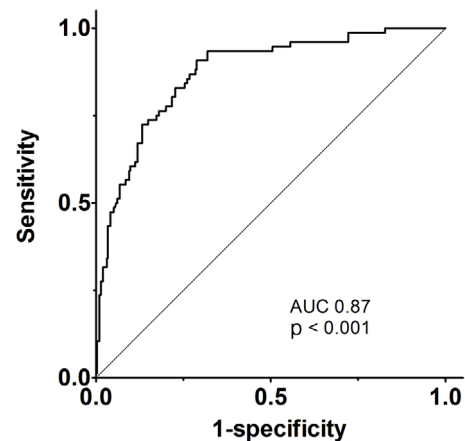


Figure 3. Receiver operating characteristic curve by the prognostic nutritional index for in-hospital death.

After dividing patients based on the baseline PNI, the patients with a lower PNI showed poorer survival curves than those with a higher PNI (Fig. 2, $p<0.001$). The survival rates at day 60 were 98%, 98%, 77%, and 31%, for patients with PNI of >40 , 30-40, 20-30, and <20 , respectively. The survival curves for PNI >40 and that for a PNI of 30-40 crossed frequently, with no significant differences in the curves for these two groups ($p=0.638$).

According to the receiver operating characteristic curve, the PNI had significant prognostic value for detecting in-hospital mortality ($p<0.001$, area under the curve 0.87) (Fig. 3).

After adjusting for other baseline variables, the baseline PNI was still associated with in-hospital death with an HR of 0.86 [95% confidence interval (CI): 0.82-0.91, $p<0.001$] (Table 3). In addition to the PNI, age (HR 1.06, 95% CI: 1.03-1.09, $p<0.001$), aspartate aminotransferase (HR 1.04, 95% CI: 1.02-1.06, $p<0.001$), and creatinine (HR 1.32, 95% CI 1.09-1.59, $p=0.004$) were found to be related to an increased risk of in-hospital death.

As a sensitivity analysis, we eliminated 13 patients who died of non-TB causes. Patients who died in-hospital had a lower PNI [median 20.2 (IQR: 18.1-26.0)] than those who were discharged alive [median 35.1 (IQR: 28.2-43.3); $Z=9.3$; $p<0.001$]. The area under the receiver operating characteristic curve was 0.87 ($p<0.001$).

Discussion

We carried out this observational study to evaluate whether or not the PNI can predict the treatment outcome of smear-positive HIV-negative pulmonary tuberculosis inpatients. First, we included a sufficient number of patients. Second, a range of analyses consistently suggested that the PNI score was related to the prognosis of TB inpatients. Third, it is biologically plausible that the serum albumin level and lymphocyte count are related to the death of TB patients.

Table 3. Multivariable Cox Proportional Hazard Analysis for All-cause Death.

	Hazard ratio (95% CI)	p value
Age (years)	1.06 (1.03-1.09)	<0.001
Sex (female)	1.31 (0.75-2.29)	0.348
Cavity on X-ray	1.58 (0.90-2.76)	0.111
Bilateral infiltration on X-ray	1.01 (0.46-2.17)	0.990
Smear on admission $\geq 2+$	1.06 (0.63-1.79)	0.820
Previous history of TB treatment	1.98 (0.92-4.28)	0.082
Concomitant extra-pulmonary TB	0.62 (0.25-1.53)	0.300
Diabetes	0.86 (0.46-1.59)	0.626
Immunosuppressant	1.22 (0.63-2.40)	0.554
Chronic cardiac disease	1.24 (0.67-2.27)	0.495
Chronic pulmonary disease	1.05 (0.51-2.17)	0.897
Chronic liver disease	1.30 (0.68-2.49)	0.419
Chronic renal disease	0.98 (0.48-2.02)	0.964
Active malignancy	1.77 (0.93-3.37)	0.084
Total protein (g/dL)	0.94 (0.66-1.33)	0.710
Hemoglobin (g/dL)	1.04 (0.89-1.21)	0.623
Aspartate aminotransferase (IU/dL)	1.04 (1.02-1.06)	<0.001
Creatinine (mg/dL)	1.32 (1.09-1.59)	0.004
Prognostic nutritional index	0.86 (0.82-0.91)	<0.001

CI: confidence interval, TB: tuberculosis

All data listed above were evaluated on admission.

In the 1980s, several researchers developed indices for evaluating preoperative patients. In that era, surgeons tried to improve the nutritional status of preoperative patients whose nutritional indices scores were poor using total parenteral nutrition. These indices usually consisted of age, albumin level, transferrin level, serum zinc level, peripheral lymphocyte count, triceps skinfold, arm circumference, and purified protein derivative skin reaction. Such indices were often criticized because they were often too complicated for practical use (14). Among the indices, Onodera's PNI was designed for patients who were scheduled to undergo gastrointestinal surgery (8). This index was useful due to its simplicity and good predictive value for postoperative complications such as ruptured suture, major gastrointestinal bleeding, and respiratory infection. Later, Onodera's PNI was further validated for assessing the risk of postoperative complications in patients with cancer of other organs. Similarly, evidence has suggested that the PNI score is associated with the short- and long-term outcomes of various cancers. In 2014, Sun et al. carried out a systematic review and a meta-analysis by collecting studies concerning the relationship between PNI and the cancer patient survival (9). This review included 14 studies involving a total of 3,414 patients with malignancies. A low PNI was associated with a poor overall survival and increased risk of post-surgery complications.

Currently, little evidence is available supporting the usefulness of PNI for evaluating non-cancer non-surgical setting patients. In 2012, Kang et al. retrospectively reviewed the clinical records of 522 peritoneal dialysis patients. The 5-year survival rates were 48.8%, 72.2%, and 77.1% in patients with a PNI of <40, 40-45, and >45, respectively (15).

In the present study, we explored the association between Onodera's PNI score and pulmonary tuberculosis. PNI may be useful as a prognostic marker of patients with other non-malignant non-surgical conditions, especially elderly patients. This is because malnutrition evaluated by albumin levels (16-18) and numbers of lymphocytes (19, 20) is a known risk factor for death in many medical conditions. Each component of the white blood cell count has a different clinical implication. For example, a high neutrophil count usually suggests both acute and chronic inflammation, which can indicate trauma, bacterial infection, chronic inflammatory disease, and adrenal deficiency. In contrast, a high lymphocyte count usually suggests a viral infection, intracellular infection, and the possibility of leukemia. A low lymphocyte count during tuberculosis infection indicates both malnutrition and an insufficient immunological response to TB infection, both of which are significantly related to a poor survival prognosis.

In the present study, PNI on admission clearly differentiated the in-hospital survival outcomes. However, the prognostic ability of PNI largely depended on the albumin level. Our previous studies revealed that many on-admission factors, such as the age, activity of daily living, oxygen requirement, and dehydration, were associated with the survival of smear-positive tuberculosis inpatients (6, 21). Among these factors, the age and albumin level seemed to be the two factors most predictive of the prognosis (6). Further studies are needed to clarify additional measurements that are related to the treatment outcome. Furthermore, why tuberculosis patients with a poor nutritional status have a higher risk of death should be investigated.

Several limitations associated with the present study warrant mention. First, its retrospective design might have adversely affected the evidence level. Second, our study lacked data on other nutritional parameters, such as transferrin and purified protein derivative skin reaction. Third, our TB cohort mainly consisted of elderly patients (Table 1). Therefore, validation in another cohort involving younger patients may be required.

In conclusion, we conducted a single-center, retrospective study to evaluate the impact of Onodera's PNI on the in-hospital death of smear-positive HIV-negative pulmonary tuberculosis inpatients. Our results showed that a low PNI was clearly related to a poor survival prognosis of in-hospital patients with smear-positive HIV-negative pulmonary tuberculosis.

The authors state that they have no Conflict of Interest (COI).

References

- Chiara I. WHO targets elimination of TB in over 30 countries. *Cent Eur J Public Health* **22**: 158, 163, 2014.
- American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: controlling tuberculosis in the United States. *Am J Respir Crit Care Med* **172**: 1169-1227, 2005.
- Prince DS, Peterson DD, Steiner RM, et al. Infection with *Mycobacterium avium* complex in patients without predisposing conditions. *N Engl J Med* **321**: 863-868, 1989.
- Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. *Am J Respir Crit Care Med* **161**: 1376-1395, 2000.
- World Health Organization. Global tuberculosis report 2016 [Internet]. 2016 [cited 2016 Nov. 22] Available from: http://www.who.int/tb/publications/global_report/en/
- Horita N, Miyazawa N, Yoshiyama T, et al. Development and validation of a tuberculosis prognostic score for smear-positive inpatients in Japan. *Int J Tuberc Lung Dis* **17**: 54-60, 2013.
- Horita N, Miyazawa N, Yoshiyama T, et al. Poor performance status is a strong predictor for death in patients with smear-positive pulmonary TB admitted to two Japanese hospitals. *Trans R Soc Trop Med Hyg* **107**: 451-456, 2013.
- Onodera T, Goseki N, Kosaki G. [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi* **85**: 1001-1005, 1984 (in Japanese, Abstract in English).
- Sun K, Chen S, Xu J, Li G, He Y. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* **140**: 1537-1549, 2014.
- Broggi MS, Patil D, Baum Y, et al. Onodera's prognostic nutritional index as an independent prognostic factor in clear cell renal cell carcinoma. *Urology* **96**: 99-105, 2016.
- Ministry of Health, Labour and Welfare, Japan. Ethical Guidelines for Medical and Health Research Involving Human Subjects [Internet]. 2015 [cited 2016 Nov. 22] Available from: http://www.lifescience.mext.go.jp/files/pdf/n1500_01.pdf#search='Ethics+Review+Procedures+concerning+Research+with+Human+Subjects+published+in+2015+by+Ministry+of+Health%2C+Labour+and+Welfare%2C+Japan'.
- Neff M, ATS, CDC, IDSA. ATS, CDC, and IDSA update recommendations on the treatment of tuberculosis. *Am Fam Physician* **68**: 1854, 1857-1858, 1861-1862, 2003.
- Sepkowitz KA. How contagious is tuberculosis? *Clin Infect Dis* **23**: 954-962, 1996.
- Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg* **139**: 160-167, 1980.
- Kang SH, Cho KH, Park JW, Yoon KW, Do JY. Onodera's prognostic nutritional index as a risk factor for mortality in peritoneal dialysis patients. *J Korean Med Sci* **27**: 1354-1358, 2012.
- Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* **341**: 403-409, 1999.
- Corti MC, Guralnik JM, Salive ME, Sorkin JD. Serum albumin level and physical disability as predictors of mortality in older persons. *JAMA* **272**: 1036-1042, 1994.
- Goldwasser P, Feldman J. Association of serum albumin and mortality risk. *J Clin Epidemiol* **50**: 693-703, 1997.
- Acanfora D, Gheorghide M, Trojano L. Relative lymphocyte count: a prognostic indicator of mortality in elderly patients with congestive heart failure. *Am Heart J* **142**: 167-173, 2001.
- Izaks GJ, Remarque EJ, Becker SV, Westendorp RG. Lymphocyte count and mortality risk in older persons. The Leiden 85-Plus Study. *J Am Geriatr Soc* **51**: 1461-1465, 2003.
- Nagai K, Horita N, Sato T, Yamamoto M, Nagakura H, Kaneko T. Age, dehydration, respiratory failure, orientation disturbance, and blood pressure score predicts in-hospital mortality in HIV-negative non-multidrug-resistant smear-positive pulmonary tuberculosis in Japan. *Sci Rep* **6**: 21610, 2016.

The Internal Medicine is an Open Access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).