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Proposed modification of the eighth edition of the AJCC-ypTNM staging system of esophageal squamous cell cancer treated with neoadjuvant chemotherapy: Unification of the AJCC staging system and the Japanese classification

Short running head: Staging system for ESCC

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19 **Disclosures:**

20 Taro Oshikiri, Hironobu Goto, Takashi Kato, Ryuichiro Sawada, Hitoshi Harada, Naoki

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2

3 **Synopsis:** Unification of the AJCC and Japanese systems yields a simpler and more precise

4 predictive system.

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1 Abstract

2 **Background**

3 The eighth edition of the American Joint Committee on Cancer (AJCC) tumor node
4 metastasis (AJCC-TNM 8th) system adopted the newly separate post-neoadjuvant
5 pathologic stage group (ypTNM). However, it is not compatible with the Japanese
6 pathologic classification after neoadjuvant chemotherapy (JPN-CT-pTNM). The aim of
7 this study is to clarify the subjects of the AJCC-ypTNM 8th and propose a unification of
8 the AJCC and Japanese systems to create novel AJCC-CT-pTNM 8th.

9 **Methods**

10 Participants were 309 esophageal squamous cell carcinoma (ESCC) patients who
11 underwent neoadjuvant chemotherapy followed by 3 stage esophagectomy between
12 2010 and 2019. Predictive probabilities of pN, pM in AJCC-ypTNM 8th and
13 JPN-CT-pTNM 11th systems were evaluated to propose novel system.

14 **Results**

15 In training data from 234 patients, the overall survival rate was statistically better for ypStage
16 IIIA than ypStage II (P=0.040) resulting in staging inversion in AJCC-ypTNM 8th. Predictive
17 probability of pathological N status in AJCC-ypTNM 8th (Akaike Information Criterion:
18 AIC=979.53) was superior to that in JPN-CT-pTNM 11th (AIC=999.07). In AJCC-ypTNM 8th,
19 71% (15/21) of ypM1 diseases were supraclavicular lymph nodes (No. 104 L/Ns as regional
20 in JPN-CT-pTNM 11th) metastases with considerably good prognosis. The predictive
21 probability of the novel AJCC-CT-pTNM 8th [unification of ypStage II and IIIA, conversion of
22 supraclavicular L/Ns metastases from ypM to ypN] (AIC=1054.24) was superior to that of the

existing AJCC-ypTNM 8th (AIC=1070.74). The feasibility of novel system was validated using test data from 70 patients.

Conclusions

Unification of the AJCC and Japanese systems yields a simpler and more precise predictive system after neoadjuvant chemotherapy.

Key words: esophageal squamous cell carcinoma (ESCC); American Joint Committee on Cancer (AJCC); post-neoadjuvant tumor node metastasis (ypTNM) staging; Japanese classification, AJCC-CT-TNM 8th

Background

The newest TNM classification for esophageal squamous cell carcinoma (ESCC), the eighth edition of the American Joint Committee on Cancer tumor node metastasis (AJCC-TNM 8th) cancer staging system, has been in use since 2017.[1,2] Significant changes relative to the AJCC-TNM 7th [3,4] included the introduction of novel classification concept for adenocarcinoma (AC) and ESCC, with the suggestion of distinguishing the clinical (c) stage group (cTNM), the classical pathologic (p) stage group (pTNM), and the newly separate post-neoadjuvant pathologic stage group (ypTNM) for both AC and ESCC.[5]

For advanced ESCC, neoadjuvant chemoradiotherapy (NACRT) or chemotherapy (NAC) followed by surgery is recognized as the standard therapy.[6-8] Thus, the introduction of ypTNM as a new category is groundbreaking because it is essential to distinguish between pre-treated and untreated patients with advanced ESCC. However, from before, there is a problem in assessing the pT0-2N1 population in the AJCC staging system. In concrete terms, in Japanese comprehensive data including more than 4,000 patients with ESCC who underwent esophagectomy and graded by AJCC-TNM 7th, the 5-year survival rate of pStage IIB (pT1-2/N1) was better than that of pStage IIA (pT3N0) (67.2% vs 58.6%).[9] In AJCC-ypTNM 8th, this problem persists: the survival rate of ypStage IIIA (pT0-2N1) is also better than that of ypStage II (pT3N0) as previous reports.[10,11] One of the conceivable reason is that AJCC-ypTNM 8th is applicated to two different populations; treated with NACRT and NAC. In comparison to NAC, there are some advantages of NACRT in increase of R0 resection and pathological complete

response leading to more complete resection and prolonged patient survival. On the contrary, increase of postoperative mortality and morbidity, radiation related complications, and prolonged treatment cycle are disadvantages.[12, 13] Thus, these two populations should be distinguished separately.

In worldwide big data to build AJCC-ypTNM 8th, majority of esophagectomies were done after NACRT. Thus, this system might not be specific to predict prognosis of patients treated with NAC which is standard neoadjuvant therapy in Japan.[8]

Moreover, there are some discrepancies between the AJCC staging system and the Japanese classification in N staging, M staging, and staging grouping, and these differences sometimes confuse surgeons. For N staging, AJCC-TNM 8th uses the number of lymph nodes (L/Ns), whereas the Japanese classification 11th (JPN-TNM 11th) uses grouping of L/Ns. In M staging, AJCC-TNM 8th treats supraclavicular L/Ns (which do not include lower cervical paratracheal nodes between the supraclavicular paratracheal space and apex of the lung) as distant metastases, whereas JPN-TNM 11th treats them as regional L/N (No. 104) metastases (Table 1).[5,14,15].

The aim of this study is to clarify the subjects of the AJCC-ypTNM 8th staging system (abbreviated as AJCC 8th) in comparison with the Japanese pathologic classification 11th after neoadjuvant chemotherapy (JPN-CT-pTNM 11th; abbreviated as JPN 11th) and propose the unification of the AJCC system and Japanese classification 11th to create novel AJCC-CT-pTNM 8th (abbreviated as Novel) staging system as simpler and more precise predictive system for NAC treated patients.

Patients and Methods

Patients and data retrieval

This was a multi-institutional, retrospective follow-up study of 309 patients with thoracic ESCC who underwent neoadjuvant therapy followed by 3 stage esophagectomy (cervical anastomosis) at Kobe University and Hyogo Cancer Center between 2010 and 2019.[16] In this population, data of 234 patients between 2010 and 2016 were used as training data and 70 patients between 2017 and 2019 were used as test data. Preoperative diagnosis was performed by endoscopy and enhanced computed tomography (CT). Lymph node metastasis was considered positive when the long axis of the lymph node measured ≥10 mm on the CT image. Positron emission tomography were also performed for almost all the patients.[17] Diagnosis of ESCC was based on the both AJCC-TNM 8th and JPN-TNM 11th.[5,14,15] As NAC, two cycles of cisplatin/5-fluorouracil (CF) were administered as preoperative chemotherapy to most patients with cT0-1N1-3M0-1 or cT2-3NanyM0-1 according to AJCC-TNM 8th.[5] According to M1 patients, they were limited to M due to supraclavicular lymph node metastasis which is treated as regional lymph node in JPN-TNM 11th. For some patients, three cycles of docetaxel/cisplatin/5-fluorouracil (DCF) were administered as part of Japanese clinical trial JCOG1109.[18] Patients who had undergone preoperative irradiation including definitive or neoadjuvant CRT were excluded. The Ethics Committee of Kobe University and the institutional review board

approved this study on December 21th, 2020 (receipt number B200304). All patients who met the inclusion criteria provided written informed consent.

Surgical procedures

All patients underwent 3 stage esophagectomy with mediastinal lymphadenectomy. At two institutions, the common practice of conducting thoracoscopic esophagectomy in the prone position was used for all surgical candidates with ESCC.[19,20] The abdominal procedure was performed by laparoscopic surgery or open laparotomy (OL). Gastric mobilization, abdominal lymphadenectomy, excision of the entire isolated esophageal specimen, and creation of the gastric conduit were performed sequentially. The conduit was generally raised via the posterior mediastinum. For patients in whom it was impossible to use gastric conduits for whatever reason, pedicled jejunum reconstruction was performed via the pre-sternal route. The site of the anastomosis was the neck. Three-field (neck, chest, and abdomen) lymph node dissection was basically performed for cT2 or 3 tumors in the upper or middle esophagus. Patients with clinical metastases to the supraclavicular lymph nodes (LNs) were also treated surgically. For three-field L/Ns dissection, the cervical nodes were removed through a collar incision. No particular change of surgical treatment was seen between 2010 and 2019.

Statistical analyses

All categorical data are presented as numbers (percentages). Differences between two groups were analyzed using the χ^2 test. Survival curves were estimated using the

Kaplan–Meier method and compared using the log-rank test. $P<0.05$ was considered statistically significant. To estimate the goodness-of-fit of each staging system based on Cox regression survival analysis, the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used. In this method of comparison, lower values of AIC and BIC indicate superior models. All statistical computations were performed using JMP 14 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

Patient characteristics are shown. A total of 304 patients (training cohort; 234 patients, test cohort; 70 patients) who underwent CF followed by 3 stage esophagectomy with two-field or three-field L/Ns dissection were included in the study. Four patients in training cohort and one patient in test cohort treated by DCF were excluded due to smallness of the number. Most patients underwent thoracoscopic esophagectomy in the prone position. In regard to resection status, negative and positive rates for residual tumor were 86% (201 patients) and 14% (circumferential margin positive; 7%, 16 patients, longitudinal margin positive; 7%, 17 patients) in training cohort. Those were 87% (61 patients) and 13% (circumferential margin positive; 7%, 5 patients, longitudinal margin positive; 6%, 4 patients) in test cohort (Supplemental Table).

Training data from 234 patients

Survival analyses and comparison using AJCC 8th and JPN 11th

Overall survival (OS) was estimated using AJCC 8th. The mean OS and median OS were 4.5 years and 5.5 years, respectively. The 5-year OS rates in AJCC 8th were as follows: ypStage I, 76% (n=52); ypStage II, 57% (n=32); ypStage IIIA, 78% (n=40); ypStage IIIB, 33% (n=69); ypStage IVA, 10% (n=20); and ypStage IVB, 24% (n=21) (Figure 1A). Prognosis of ypStage IIIA (ypT0-2N1) was statistically better than that of ypStage II (ypT3N0) (P=0.040). Prognosis of ypStage IVB (ypTanyNanyM1) was better than that of ypStage IVA, although the difference was not statistically significant. On the other hand, there was no OS inversion between each stage category in JPN 11th: CT-pStage 0, 79% (n=23); CT-pStage I, 76% (n=17); CT-pStage II, 65% (n=90); CT-pStage III, 29% (n=91); CT-pStage IVA, 9% (n=11); and CT-pStage IVB, 0% (n=2) (Figure 1B). All of the ypStage II patients (ypT3N0, n=32/32, 100%) and almost all ypStage IIIA patients (ypT0-2N1, n=36/40, 90%) in AJCC 8th were considered CT-pStage II according to JPN 11th (Table 1).

Evaluation of ypN (AJCC 8th)/CT-pN (JPN 11th) status

Among whole cohort, 15 patients who were positive for supraclavicular L/Ns (No. 104) were excluded from 234 patients because they were treated as ypM1 in AJCC 8th.[5,14,15] Hence, we estimated the correlation of ypN (AJCC 8th)/CT-pN (JPN 11th) status in 219 patients. On the whole, the two categories were significantly correlated. Especially, 74% (55/74) of ypN1 and 77% (55/71) of CT-pN1 coincide with each other. (P<0.0001). Next, we estimated the 5-year OS curves of ypN (AJCC 8th)/CT-pN (JPN 11th) (Figure 1C,D). Higher categories were associated with worse OS in ypN (AJCC 8th): ypN0, 68%

(n=83); ypN1, 59% (n=74); ypN2 28% (n=40); and ypN3 9% (n=22) (Figure 1C). Finally, predictive values were compared using AIC and BIC; ypN (AJCC 8th) was slightly superior to the CT-pN (JPN 11th) staging system regarding prognostication (AJCC 8th: AIC=979.53, BIC=989.58; JPN 11th: AIC=999.07, BIC=1012.44).

Evaluation of ypM (AJCC 8th)/ CT-pM (JPN 11th) status

The OS curves of ypM (AJCC 8th), CT-pM (JPN 11th), and the proportion of these patients positive for supraclavicular L/Ns (No. 104), were estimated (Figure 2A–C). The 5-year OS rates were as follows: ypM0, 53% (n=213) and ypM1 24% (n=21) in AJCC 8th (Figure 2A), and CT-pM0 51% (n=232) and CT-pM1 0% (n=2) in JPN 11th (Figure 2B). In the ypM1 group in AJCC 8th (n=21), 15 patients (71%) were positive for supraclavicular L/Ns (No. 104). As characteristics of primary tumors in this population, 60% were pT3 or 4, 80% were located in the upper or middle esophagus, and L/Ns metastases were seen in 80% patients. The 5-year OS rate of this population was 33% (Figure 2C). Fifteen of 21 (71%) ypStage IVB patients in AJCC 8th were considered CT-pStage III in JPN 11th because positivity for supraclavicular L/Ns (No. 104) is CT-pN2 or 3 rather than CT-pM1 in JPN 11th.

Unification of AJCC 8th and JPN 11th, leading to the novel staging system

The proposed unification of AJCC 8th and JPN 11th is shown below. In concrete terms, the novel pT and pN categories remain in the present state of AJCC 8th. In novel pM, supraclavicular L/Ns (No. 104) are treated as regional according to JPN 11th and

incorporated into novel pN. ypStage II, IIIA should be incorporated into novel pStageII. Consequently, ypStage IIIB is treated as a unique novel pStageIII (Table 1). The 5-year OS of the new staging system is shown in Figure 3A as the novel AJCC-CT-pTNM 8th: CT-pStage I, 76% (n=51); CT-pStage II, 70% (n=75); CT-pStage III, 34% (n=75); CT-pStage IVA, 7% (n=27); and CT-pStage IVB 0% (n=6) (Figure 3A, P<0.0001). Finally, predictive values were compared using AIC and BIC. The novel staging system was superior in terms of prognostication (novel: AIC=1054.24, BIC=1067.88; AJCC 8th: AIC=1070.74, BIC=1087.76; JPN 11th: AIC=1086.15, BIC=1103.16) (Table 2A).

Test data from 70 patients

The 3-year OS of the AJCC 8th using test data is shown in Figure 3B with inversions between some stages: ypStage I, 81% (n=14); ypStage II, 52% (n=9); ypStage IIIA, 64% (n=14); ypStage IIIB, 53% (n=22); ypStage IVA, 25% (n=4); and ypStage IVB, 0% (n=7) (Figure 3B). On the other hand, there was no OS inversion between each stage category in the novel AJCC-CT-pTNM 8th: CT-pStage I, 81% (n=14); CT-pStage II, 57% (n=24); CT-pStage III, 50% (n=25); and CT-pStage IVA, 14% (n=7) (Figure 3C, P<0.0001). Finally, predictive values were compared using AIC and BIC. The novel staging system using test data was also superior in terms of prognostication (novel: AIC=204.54, BIC=210.92; AJCC 8th: AIC=206.76, BIC=216.06) (Table 2b).

Discussion

The reason we problematize the AJCC 8th, which is utilized for not only NACRT

but NAC treated patients, is that more precise system to reflect each modality should be built. Indeed, there was some staging inversion in the AJCC 8th staging system to stratify patients with ypStage II vs. IIIA. In our training data, 5-year OS was statistically better for ypStage IIIA (ypT0-2N1) than ypStage II (ypT3N0). We hypothesize that this inversion might occur due to the difference of neo-treatment between Japan and Western countries; Japanese standard is NAC and the Western countries' is NACRT. For same clinical stage patients, difference between NACRT and NAC as neo-treatment might cause different affect for pathological staging. Accordingly, each staging system is needed for NACRT and NAC treated populations, respectively. Considering that all ypStage II patients (ypT3N0, n=32/32, 100%) and almost all ypStage IIIA patients (ypT0-2N1, n=36/40, 90%) in AJCC 8th were considered CT-pStage II in JPN 11th, in which no staging inversion was seen in prognosis (higher-stage categories were associated with OS), these two populations (ypStage II and IIIA) should be unified as novel pStage II for NAC treated population. Consequently, ypStage IIIB will be simplified to a unique novel pStage III.

The Japanese classification has subdivided the lymph node mapping system and uses different definitions of N staging than the AJCC system. Comparing AJCC 8th and JPN 11th staging, 72% (54/75) of ypN1 and 76% (54/71) of CT-pN1 coincide with each other. However, the rates of concordance decreased as N status progressed. Therefore, it is important to estimate which is the superior predictive system. In OS, JPN 11th failed to stratify patients with CT-pN2 vs. CT-pN3 even though AJCC 8th reflects an appropriate prognosis. This may be because JPN 11th staging depends on lymph node group but not

number. Therefore, if many L/Ns metastases are concentrated in group 1 only, the diagnosis would be CT-pN1, and the effect of the number of metastatic L/Ns would not be reflected. Finally, AIC and BIC, used as parameters for goodness-of-fit, showed that AJCC 8th was slightly superior to JPN 11th in terms of prognostication.

Supraclavicular L/N (No. 104) metastases are treated as distant metastases (ypM1) in AJCC 8th and regional L/N metastases in JPN 11th. It is very important to determine whether supraclavicular L/Ns (No. 104) should be considered as regional L/Ns. The 5-year OS of ypM1 in AJCC 8th is considerably good comparing with that of CT-pM1 in JPN 11th. This may be because the 5-year OS of patients with supraclavicular L/Ns (No. 104) metastases, occupying 71% (15/21) of the ypM1 group, was 33%, which was better than that of the ypN2 group (28%). Inversion of 5-year OS between ypStage IVB (=ypTanyNanyM1) and ypStage IVA (24% vs 11%) can also be explained by the same reason. Consequently, supraclavicular L/Ns (No. 104) should be treated as regional L/Ns.

Based on these results, we proposed the unification of AJCC 8th and JPN 11th leading to the novel staging system [preserving the ypT and ypN staging system, converting supraclavicular L/N metastases from ypM to ypN, and unifying ypStage II and IIIA] for patients treated with NAC. The novel staging system predicts survival of NAC treated population well and was easy to use, as shown by AIC and BIC. In test data, even though the number of patients was small and follow up period was relatively short, feasibility of the novel staging system was validated largely.

As we mentioned above, both preoperative and surgical treatment strategies should be discussed. All of the patients in this study underwent NAC. On the other hand,

AJCC 8th staging system was based on the worldwide data of esophageal cancer patients who underwent neoadjuvant therapy where the majority of patients underwent NACRT rather than NAC.[21] It is controversial to treat NAC and NACRT as if they were identical. Strictly, validation might be done for each strategy. Next, there is difference in lymph node dissection between Western and Eastern countries. Approximately half of patients underwent three-field L/Ns dissection in our study. On the other hand, most of Western patients underwent esophagectomy with two-field L/Ns dissection. Classifying supraclavicular L/Ns (No. 104) as regional on the clinical staging of ESCC in the AJCC system would represent a major paradigm shift in many Western centers. However, as we showed, the number of positive nodes including supraclavicular L/Ns (No. 104) is better prognostic factor for post-neoadjuvant patients. Additionally, as Tachimori et al. reported, therapeutic lymphadenectomy effects for patients with supraclavicular L/Ns (No. 104) metastasis are sufficient.[22,23] According to the tumor locations, the 5-year survival rates for these patients were 42.3%, 40.5% and 30.0% in upper, middle, and lower esophageal cancers, respectively.[23] Thus, these nodes should be treated not as distant lesions but as regional nodes for all cohort even if those are bilateral and/or bulky. Concerning the prophylactic supraclavicular L/Ns dissection, however, it remains controversial. We reported that it is not necessary because there were no oncologic benefits [24]. Other investigator also reported that it may be omitted for NAC treated patients with clinically negative supraclavicular L/Ns (No. 104) [25]. Instead of it, asynchronous resection for single recurrence of supraclavicular L/Ns might be effective. Consequently, three-field L/Ns dissection might only be performed for clinically supraclavicular L/Ns positive

cases.

A limitation of this study is that the datasets were small and obtained from only two institutions. Additionally, it is unclear whether unification of the two systems is possible in Western countries' patients with NAC. To create a better staging system, multicentral cohort study using the Japanese National Clinical Database is currently in progress.

Conclusions

In summary, unification of the AJCC system and the Japanese classification for NAC treated patients yields a simpler and more precise predictive system that will prevent surgeons from becoming confused. We hope that our results will provide some insights for consideration during the next iteration of the AJCC staging system.

Acknowledgments

Informed consent was obtained from patients for the publication of this report and any accompanying data. Patient anonymity was maintained.

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Figure legends

Figure 1

In training data,

A) Prognosis was statistically better for ypStage IIIA (ypT0-2N1) than ypStage II (ypT3N0) (P=0.040) in AJCC-ypTNM 8th (AJCC 8th) with staging inversion. Also, prognosis of ypStage IVB (ypTanyNanyM1) was better than that of ypStage IVA.

B) Higher-stage categories were associated with OS in JPN-CT-pTNM 11th (JPN 11th) without staging inversion.

C) Higher categories of ypN were associated with worse OS in AJCC-ypTNM 8th (AJCC 8th).

D) Staging inversion was seen between CT-pN3 and CT-pN2 in JPN-CT-pN 11th.

Figure 2

A) 5-year OS rates were 53% (n=213) for ypM0 and 24% (n=21) for ypM1 in AJCC-ypTNM 8th (AJCC 8th).

B) 5-year OS rates were 51% (n=232) for CT-pM0 and 0% (n=2) for CT-pM1 in JPN-CT-pTNM 11th (JPN 11th).

C) 5-year OS rate of 15 patients positive for supraclavicular L/Ns (No. 104), representing 71% of 21 ypM1 patients in AJCC-ypTNM 8th (AJCC 8th), was 33%.

Figure 3

In training data,

A) higher-stage categories were associated with OS in the novel AJCC-CT-pTNM 8th staging system ($P<0.0001$).

In test data,

B) Prognosis was better for ypStage IIIA and IIIB than ypStage II in AJCC-ypTNM 8th (AJCC 8th) with staging inversion. Also, prognosis of ypStage IVB was better than that of ypStage IVA until postoperative year 2.

C) Higher-stage categories were associated with OS in the novel AJCC-CT-pTNM 8th staging system ($P<0.0001$).

Table 1 Pathological staging based on the each system

AJCC 8th

	ypN0	ypN1	ypN2	ypN3	ypM1
ypT0	I	IIIA	IIIB	IVA	IVB
ypT1	I	IIIA	IIIB	IVA	IVB
ypT2	I	IIIA	IIIB	IVA	IVB
ypT3	II	IIIB	IIIB	IVA	IVB
ypT4a	IIIB	IVA	IVA	IVA	IVB
ypT4b	IVA	IVA	IVA	IVA	IVB

JPN 11th

	pN0	pN1	pN2	pN3	pN4	pM1
pT0,1a	0	II	II	III	IVa	IVb
pT1b	I	II	II	III	IVa	IVb
pT2	II	II	III	III	IVa	IVb
pT3	II	III	III	III	IVa	IVb
pT4a	III	III	III	III	IVa	IVb
pT4b	IVa	IVa	IVa	IVa	IVa	IVb

Novel

	ypN0	ypN1	ypN2	ypN3	pM1
ypT0	I	II	III	IVA	IVB
ypT1	I	II	III	IVA	IVB
ypT2	I	II	III	IVA	IVB
ypT3	II	III	III	IVA	IVB
ypT4a	III	IVA	IVA	IVA	IVB
ypT4b	IVA	IVA	IVA	IVA	IVB

AJCC 8th; AJCC-ypTNM 8th

JPN 11th; JPN-CT-pTNM 11th

Novel; novel AJCC-CT-pTNM 8th

ypN; using the number of L/Ns, pN; grouping the L/Ns * supraclavicular L/Ns (No.104) are treated as regional

ypM; including supraclavicular L/Ns (No.104), pM; not including supraclavicular L/Ns (No.104)

Table 2a. Comparison AIC and BIC values between the novel, AJCC 8th and JPN 11th in training data

	AIC*	BIC**
Novel	1054.24	1067.88
AJCC 8th	1070.74	1087.76
JPN 11th	1086.15	1103.16

Novel; novel AJCC-CT-pTNM 8th

AJCC 8th; AJCC-ypTNM 8th

JPN 11th; JPN-pTNM 11th

* Akaike Information Criterion: AIC

** Bayesian Information Criterion: BIC

Table 2b Comparison AIC and BIC values between the novel and AJCC 8th in test data

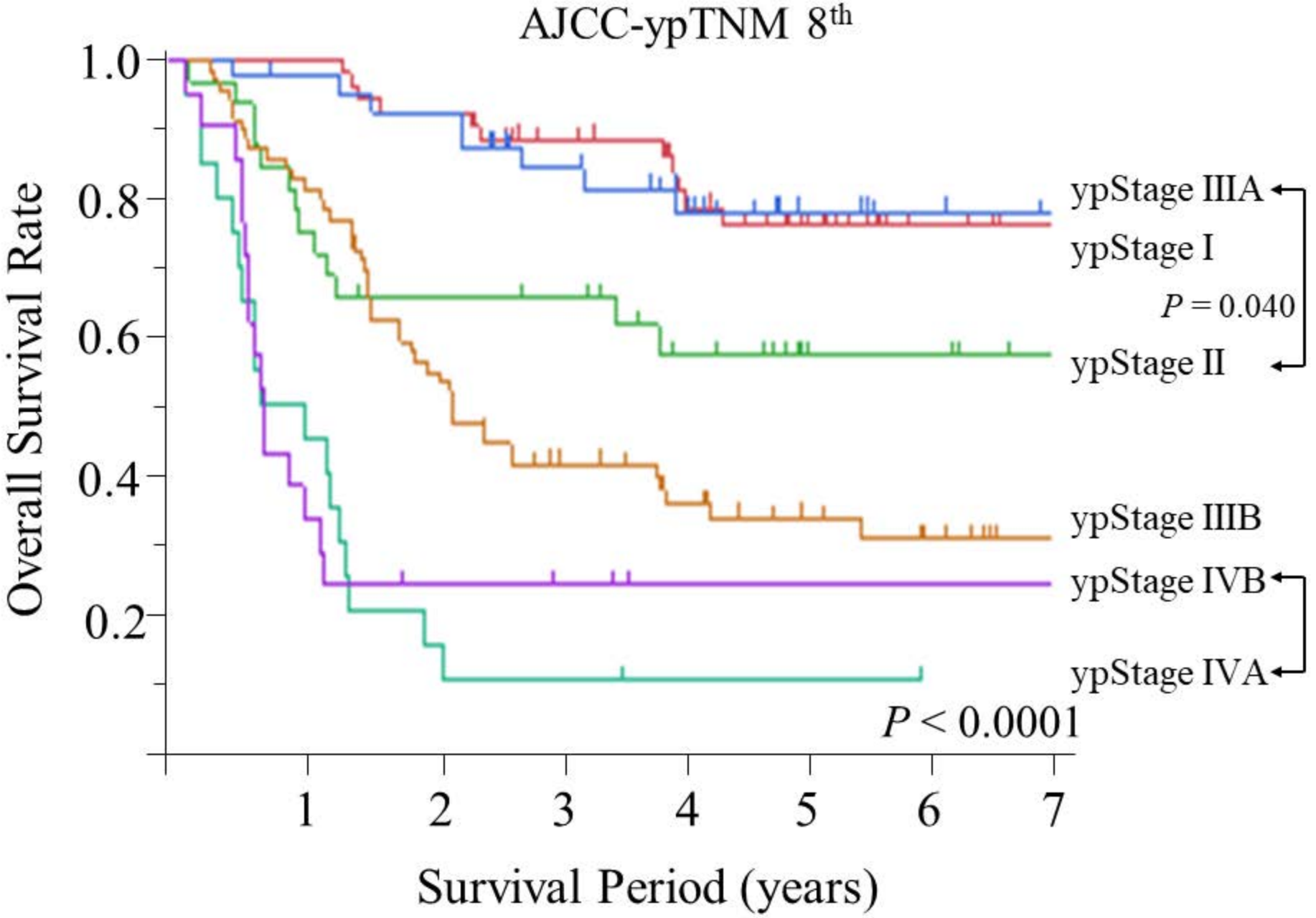
	AIC*	BIC**
Novel	204.54	210.92
AJCC 8th	206.76	216.06

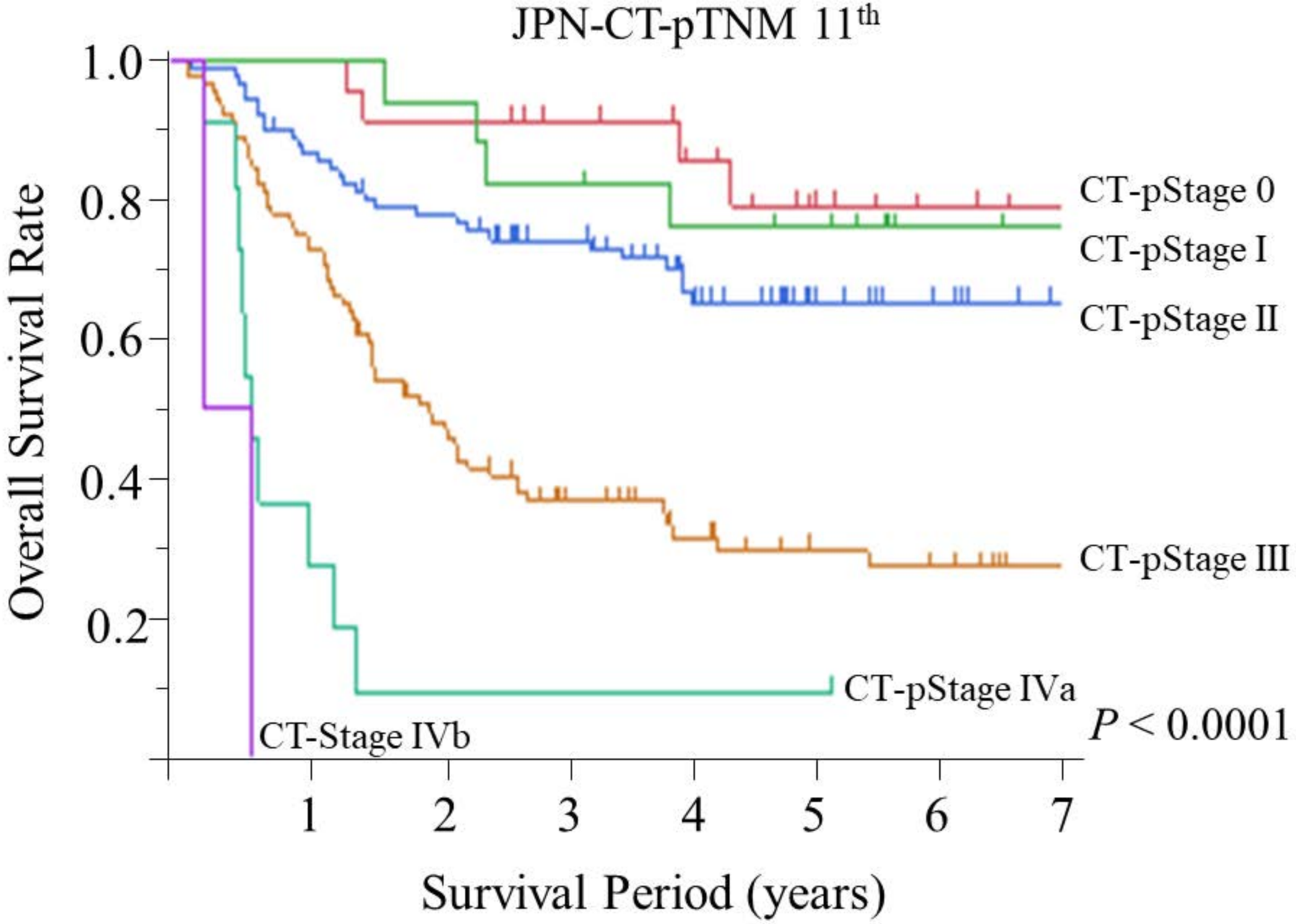
Novel; novel AJCC-CT-pTNM 8th

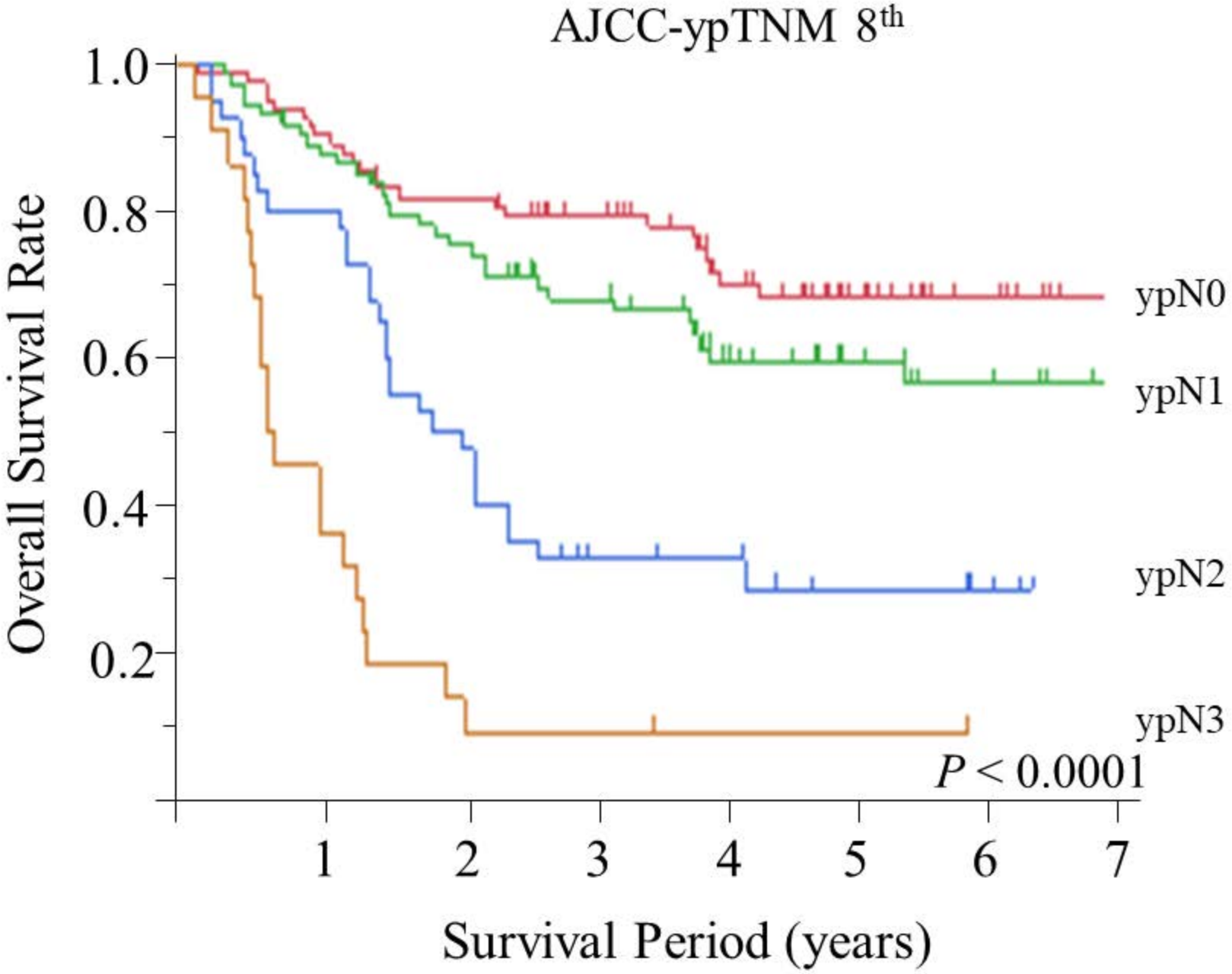
AJCC 8th; AJCC-ypTNM 8th

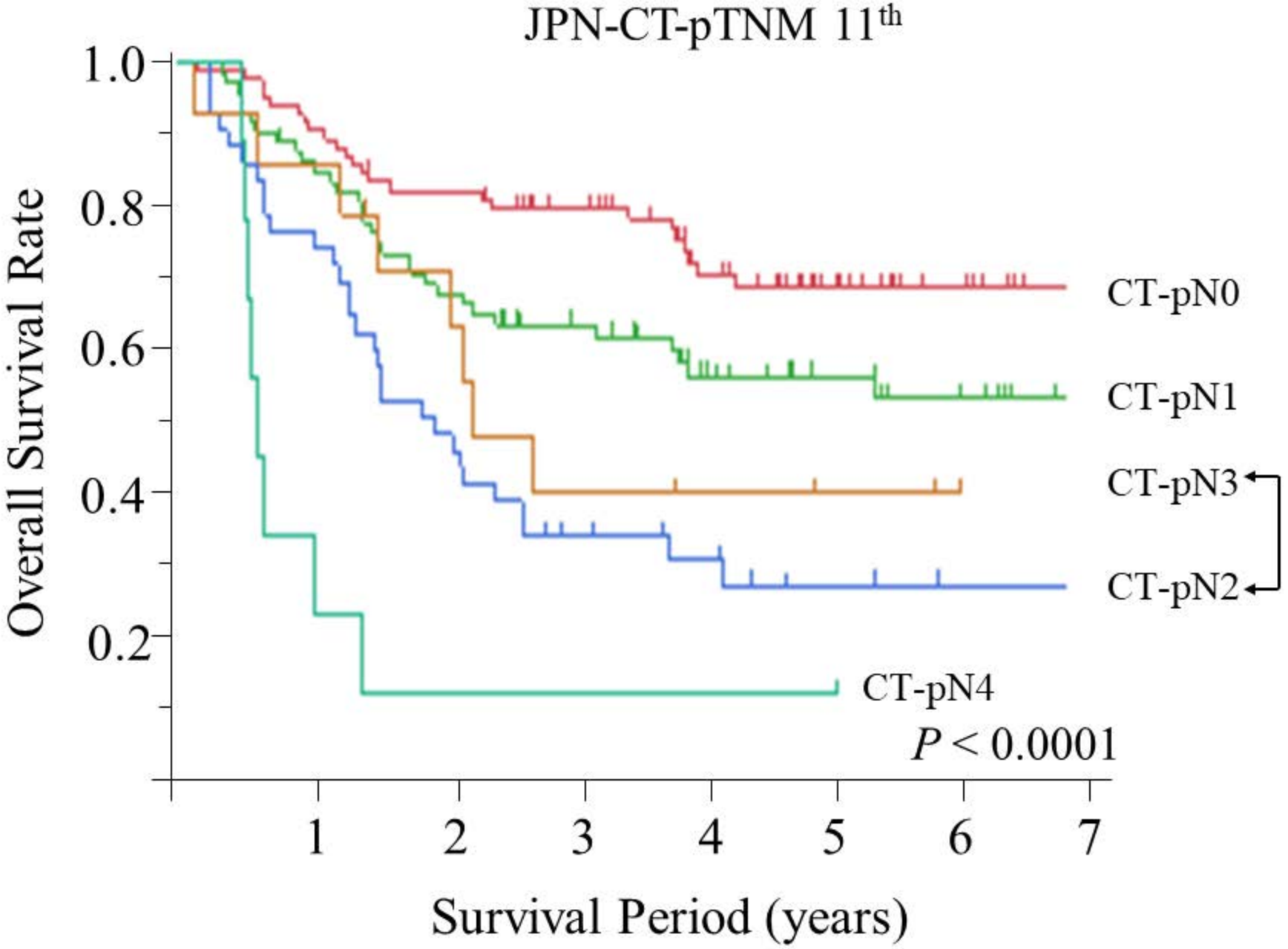
* Akaike Information Criterion: AIC

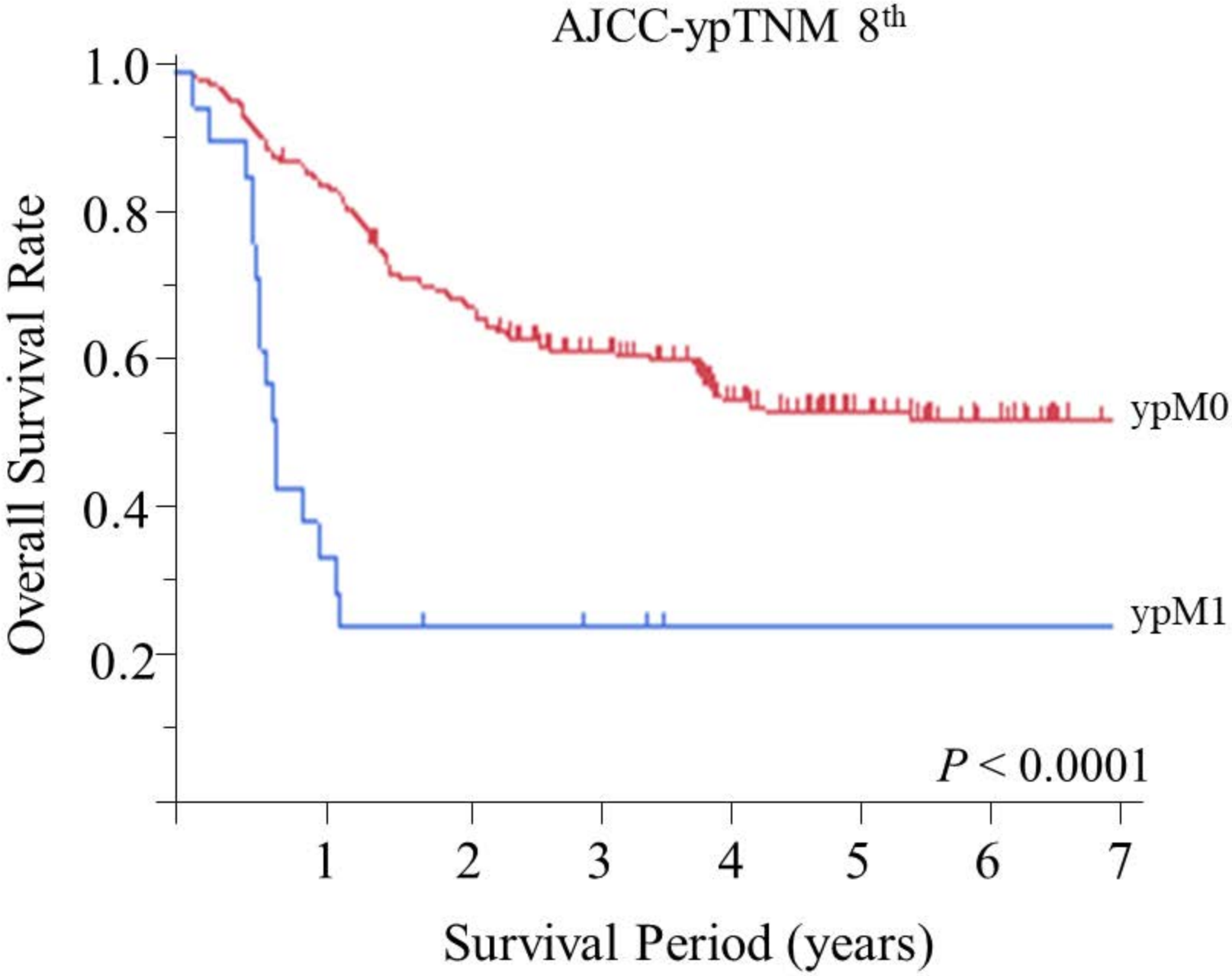
** Bayesian Information Criterion: BIC

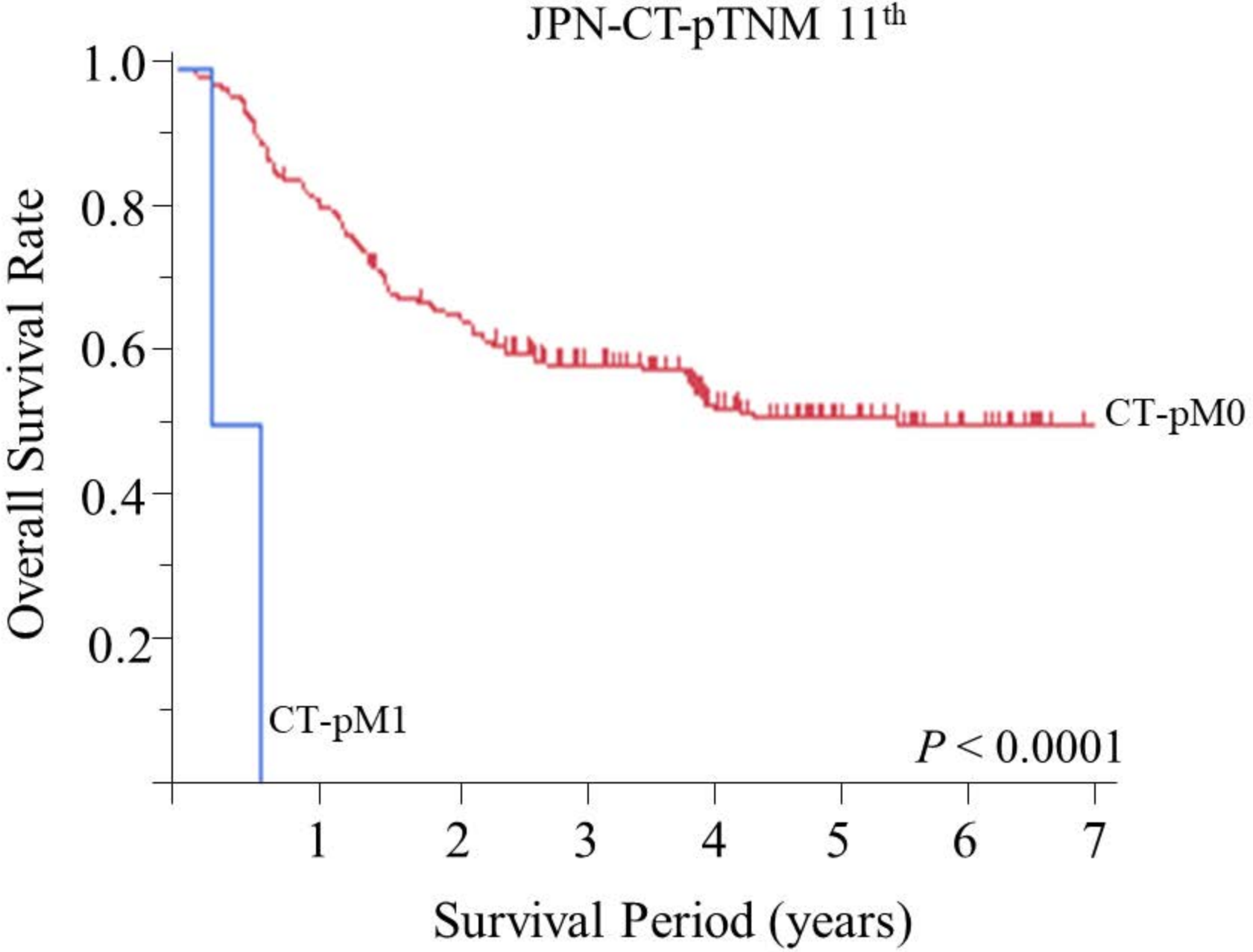

AJCC-ypTNM 8th
1.0
0.8
0.6
0.4
0.2
Overall Survival Rate
ypStage IIIA
ypStage I
P = 0.040
ypStage II
ypStage IIIB
ypStage IVB
ypStage IVA
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)

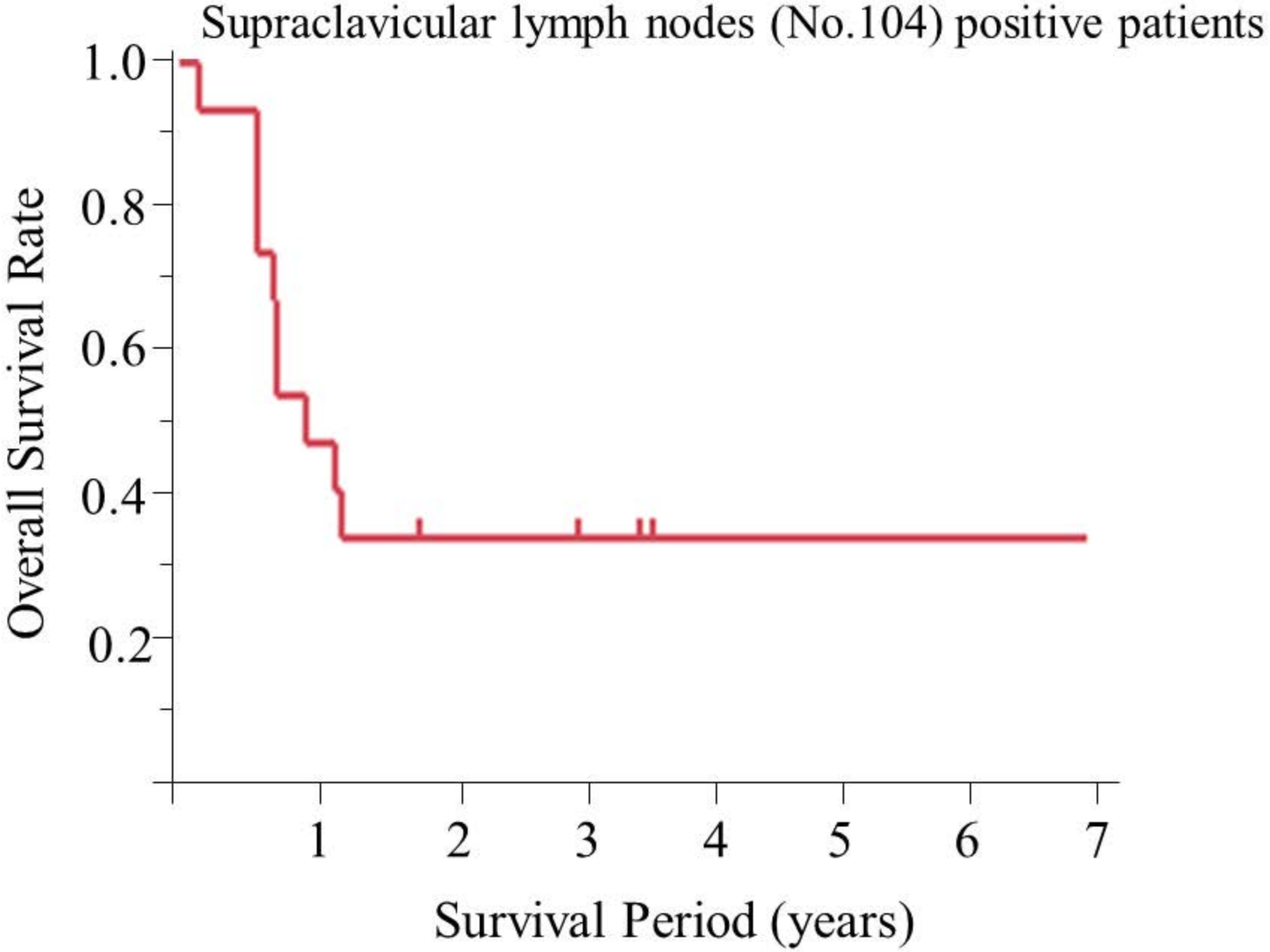

JPN-CT-pTNM 11th
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
1
2
3
4
5
6
7
Survival Period (years)
CT-pStage 0
CT-pStage I
CT-pStage II
CT-pStage III
CT-pStage IVa
CT-Stage IVb
P < 0.0001

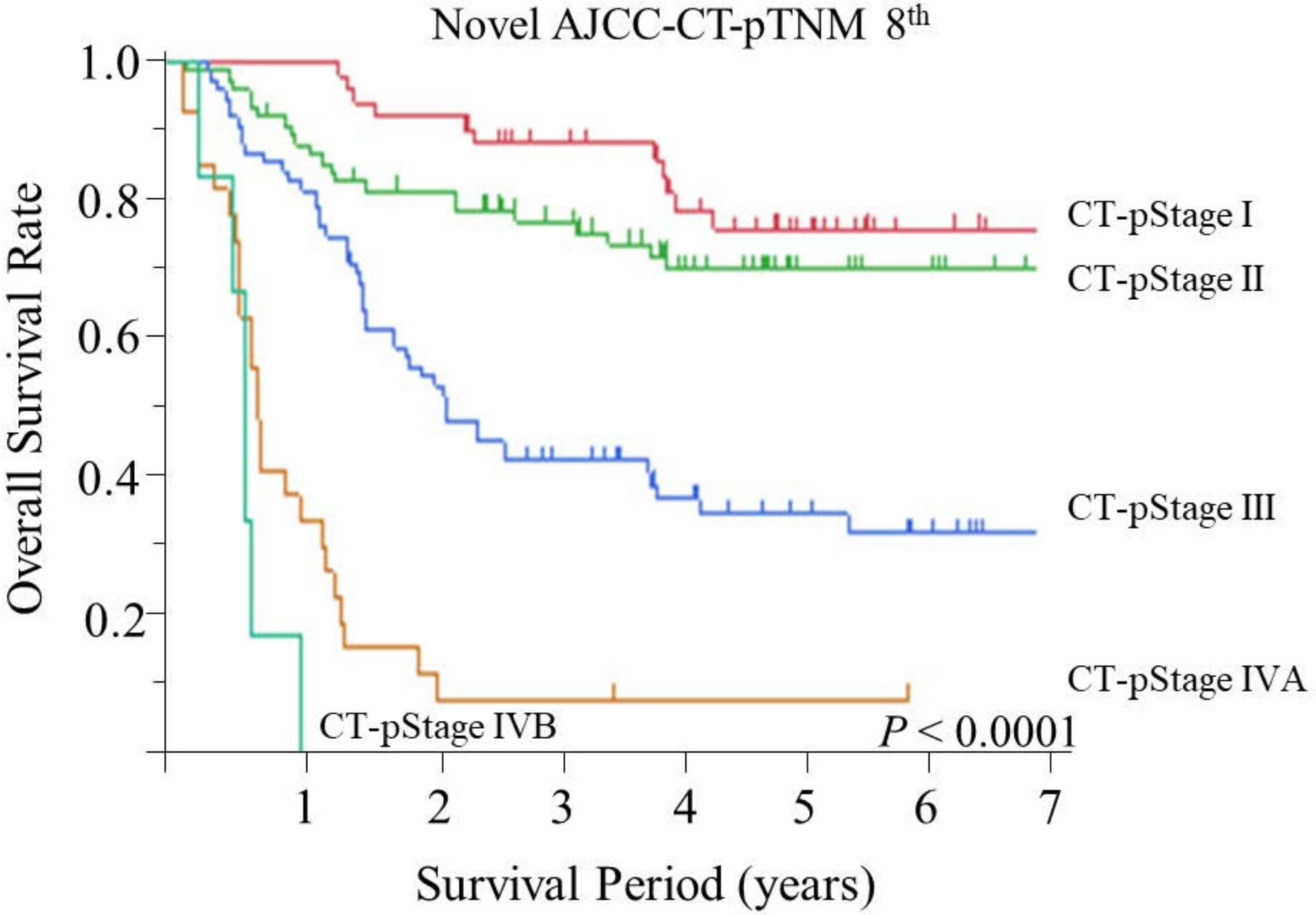

AJCC-ypTNM 8th
1.0
0.8
0.6
0.4
0.2
Overall Survival Rate
ypN0
ypN1
ypN2
ypN3
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)

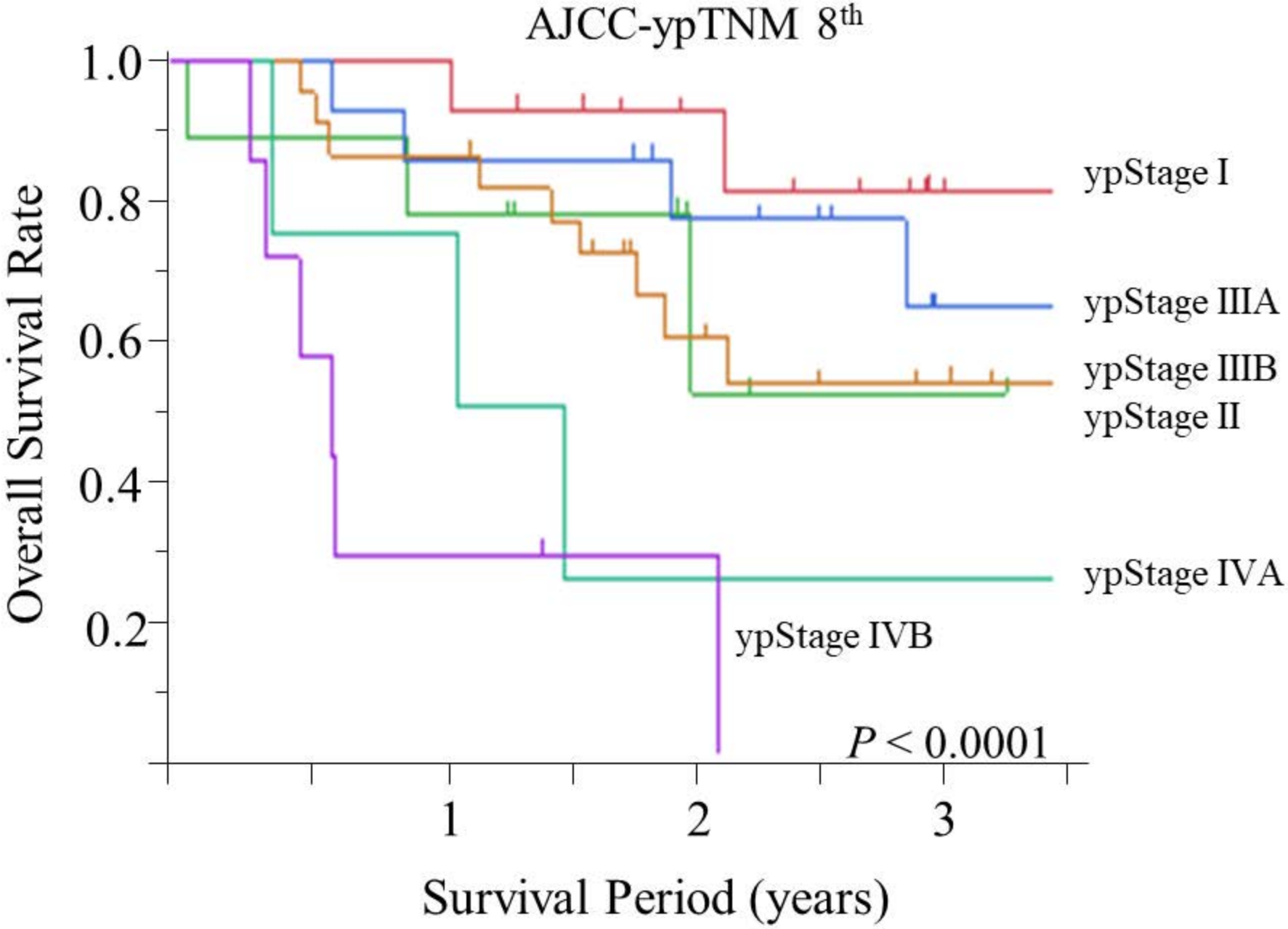

JPN-CT-pTNM 11th
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
CT-pN0
CT-pN1
CT-pN3
CT-pN2
CT-pN4
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)

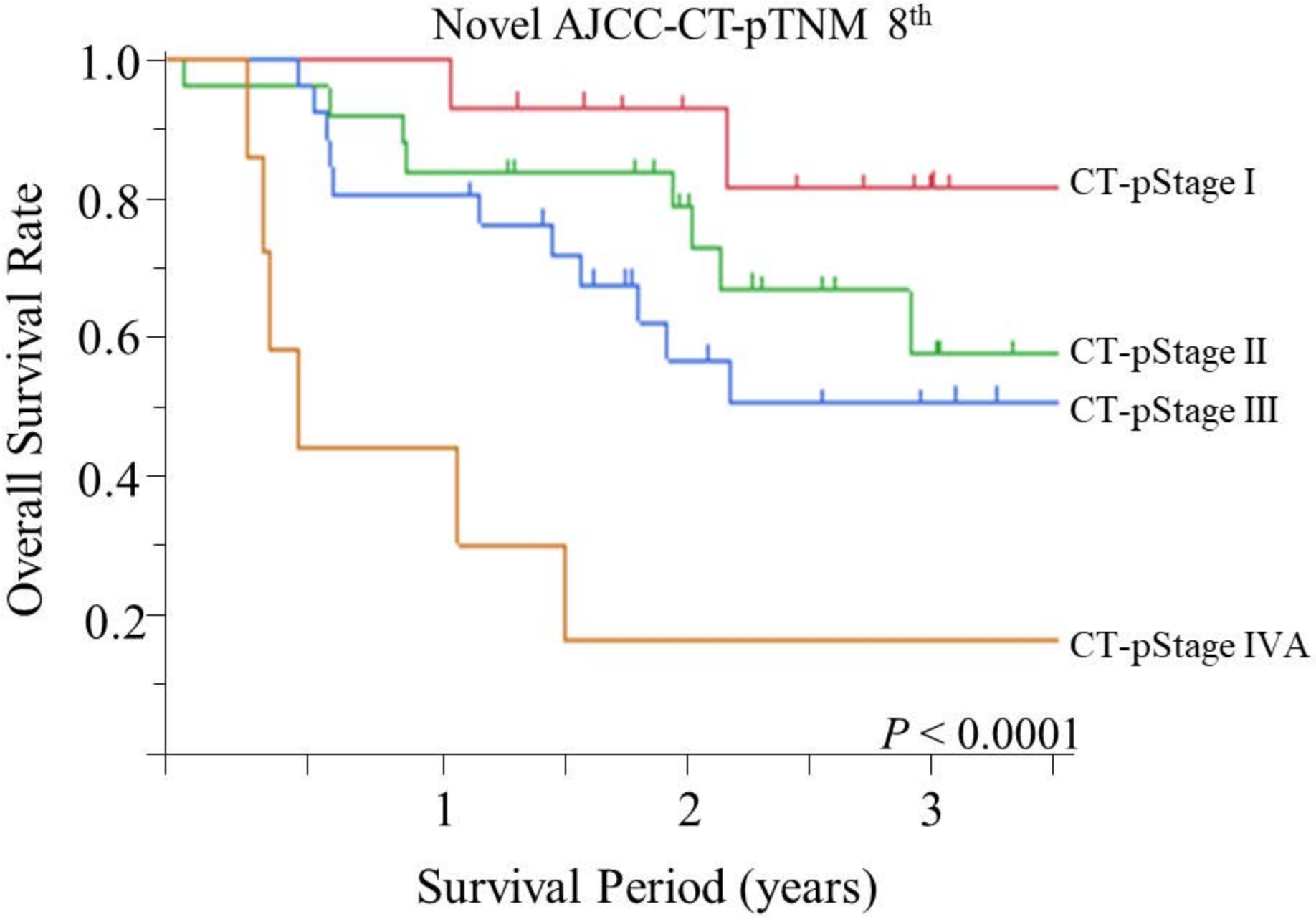

AJCC-ypTNM 8th
1.0
0.8
0.6
0.4
0.2
Overall Survival Rate
ypM0
ypM1
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)


JPN-CT-pTNM 11th
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
CT-pM0
CT-pM1
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)


Supraclavicular lymph nodes (No.104) positive patients
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
1
2
3
4
5
6
7
Survival Period (years)


Novel AJCC-CT-pTNM 8th
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
CT-pStage I
CT-pStage II
CT-pStage III
CT-pStage IVA
CT-pStage IVB
P < 0.0001
1
2
3
4
5
6
7
Survival Period (years)


AJCC-ypTNM 8th
Overall Survival Rate
1.0
0.8
0.6
0.4
0.2
ypStage I
ypStage IIIA
ypStage IIIB
ypStage II
ypStage IVA
ypStage IVB
P < 0.0001
1
2
3
Survival Period (years)


Novel AJCC-CT-pTNM 8th
1.0
0.8
0.6
0.4
0.2
Overall Survival Rate
CT-pStage I
CT-pStage II
CT-pStage III
CT-pStage IVA
P < 0.0001
1
2
3
Survival Period (years)