

Supplemental Online Content

Lin J, Zhao Y, Zhou Y, et al. Comparison of survival and patterns of recurrence in gastric neuroendocrine carcinoma, mixed adenoneuroendocrine carcinoma, and adenocarcinoma. *JAMA Netw Open*. 2021;4(7):e2114180.
doi:10.1001/jamanetworkopen.2021.14180

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Distribution of Multicenter Patients

Center	number of patients
Fujian Medical University Union Hospital	155
West district of The First Affiliated Hospital of USTC	115
The Affiliated Hospital of Qingdao University	84
Cancer Hospital Affiliated to Chinese Academy of Medical Sciences	83
The First Affiliated Hospital of Fujian Medical University	80
Huashan Hospital Affiliated to Fudan University	66
The First Affiliated Hospital of Anhui Medical University	53
Yantai Yuhuangding Hospital	51
Renji Hospital Affiliated to Shanghai Jiaotong University	50
The Affiliated Hospital of Putian University	43
The First Hospital of Putian	36
Henan Cancer Hospital	30
Fujian Provincial Hospital	13
The Second People's Hospital of Liaocheng	7
Tianjin Medical University General Hospital	6
The First Affiliated Hospital of Nanjing Medical University	6
Guangdong Provincial People's Hospital	5
Quanzhou First Hospital Affiliated to Fujian Medical University	5
The First Affiliated Hospital of Soochow University	4
Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine	4
Zhangzhou Affiliated Hospital of Fujian Medical University	3
Meizhou People's Hospital	3
Second Affiliated Hospital of Nanchang University	2

eTable 2. Comparison of Stages Between Different Pathological Types in the Original and the Matched Data Sets

Baseline Variable	Before matching			After matching		
	AC (n=2785, %)	NEC (n=503, %)	P value	AC (n=1573, %)	NEC (n=500, %)	P value
Age, median (IQR), y	61 (54-68)	64 (58-69)	<.001	63 (58-69)	64 (58-69)	.40
Sex			.002			.74
Male	2035 (73.1)	400 (79.5)		1263 (80.3)	398 (79.6)	
Female	750 (26.9)	103 (20.5)		310 (19.7)	102 (20.4)	
Pathologic TNM stage			<.001			.32
I	862 (31.0)	47 (9.3)		186 (11.8)	47 (9.4)	
II	659 (23.7)	144 (28.6)		433 (27.5)	144 (28.8)	
III	1264 (45.4)	312 (62.0)		954 (60.6)	309 (61.8)	
	AC (n=2785, %)	MANEC (n=401, %)	P value	AC (n=1355, %)	MANEC (n=394, %)	P value
Age, median (IQR), y	61 (54-68)	64 (58-70)	<.001	63 (57-69)	64 (58-70)	.09
Sex			.03			.69
Male	2035 (73.1)	313 (78.1)		1082 (79.9)	311 (78.9)	
Female	750 (26.9)	88 (21.9)		273 (20.1)	83 (21.1)	
Pathologic TNM stage			<.001			.56
I	862 (31.0)	48 (12.0)		190 (14.0)	48 (12.2)	
II	659 (23.7)	105 (26.2)		361 (26.6)	102 (25.9)	
III	1264 (45.4)	248 (61.8)		804 (59.3)	244 (61.9)	

Abbreviations: NEC, neuroendocrine carcinoma; MANEC, mixed adenoneuroendocrine carcinoma; AC, adenocarcinoma; Sdiff, standardized difference.

eTable 3. Univariable and Multivariable Logistic Regression Analyses of Factors Potentially Associated with Distant Recurrence in the Matched Data Sets of AC and NEC

Clinicopathological features	Univariable Analysis		Multivariable analysis	
	Odds Ratio (CI)	P	Odds Ratio (CI)	P
Age	1.02 (1.00-1.03)	.02	1.02 (1.00-1.03)	.04
Sex				
Male	1		1	
Female	0.63 (0.46-0.86)	.003	0.66 (0.47-0.93)	.02
Center volume				
Low	1			
High	1.04 (0.39-2.78)	.94		
Location				
Lower	1		—	
Middle	1.15 (0.82-1.61)	.42	—	.17
Upper	1.47 (1.12-1.94)	.006	—	.59
Mix	1.51 (1.03-2.22)	.04	—	.61
Tumor size	1.16 (1.11-1.22)	<.001	—	.59
Lymph nodes examined	1.00 (1.00-1.01)	.43		
The number of metastatic lymph nodes	1.08 (1.07-1.10)	<.001	1.06 (1.05-1.08)	<.001
Vascular invasion	1.48 (1.17-1.88)	.001	—	.17
Neural invasion	1.30 (1.03-1.66)	.03	—	.10
Pathologic T stage				
T1-2	1		1	
T3-4	4.43 (2.92-6.71)	<.001	2.19 (1.40-3.41)	.001
Pathologic N stage				
N0	1		1	
N1-3	5.43 (3.64-8.10)	<.001	2.94 (1.89-4.55)	<.001
Type of resection				
Total gastrectomy	1		1	
Subtotal gastrectomy	0.57 (0.45-0.72)	<.001	0.77 (0.59-1.00)	.05
Received neoadjuvant chemotherapy				
No	1		1	
Yes	2.95 (1.57-5.55)	.001	2.86 (1.44-5.67)	.003
Received adjuvant chemotherapy				
No	1		1	
Yes	1.46 (1.13-1.89)	.004	—	.91
Pathological type				
AC	1		1	
NEC	1.46 (1.12-1.89)	.005	2.22 (1.66-2.98)	<.001

Abbreviations: NEC, neuroendocrine carcinoma; AC, adenocarcinoma; CI, confidence interval.

eTable 4. Univariate and Multivariable Logistic Regression Analyses of Factors Potentially Associated with Distant Recurrence in the Matched Data Sets of AC and MANEC

Clinicopathological features	Univariable Analysis		Multivariable analysis	
	Odds Ratio (CI)	P	Odds Ratio (CI)	P
Age	1.01 (1.00-1.03)	.09		
Sex				
Male	1		1	
Female	0.67 (0.48-0.94)	.02	0.69 (0.48-1.00)	.05
Center volume				
Low	1			
High	0.81 (0.22-2.96)	.75		
Location				
Lower	1		—	
Middle	1.03 (0.73-1.47)	.86	—	.07
Upper	1.54 (1.14-2.08)	.005	—	.06
Mix	1.51 (0.99-2.29)	.06	—	.63
Tumor size	1.17 (1.11-1.22)	<.001	—	.97
Lymph nodes examined	1.00 (0.99-1.01)	.61		
The number of metastatic lymph nodes	1.09 (1.07-1.11)	<.001	1.07 (1.05-1.09)	<.001
Vascular invasion	1.62 (1.25-2.09)	<.001	—	.73
Neural invasion	1.48 (1.14-1.92)	.003	—	.43
Pathologic T stage				
T1-2	1		1	
T3-4	6.81 (4.11-11.27)	<.001	3.52 (2.08-5.97)	<.001
Pathologic N stage				
N0	1		1	
N1-3	5.12 (3.35-7.84)	<.001	2.08 (1.30-3.32)	.002
Type of resection				
Total gastrectomy	1			
Subtotal gastrectomy	0.63 (0.48-0.81)	<.001		
Received neoadjuvant chemotherapy				
No	1		1	
Yes	2.89 (1.41-5.92)	.004	2.97 (1.40-6.33)	.005
Received adjuvant chemotherapy				
No	1		1	
Yes	1.78 (1.34-2.36)	<.001	—	.48
Pathological type				
AC	1		1	
MANEC	1.39 (1.03-1.86)	.03	1.70 (1.24-2.34)	.001

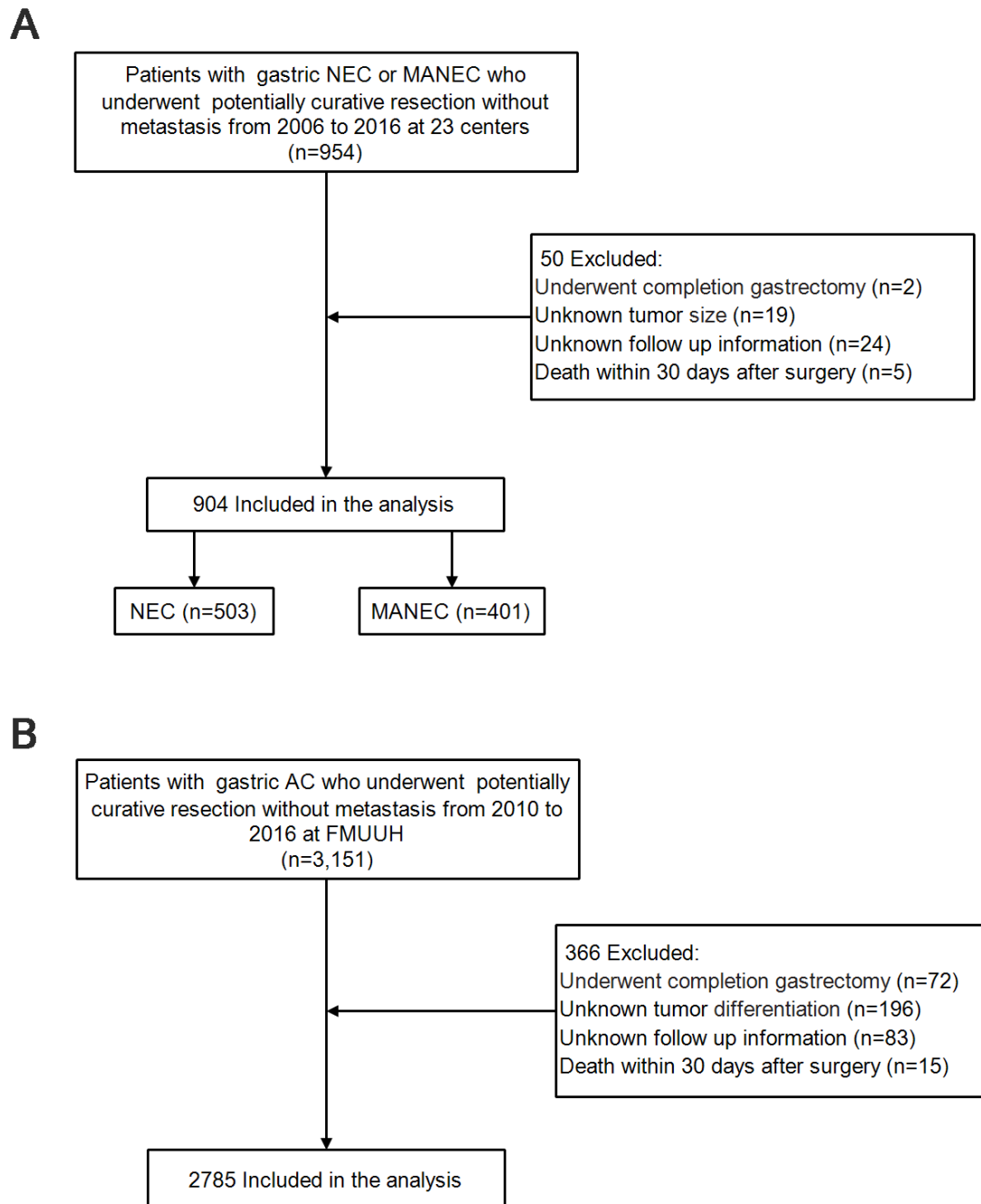
Abbreviations: MANEC, mixed adenoneuroendocrine carcinoma; AC, adenocarcinoma; CI, confidence interval.

eTable 5. Univariable and Multivariable Logistic Regression Analyses of Pathological Factors Potentially Associated with Distant Recurrence in Patients with NEC and MANEC

Clinicopathological features	Univariable Analysis		Multivariable analysis	
	Odds Ratio (95%CI)	P	Odds Ratio (95%CI)	P
Location				
Lower	1		—	
Middle	0.50 (0.29-0.86)	.01	—	.08
Upper	0.77 (0.52-1.14)	.20	—	.51
Mix	0.72 (0.32-1.60)	.42	—	.87
Tumor size	1.04 (0.98-1.11)	.20		
Lymph nodes examined	1.01 (0.99-1.02)	.47		
Vascular invasion	1.16 (0.80-1.66)	.44		
Neural invasion	0.90 (0.60-1.33)	.58		
Ki-67 (%)				
≤20	1		—	
>20	2.37 (1.05-5.37)	.04	—	.11
Unknown	0.78 (0.28-2.18)	.63	—	.47
Pathological type				
NEC	1			
MANEC	0.96 (0.68-1.34)	.79		
Pathologic T stage				
T1-2	1		1	
T3-4	3.47 (1.94-6.19)	<.001	2.84 (1.57-5.14)	.001
Pathologic N stage				
N0	1		1	
N1-3	2.40 (1.57-3.65)	<.001	2.01 (1.31-3.10)	.002

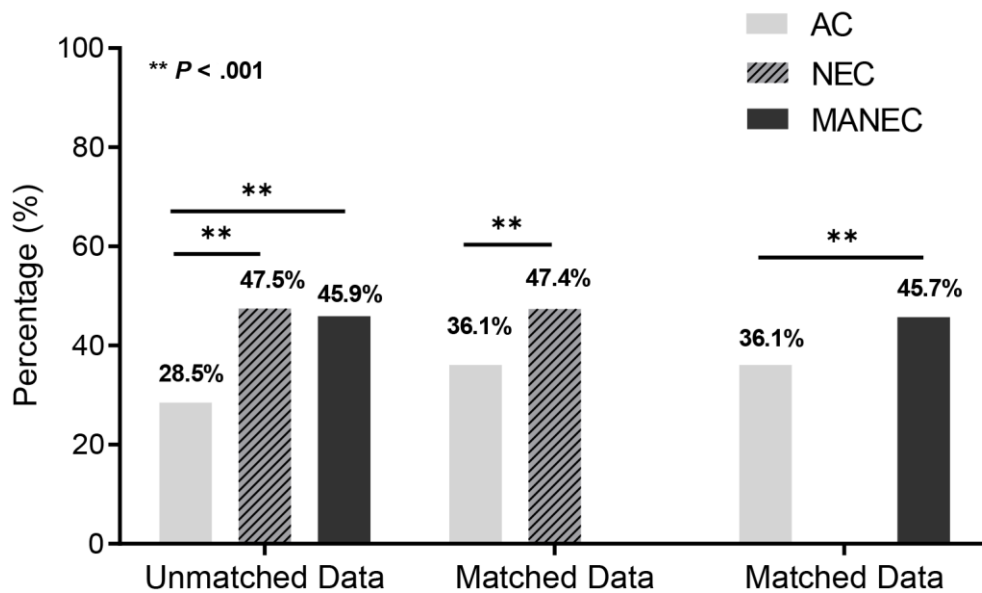
Abbreviations: NEC, neuroendocrine carcinoma; MANEC, mixed adenoneuroendocrine carcinoma; CI, confidence interval.

eFigure 1. Diagram Representing the Selection of the Study Population



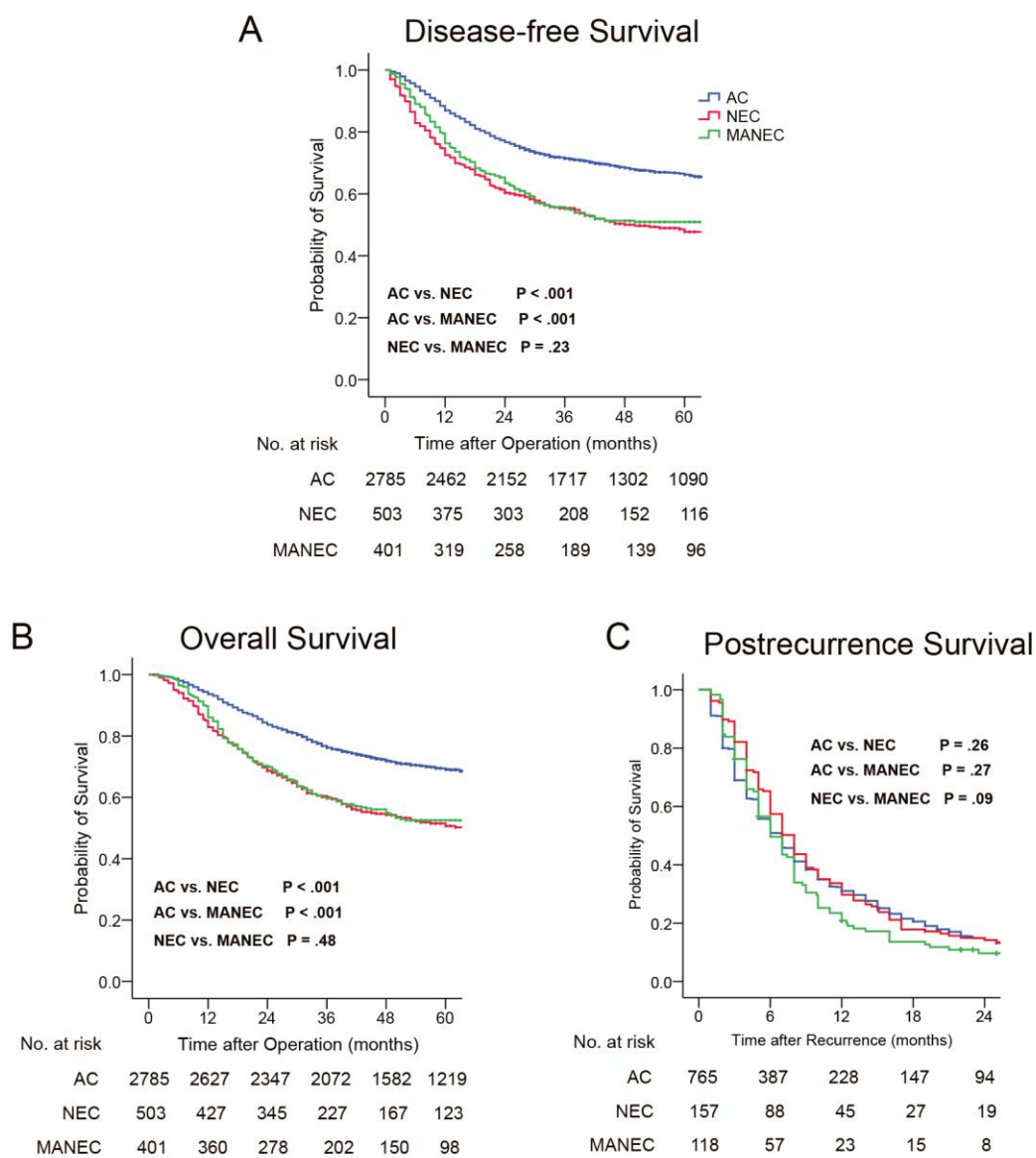
(A) Patients with gastric neuroendocrine carcinoma (NEC) and mixed adenoneuroendocrine carcinoma (MANEC). (B) Patients with gastric adenocarcinoma (AC). Abbreviations: FMUUH, Fujian Medical University Union Hospital.

eFigure 2. Incidence of Recurrence According to Histologic Subtype in Original Data and Matched Data



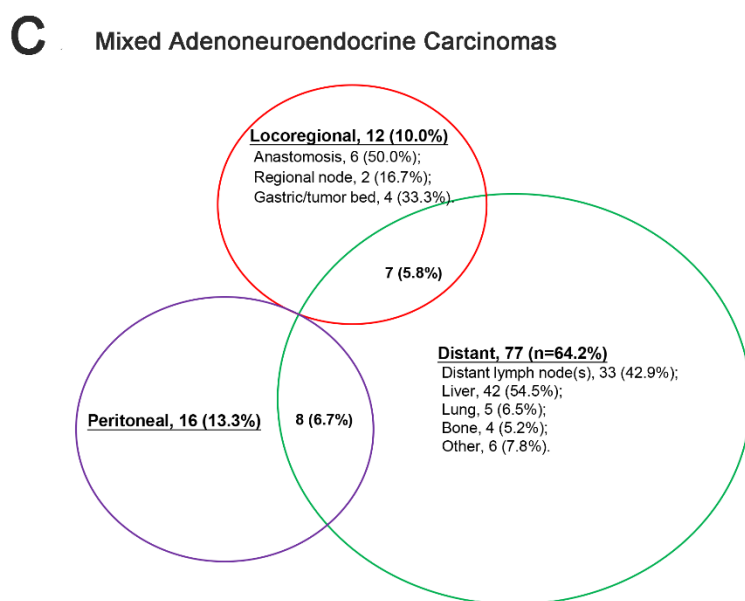
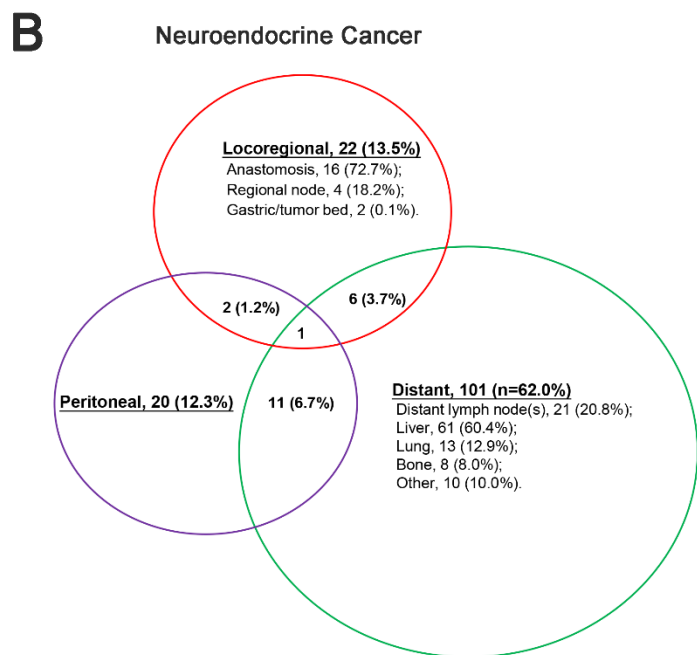
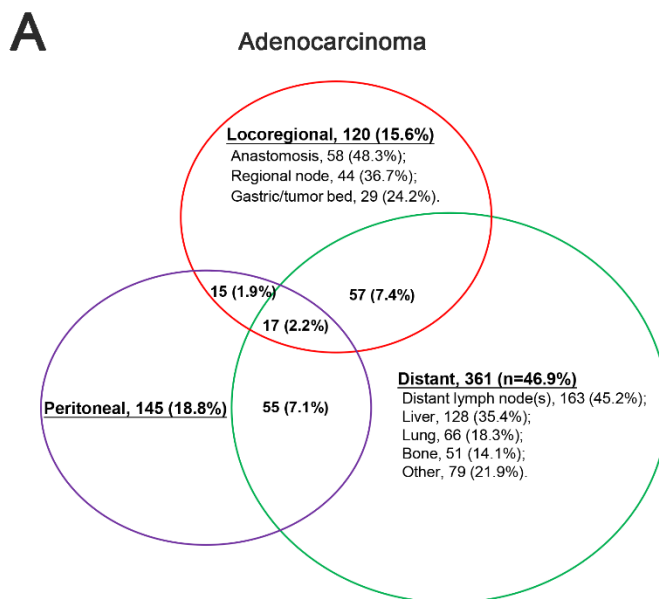
Abbreviations: NEC, neuroendocrine carcinoma. MANEC, mixed adenoneuroendocrine carcinoma. AC, adenocarcinoma

eFigure 3. Kaplan-Meier Survival Curves for Patients With Gastric Neuroendocrine Carcinoma (NEC), Mixed Adenoneuroendocrine Carcinoma (MANEC), or Adenocarcinoma (AC) in Original Data



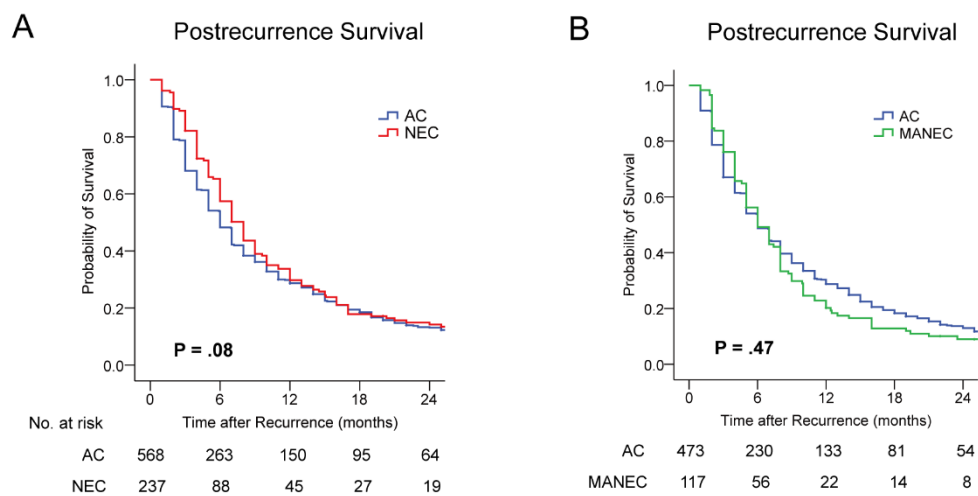
(A) Disease-free survival (DFS), (B) Overall survival (OS), and (C) postrecurrence survival (PRS).

eFigure 4. Recurrence Patterns According to Histologic Subtype in the Original Data



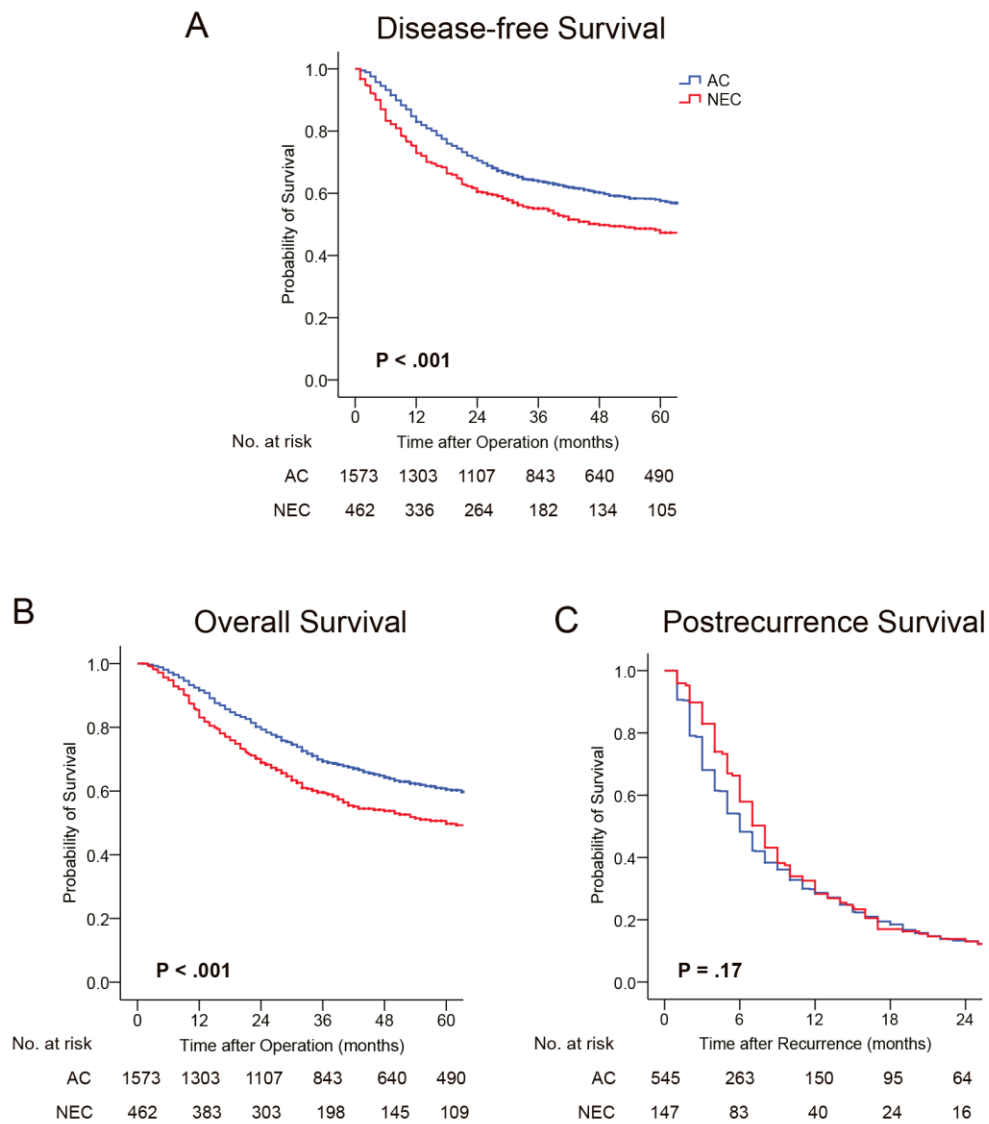
(A) adenocarcinoma, (B) neuroendocrine carcinoma, and (C) mixed adenoneuroendocrine carcinoma. Sizes of circles are proportional to the number of patients.

eFigure 5. Kaplan-Meier Survival Curves for Postrecurrence Survival for Patients With Different Histologic Subtypes in the Matched Data



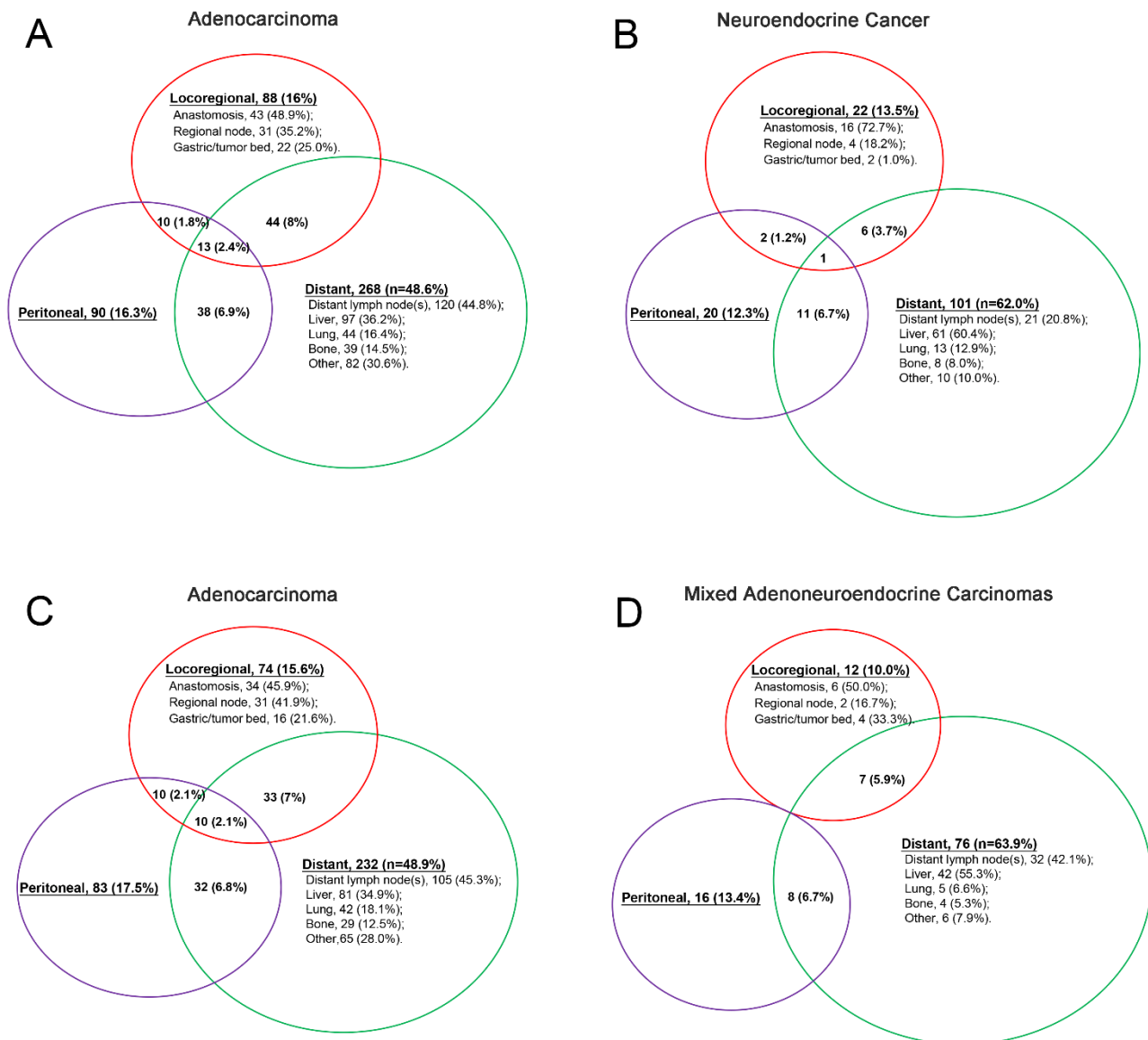
(A) gastric neuroendocrine carcinoma (NEC) versus adenocarcinoma (AC); (B) gastric mixed adenoneuroendocrine carcinoma (MANEC) versus AC.

eFigure 6. Kaplan-Meier Survival Curves for Patients With Gastric Neuroendocrine Carcinoma (NEC) and Adenocarcinoma (AC) in High-Volume Centers



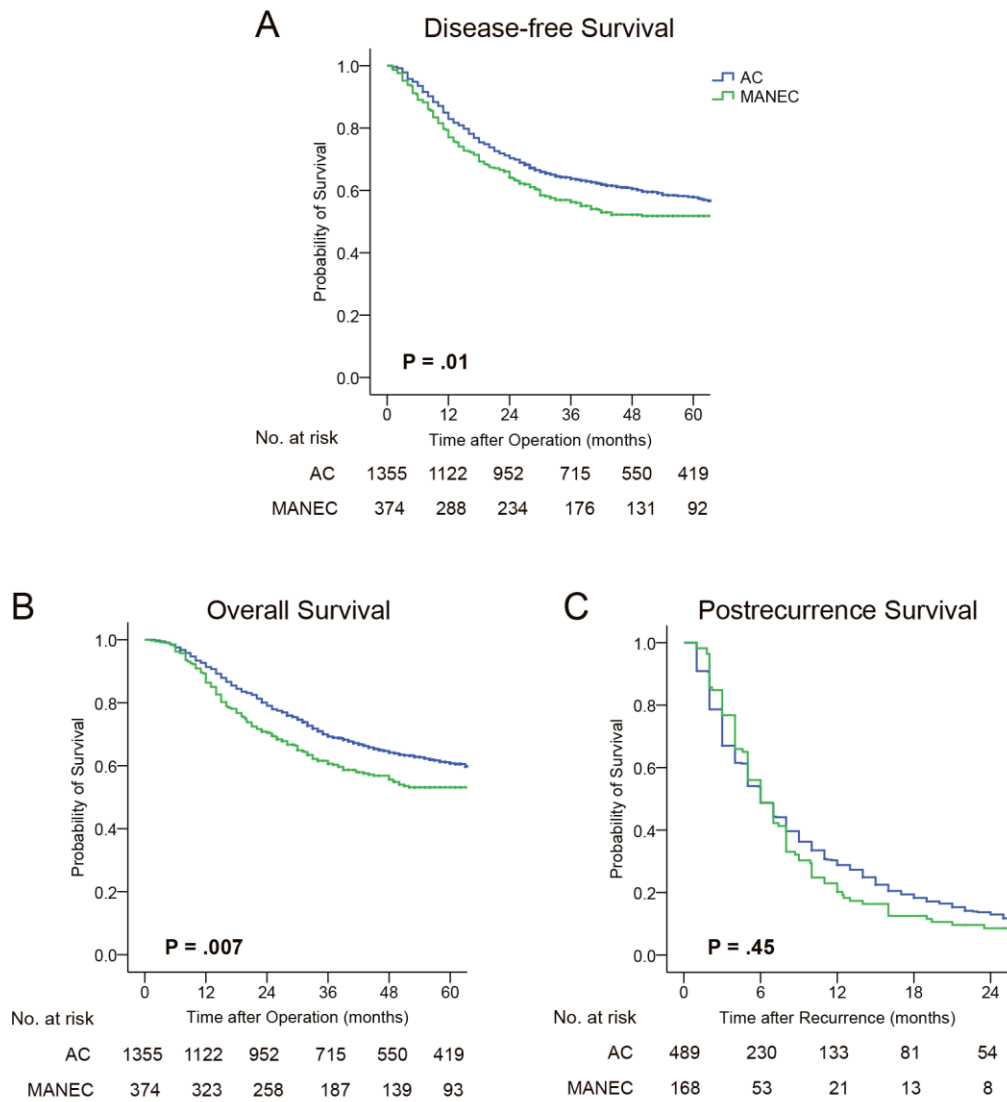
(A) Disease-free survival (DFS), (B) Overall survival (OS), and (C) postrecurrence survival (PRS).

eFigure 7. Recurrence Patterns According to Histologic Subtype in the Matched Data



(A-B) matched adenocarcinoma and neuroendocrine carcinoma patients; (C-D) matched adenocarcinoma and mixed adenoneuroendocrine carcinoma patients. Sizes of circles are proportional to the number of patients.

eFigure 8. Kaplan-Meier Survival Curves for Patients With Gastric Mixed Adenoneuroendocrine Carcinoma (MANEC) and Adenocarcinoma (AC) in High-Volume Centers



(A) Disease-free survival (DFS), (B) Overall survival (OS), and (C) postrecurrence survival (PRS).