The influence of American Society of Anesthesiologists Physical Status on patient morbidity and survival after total thyroidectomy

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Abstract. In cases of thyroid papillary carcinoma, a less aggressive cancer, surgeons may hesitate to perform total thyroidectomy on patients with poor general condition because these may experience longer survival without undergoing surgery. To investigate the influence of general patient condition on the patients’ survival who received total thyroidectomy, we utilized the American Society of Anesthesiologists Physical Status (ASA-PS). We retrospectively reviewed all patients undergoing total thyroidectomy under general anesthesia and graded by ASA-PS between 2004 and 2014. Patients with anaplastic carcinoma and metastatic thyroid renal cell carcinoma were excluded. There were 77 (30%), 149 (58%), and 30 (12%) ASA-PS 1, 2, and 3 cases, respectively. Patient age increased significantly with increasing ASA-PS score (median age of 53, 64, and 71 years for ASA-PS 1, 2, and 3). Hospitalization periods extended significantly for patients with ASA-PS 3. Twenty patients died during the study (3.89 median years). Five-year overall survival rates were 100%, 93%, and 79% for ASA-PS 1, 2 and 3, respectively. Patients in the ASA-PS 1 group had significantly better prognosis by log-rank test. Univariate analysis showed an increased risk of death as ASA-PS score increased (hazard ratio: 3.03, 95% confidence interval: 1.55–5.92, \( p = 0.00 \)). In multivariate analysis, including patient age and presence of malignancy, patient age was the only significant predictor of overall survival (hazard ratio: 1.09 by year, 95% confidence interval: 1.03–1.14, \( p = 0.00 \)). We concluded that a high ASA-PS score should not inhibit performance of total thyroidectomy if a patient’s age is suitable for the surgery.

Key words: Total thyroidectomy, ASA-PS, General condition, Morbidity, Overall survival
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We excluded three patients with anaplastic carcinoma and two patients with metastatic renal cell carcinoma because of their poor prognoses. Finally, 256 patients were enrolled in this study. Clinical information was collected by chart review including age at diagnosis, sex, treatment, postoperative morbidity, and survival. The patients comprised 57 men and 199 women, with ages ranging from 14 to 86 (median, 62) years. The distribution of tumor pathology was as follows: 182 malignant lesions (157 papillary carcinomas, 8 follicular carcinomas, 3 medullary carcinomas, and 14 poorly differentiated carcinomas) and 74 benign lesions (46 cases of adenomatous goiter; 26 of Grave’s disease, and 2 of Hashimoto thyroiditis). Patient characteristics are shown in Table 1.

The ASA-PS score was collected by preoperative anesthesiology charts and re-evaluated by board certified anesthesiologists (K.Y. and K.Y.). The ASA-PS was the primary independent variable. It ranges from 1 to 5, where 1 is “a normal healthy patient”, 2 is “a patient with mild systemic disease”, 3 is “a patient with severe systemic disease”, 4 is “a patient with severe systemic disease that is a consistent threat to life”, and 5 is “a moribund patient who is not expected to survive without the operation”. The last modification was approved by the ASA House of Delegates on October 15, 2014 [8].

To compare the patients’ characteristic and perioperative values among ASA scores, we collected data on the distribution of age, sex, presence of malignancy, duration of hospitalization, duration of postoperative stay, rate of preoperative heparinization or anticoagulant administration, and postoperative mortality. We also examined the distribution of postoperative morbidities by ASA classification. Finally, we estimated the influence of ASA classification on patient overall survival.

For the purpose of comparing the distribution between groups, the Chi-squared test was used to estimate differences. The Mann–Whitney U test was used to compare variables, such as age, days of postoperative stay, and days of hospitalization. The Kaplan–Meier method and log-rank test were adopted to analyze the differences in overall survival among the ASA-PS groups. The Cox regression model was adopted for univariate and multivariate analyses. These analyses were performed with Excel Tokiei 2010 (SAS institute Inc. Cary North Carolina), and P-values < 0.05 were regarded as significant.

Results

There were 77 ASA-PS 1 cases (30%), 149 ASA-PS 2 cases (58%) and 30 ASA-PS 3 cases (12%). The incidence of comorbidities and specific medications in ASA-PS2 and ASA-PS3 was shown in Table 2 and Table 3. The circulatory comorbidities were the most common in both ASA-PS 2 and ASA-PS 3 groups. There were some patients who received administration of antiplatelet or anticoagulant in ASA-PS2 and 3 groups.

Distributions of patient characteristics by ASA classification are shown in Table 4. Patient age increased significantly with increasing ASA-PS score (median age of 53, 64, and 71 years for respective ASA-PS 1, 2, and 3). Duration of the hospitalization and duration of postoperative hospitalization were significantly longer in the ASA-PS 3 group. The proportion of patients needing preoperative heparinization was also significantly higher in the ASA-PS 3 group. Compared with the other two groups, the proportion of malignant disease was the highest in the ASA-PS 1 group.

Table 1 Patient baseline characteristics

| Characteristic                              | N = 256 |
|--------------------------------------------|---------|
| Males                                      | 57      |
| Females                                    | 199     |
| Pathology                                  |         |
| Malignant                                  | 182     |
| Papillary adenocarcinoma                   | 157     |
| Follicular adenocarcinoma                  | 8       |
| Medullary adenocarcinoma                   | 3       |
| Poorly differentiated carcinoma             | 14      |
| Benign                                     | 74      |
| Adenomatous Goiter                         | 46      |
| Grave’s disease                            | 26      |
| Hashimoto Thyroiditis                      | 2       |
| Age, years                                 | 62 (14–86) |
| Additional surgical procedure with total thyroidectomy |         |
| Unilateral neck dissection                 | 53      |
| Bilateral neck dissection                   | 15      |
| Tracheostomy                               | 7       |
| Median postoperative stay, days            | 7 (3–103) |
| Median hospitalization, days               | 10 (7–105) |

Data in the table are presented as number of patients and median (range).
The distribution of the postoperative complications is shown in Table 5. Among 30 patients with postoperative recurrent nerve palsy (RNP), seven patients had RNP secondary to cancer invasion prior to surgery, and seven newly emergent RNPs were caused by resecting or shaving the nerve during the operation because of cancer invasion. The RNP was unrelated to cancer invasion in 16 patients (6.3%); it was transient in 14 and permanent 2 (0.8%) patients. No RNP was seen in patients with benign tumors. There was no relationship between morbidity of RNP and ASA-classification (Table 3). Life-threatening complications, such as pulmonary embolism and tracheal breakdown, were mostly seen in the ASA-PS 3 group. As a result, 2 patients in the ASA-PS 3 group died during the postoperative hospitalization (Table 2), one died of aspiration pneumonia on postoperative day 92 and the other died of pulmonary embolism on postoperative day 25. The former was an 80-year-old man with Parkinson disease, cognitive problems and severe diabetes mellitus, who underwent surgery for advanced medullary carcinoma. During surgery, one side of the recurrent laryngeal nerve and tracheal wall were resected because of cancer invasion. The patient’s condition was managed with a tracheal tube, but he had frequent troubles with the tube, which worsened his general condition. The latter was a 67-year-old man with hypertension, severe diabetes mellitus, atrial fibrillation under anticoagulant therapy, and a history of percutaneous coronary intervention, who underwent total thyroidectomy and tracheostomy for advanced papillary carcinoma with bilateral vocal cord paralysis. We replaced

| Table 2 | Distributions of the patient characteristic by ASA classification group |
|---|---|---|
| | ASA-PS 1 | ASA-PS 2 | ASA-PS 3 |
| N (%) | 77 (30) | 149 (58) | 30 (12) |
| Age, years, median (range) | 53 (14–75) | 64 (23–86) | 71 (40–86) |
| Males, n (%) | 16 (21) | 32 (21) | 9 (30) |
| Females, n | 61 | 117 | 21 |
| Malignant, n (%) | 53 (81) | 97 (66) | 22 (73) |
| Benign | 14 | 52 | 8 |
| Postoperative stay, days, median (range) | 7 (5–15) | 7 (3–86) | 8 (5–103) |
| Hospitalization, days, median (range) | 10 (7–18) | 10 (7–88) | 11.5 (7–105) |
| Preoperative heparinization | 0 (0) | 4 (3) | 4 (13) |
| Operation under anticoagulant | 0 (0) | 3 (2) | 0 (0) |
| Death in hospital without discharge | 0 (0) | 0 (0) | 2 (6.7) |

ASA-PS, American Society of Anesthesiologists Physical Status.

| Table 3 | Comorbidities and specific medications in ASA-PS2 patients |
|---|---|
| Disease status | n | % |
| Hypertension | 75 | 50% |
| Hyperlipidemia | 38 | 26% |
| Diabetes Mellitus | 32 | 21% |
| Hyperthyroidism | 16 | 11% |
| Bronchopulmonary disease | 14 | 9% |
| Previous stroke | 10 | 7% |
| Hepatitis | 8 | 5% |
| Dysrhythmia | 7 | 5% |
| Angina Pectoris | 7 | 5% |
| Chemotherapy for other malignancy | 6 | 4% |
| Previous myocardial infarction | 6 | 4% |
| Collagen disease | 6 | 4% |
| Psychiatric disorder | 4 | 3% |
| Gastrointestinal disease | 3 | 2% |

| Specific medication | n | % |
| Antiplatelet | 17 | 11% |
| Anticoagulant | 5 | 3% |

| Table 4 | Comorbidities and specific medications in ASA-PS3 patients |
|---|---|
| Disease status | n | % |
| Cardiac Dysfunction | 16 | 53% |
| (Implanted Pacemaker) | (4) | 13% |
| Poorly controlled diabetes mellitus | 8 | 27% |
| Renal failure undergoing dialysis | 6 | 20% |
| Poorly controlled hypertension | 2 | 7% |
| Severe bronchopulmonary disease | 2 | 7% |
| Severe thrombopenia | 2 | 7% |
| Parkinsonism | 2 | 7% |
| Rheumatic Arthritis | 2 | 7% |
| Specific medication | n | % |
| Antiplatelet | 4 | 13% |
| Anticoagulant | 7 | 23% |
The oral anticoagulant with intravenous heparin during the perioperative period; however, he presented a pulmonary embolism. Including these two deaths, there were 20 deaths during the observation period (3.89 median years): seven deaths were attributed to thyroid cancer and 13 deaths to other causes. Overall survival curves of each ASA-PS group are shown in Fig. 1. Five-year overall survival rates were 100%, 93%, and 79% for ASA-PS 1, 2 and 3 groups, respectively. Patients with ASA-PS 1 showed significantly better prognosis by log-rank test compared with those in the ASA-PS categories. The Cox proportional hazard model test was performed to investigate which factors among age, malignancy, and ASA-PS score, exerted a greater influence on patient overall survival (Table 6). Univariate analysis demonstrated increased risk of death with increasing ASA-PS score (hazard ratio: 3.03, 95% confidence interval: 1.55–5.92, \( p = 0.00 \)). However, multivariate analysis indicated that patient age was the only factor associated with overall survival (hazard ratio: 1.09 by year, 95% confidence interval: 1.03–1.14, \( p = 0.00 \)).

### Discussion

The ASA-classification was introduced in 1941 by Saklad in an attempt to provide a basis for comparison of statistical data in anesthesia [9]. This classification was revised in 1963 with the number of classes being reduced from seven to five [10]. Several retrospective studies have demonstrated a correlation between ASA classification and postoperative mortality, and the

| Table 5 | Distributions of postoperative complications by ASA classification |
|---------|---------------------------------------------------------------|
|         | ASA-PS 1 (n=77) | ASA-PS 2 (n=149) | ASA-PS 3 (n=30) |
| Postoperative RNP | 11 | 16 | 3 |
| Temporal RNP without cancer invasion | 7 | 7 | 0 |
| Permanent RNP without cancer invasion | 1 | 1 | 0 |
| Laryngeal edema | 0 | 7 | 1 |
| Hematoma (required re-operation) | 0 | 1 | 1 |
| Lymphorrhea | 2 | 4 | 0 |
| Pneumonia | 0 | 2 | 1 |
| Pulmonary embolism | 0 | 0 | 1 |
| Skin flap breakdown | 0 | 1 | 1 |
| Tracheal breakdown | 0 | 0 | 1 |

ASA-PS, American Society of Anesthesiologists Physical Status; RNP, Recurrent laryngeal nerve palsy. Data in the table are presented as number of patients.
proportion of patients corresponding to each class has been changing by the decade [5-7]. Vacanti examined 68,388 cases between 1964 and 1966 in 11 U.S. Naval Hospitals, and the proportion of patients in each class was 74%, 18%, and 5% for ASA-PS 1 to 3, respectively [6]. According to the report by Wolters in 1996, the proportion of patients in ASA-PS 1 decreased to 18% and those of ASA-PS 2 and 3 increased to 43% and 35% [7]. In 2015, Hackett et al. analyzed the data of a cohort of 2,297,629 patients from the 2012 ACS NSQIP database in order to evaluate patients across distinct surgical specialties [5]. Though they excluded patients with cardiac surgery, the proportion of patients in ASA-PS 1, 2, and 3 were 10%, 46%, and 38%, respectively. They also reported the postoperative morbidity and mortality increased with increasing ASA-PS. By ASA-PS 1, 2, and 3 categories, the morbidities were 2%, 5% and 14%, and the mortality was 0.02%, 0.14% and 1.41%, respectively. In the present study, the distribution of the ASA-classification was 30%, 58% and 12% for ASA-PS 1, ASA-PS 2, and ASA-PS 3, and the proportion of the patients with low risk seemed higher than that reported by Hackett et al. This is mainly because thyroid disease requiring total thyroidectomy occurred in comparatively younger and healthy individuals.

In the group of ASA-PS 3 patients, we had two cases of treatment-related death and one was considered as a postoperative death because this patient died within 30 postoperative days. Thus, the postoperative mortality in all patients was 0.4% and 3.3% in ASA-PS 3 patients. In past reports, the most frequent cause of postoperative death after thyroidectomy was hematoma [11, 12]. Especially among patients undergoing antiplatelet or anticoagulation therapy, the odds ratio of presenting postoperative hematoma was 2.12 [12]. In the present study, 12 patients were preoperatively treated with anticoagulants and 21 patients with antiplatelet therapy. Eight patients needed a high preoperative dose of heparinization, and three patients underwent total thyroidectomy while receiving antiplatelet therapy. Two patients in the ASA-PS 2 and ASA-PS 3 groups each presented postoperative cervical hematoma and required re-operation. One patient did not require anticoagulant or antiplatelet therapy and the other required perioperative intravenous heparinization instead of anticoagulant therapy. The morbidity of cervical hematoma was 0.8%, which was almost identical to that in past reports [12-14]. Fortunately, both hematomas were promptly controlled after the revision surgery.

Permanent RNP is the most common complication specific to thyroidectomy, with the morbidity in the past report ranging from 1% to 3% [14-18]. In the present case series, two cases of permanent RNP were unrelated to cancer invasion in the ASA-PS 1 and ASA-PS 2 groups. The morbidity of permanent RNP was 0.8%, which was not higher than the past report. Neither poorer general condition nor age was shown to be a risk factor of permanent RNP in this study. Further, of the 30 patients with postoperative RNP, seven patients already had palsy secondary to cancer invasion prior to the operation and seven newly emergent palsies were caused by resecting or shaving the nerve trans-operatively because of cancer invasion into the nerve. In the ASA-PS 3 group, one patient had preoperative palsy in both vocal cords and two patients presented postoperative RNP because of the intraoperative resection of the recurrent nerve owing to cancer invasion. Among these three patients, two died during postoperative hospitalization because of circulation–respiratory complications. Maximum care should be taken for patients in poorer general condition having RNP, because these patients present dysphagia that is caused by RNP, which can easily lead to serious consequences such as aspiration pneumonia.

Concerning the overall survival, univariate analysis revealed that the hazard ratio of death became more than three as ASA-PS increased by one category in this study. This result, added to the higher postoperative mortality rate up to 3.3% in the ASA-PS 3 group, may be an excuse to avoid total thyroidectomy in patients in poorer general conditions with thyroid cancer, which is comparatively less aggressive than cancers affecting other organs. Surgeons sometimes think that patients in poorer condition may benefit from a longer survival period without undergoing the indicated operation. However, multivariate analysis revealed that patient age was the only factor associated with overall survival and that higher ASA score was not a significant risk factor for poor overall survival. Moreover the incidences of permanent RNP or hematoma were not significantly different between hemi-thyroidectomy and total thyroidectomy in a large number of the report [14]. Based on these findings, we consider that a high ASA-PS score should not inhibit performance of total thyroidectomy if a patient’s age is suitable for the surgery.
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Conflict of Interest Disclosure

None of the authors have any potential conflicts of interest associated with this research.

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