



Effect of sarcopenia on short- and long-term outcomes in patients with gastric neuroendocrine neoplasms after radical gastrectomy: Results from a large, two-institution series

Running title:Sarcopenia and g-NENs



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Background

The relationship between sarcopenia and prognoses of patients with gastric neuroendocrine neoplasms (g-NENs) is unclear.

Objective

This study was designed to explore the effects of sarcopenia on short-term and long-term outcomes of patients with g-NENs after radical gastrectomy.

Methods

This study retrospectively collected data of 138 patients with g-NENs after radical gastrectomy. The skeletal muscle index (SMI) diagnostic threshold for sarcopenia was determined using X-tile software. Cox regression were used to determine the independent risk factors for 3-year overall survival (OS) and 3-year recurrence-free survival (RFS).

Results

- Clinicopathologic Characteristics
- Effects of Sarcopenia on Postoperative Complications
- Effects of Sarcopenia on the Prognosis of g-NENs Patients
- Effects of Sarcopenia on the Prognosis of Patients with Different Types of g-NENs

Table 1. Clinicopathological characteristics

Variable	All (n = 138)	Low (n = 59)	High (n = 79)	P
Gender				0.014
Male	105	51	54	
Female	33	8	25	
Age(years)				0.004
< 65	80	26	54	
≥ 65	58	33	25	
BMI(kg/m ²)				0.007
< 25	115	55	60	
≥ 25	23	4	19	
ASA				0.664
1	69	28	41	
2	54	23	31	
3	15	8	7	
Comorbidities				0.471
No	40	19	21	
Yes	98	40	58	
Tumor diameter(mm)				0.037
< 50	68	23	45	
≥ 50	70	36	34	
Tumor location				0.783
Upper	63	26	37	
Middle	27	12	15	
Lower	33	16	17	
Mix	15	5	10	
T stage				0.471
T1 + T2	77	35	42	
T3 + T4	61	24	37	
N stage				0.181
N0	46	16	30	
N1	92	43	49	
Surgical method				0.103
Open	43	14	29	
Laparoscopic	95	45	50	
Gastrectomy extent				0.67
Total	101	45	56	
Distal	33	13	20	
Proximal	4	1	3	
Pathological type				0.318
NET	12	3	9	
NEC	52	21	31	
MANEC	74	35	39	
Ki-67 positive index (%)				0.439
< 60	59	23	36	
≥ 60	79	36	43	
Complications				0.984
No	82	35	47	
Yes	56	24	32	
Adjuvant chemotherapy				0.193
No	66	32	34	
Yes	72	27	45	

SMI: Skeletal muscle index, BMI: Body mass index, ASA: American Society of Anesthesiologists, NET: Neuroendocrine tumor, NEC: Neuroendocrine carcinoma, MANEC: Mixed adenoneuroendocrine carcinoma

Table 2. Postoperative complications in 138 patients[Case(%)]

	Sarcopenia	Nonsarcopenia	P
Total complications	20 (33.9)	24 (30.4)	0.661
Serious complications	0 (0)	3 (3.7)	0.26
Surgical complications	8 (13.6)	12 (15.2)	0.788
Systemic complications	12 (20.3)	12 (15.2)	0.43
Physical location			

Pulmonary infection	12 (20.3)	12 (15.2)	0.43
Abdominal infection	4 (6.8)	3 (3.8)	0.461
Incisional infection	1 (1.7)	0 (0)	0.428
Chylous fistula	0 (0)	3 (3.8)	0.26
Intestinal obstruction	0 (0)	2 (2.5)	0.507
Anastomotic fistula	1 (1.7)	2 (2.5)	1
Abdominal bleeding	1 (1.7)	2 (2.5)	1
Anastomotic stenosis	1 (1.7)	0 (0)	0.428

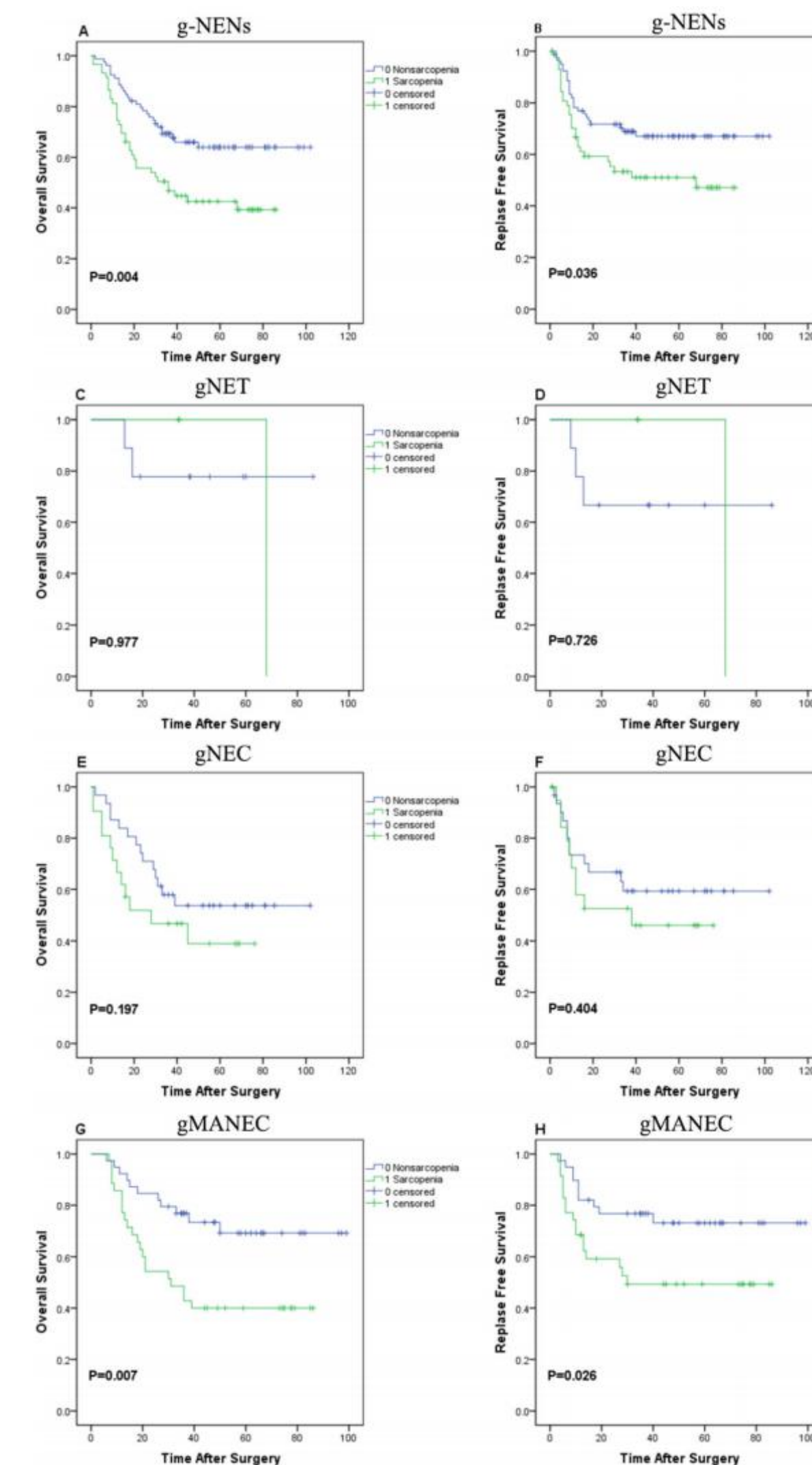


Fig. 1 Kaplan-Meier analysis of the 3-year overall survival (OS) and recurrence-free survival (RFS) rates of patients with gastric neuroendocrine neoplasms (g-NENs) stratified according to the presence of sarcopenia (a-b) and pathological types: c-d gastric neuroendocrine tumor (gNET), e-f gastric neuroendocrine carcinoma (gNEC), and (g-h) gastric mixed adenoneuroendocrine carcinoma (gMANEC)

Table 3 Uni- and multivariate analyses of factors associated with 3-year overall survival (OS) and recurrence-free survival (RFS) rates in g-NENs patients

Variable	Univariate analysis 3-year OS HR (95% CI)	P	Multivariate analysis 3-year OS HR (95% CI)	P	Univariate analysis 3-year RFS HR (95% CI)	P	Multivariate analysis 3-year RFS HR (95% CI)	P
Gender								
Male	1		1		1		1	
Female	0.800 (0.338-1.248)	0.195			0.813 (0.419-1.580)	0.542		
Age (years)								
< 65	1		1		1		1	
≥ 65	1.112 (0.660-1.887)	0.683			0.861 (0.486-1.483)	0.589		
BMI(kg/m ²)								
< 25	1		1		1		1	
≥ 25	0.694 (0.330-1.460)	0.336			0.709 (0.320-1.570)	0.396		
ASA								
1	1		1		1		1	
2	1.034 (1.146-3.347)	0.018	1.880 (1.089-3.287)	0.028	2.118 (1.196-3.748)	0.010	2.191 (1.273-3.826)	0.008
3	2.04 (1.172-5.504)	0.018	2.039 (0.917-4.686)	0.081	1.204 (0.487-3.437)	0.605	0.875 (0.324-2.341)	0.791
Comorbidity								
No	1		1		1		1	
Yes	1.246 (0.751-2.411)	0.318			0.993 (0.552-1.782)	0.981		
Tumor (mm)								
< 50	1		1		1		1	
≥ 50	1.096 (0.557-2.609)	0.073			1.449 (0.841-2.496)	0.181		
Tumor location								
Upper	1		1		1		1	
Middle	0.664 (0.314-1.403)	0.283			0.778 (0.349-1.734)	0.540		
Lower	0.817 (0.484-1.352)	0.389			1.164 (0.571-2.323)	0.349		
Mix	1.253 (0.353-2.646)	0.155			1.147 (0.494-2.664)	0.749		
T stage								
T1 + T2	1		1		1		1	
T3 + T4	1.748 (1.054-2.896)	0.031	1.645 (0.843-2.476)	0.181	1.569 (0.914-2.693)	0.103		
N stage								
N0	1		1		1		1	
N1	5.032 (2.385-10.616)	<0.001	3.504 (1.624-7.778)	0.002	3.882 (2.007-7.486)	<0.001	4.710 (1.966-11.283)	0.001
Surgical method								
Open	1		1		1		1	
Laparoscopic	0.767 (0.472-1.244)	0.295			0.875 (0.496-1.546)	0.647		
Gastrectomy extent								
Total	1		1		1		1	
Distal	0.74 (0.400-1.368)	0.337			1.080 (0.584-1.994)	0.807		
Proximal	0.418 (0.074-3.027)	0.388			0.538 (0.077-3.852)	0.529		
Pathological type								
NET	1		1		1		1	
NEC	2.352 (0.712-7.777)	0.161			1.521 (0.524-4.414)	0.441		
MANEC	1.839 (0.563-6.006)	0.313			1.172 (0.410-3.350)	0.767		
Ki-67 positive index (%)								
< 60	1		1		1		1	
≥ 60	4.753 (2.465-9.132)	<0.001	3.492 (1.772-6.876)	<0.001	3.978 (2.010-7.718)	<0.001	4.304 (1.981-9.333)	<0.001
Complication								
No	1		1		1		1	
Yes	1.645 (0.994-2.722)	0.053			1.245 (0.699-2.232)	0.457		
Adjuvant chemotherapy								
No	1		1		1		1	
Yes	1.409 (0.843-2.355)	0.181			1.029 (0.594-1.776)	0.117		
Martin et al. [27]								
High	1		1		1		1	
Low	1.181 (0.709-1.986)	0.523			1.377 (0.790-2.406)	0.240		
Stage								
Low	1		1		1		1	
High	2.061 (1.243-3.425)	0.005	2.098 (1.239-3.531)	0.006	1.758 (1.029-3.016)	0.041	1.780 (1.029-3.076)	0.039

Table 4 Uni- and multivariate analyses of factors associated with 3-year overall survival (OS) and recurrence-free survival (RFS) rates in gMANEC patients

Variable	Univariate analysis 3-year OS HR (95% CI)	P	Multivariate analysis 3-year OS HR (95% CI)	P	Univariate analysis 3-year RFS HR (95% CI)	P	Multivariate analysis 3-year RFS HR (95% CI)	P
Gender								
Male	1		1		1		1	
Female	0.788 (0.341-1.823)	0.578			1.030 (0.431-2.412)	0.964		
Age (years)								
< 65	1		1		1		1	
≥ 65	1.234 (0.616-2.472)	0.554			0.929 (0.431-2.002)	0.851		
BMI(kg/m ²)								
< 25	1		1		1		1	
≥ 25	0.856 (0.300-2.442)	0.772			0.809 (0.243-2.687)	0.729		
ASA								
1	1		1		1		1	
2	2.261 (1.038-4.929)	0.04	1.548 (0.701-3.422)	0.280	2.572 (1.141-5.801)	0.041	2.089 (0.917-4.758)	0.080
3	3.752 (1.371-10.146)	0.01	1.688 (0.636-4.578)	0.296	1.560 (0.426-5.660)	0.499	0.744 (0.197-2.813)	0.643
Comorbidity								
No	1		1		1		1	
Yes	0.846 (0.401-1.789)	0.662			0.528 (0.245-1.136)	0.104		
Tumor (mm)								
< 50	1		1		1		1	
≥ 50	1.528 (0.754-3.098)	0.239			1.264 (0.591-2.701)	0.546		
Tumor location								
Upper	1		1		1		1	
Middle	0.573 (0.186-1.741)	0.326			0.802 (0.275-2.321)	0.706		
Lower	0.852 (0.360-1.979)	0.708			1.100 (0.450-2.666)	0.837		
Mix	1.625 (0.383-6.513)	0.313			1.140 (0.317-4.094)	0.841		
T stage								
T1 + T2	1		1		1		1	
T3 + T4	2.197 (1.082-4.464)	0.029	2.145 (0.985-4.686)	0.055	1.753 (0.818-3.756)	0.149		
N stage								
N0	1		1		1		1	
N1	4.350 (1.756-11.979)	0.002	3.134 (1.146-8.531)	0.026	4.358 (1.568-13.248)	0.005	3.956 (1.313-11.917)	0.015
Surgical method								
Open	1		1		1		1	
Laparoscopic	0.698 (0.330-1.474)	0.346			0.778 (0.340-1.776)	0.552		
Gastrectomy extent								
Total	1		1		1		1	
Distal	0.691 (0.310-1.540)	0.366			1.201 (0.539-2.672)	0.654		
Proximal	0.160	0.982			0.980	0.984		
Ki-67 positive index (%)								
< 60	1		1		1		1	
≥ 60	4.874 (1.872-12.646)	0.001	3.701 (1.372-10.033)	0.010	11.552 (2.729-48.913)	0.001	8.210 (1.912-35.256)	0.005
Complication								
No	1		1		1		1	
Yes	1.645 (0.820-3.298)	0.161			1.200 (0.525-2.742)	0.666		
Adjuvant chemotherapy								
No	1		1		1		1	
Yes	1.428 (0.697-2.923)	0.31			1.248 (0.579-2.691)	0.572		
Martin et al. [27]								
High	1		1		1		1	
Low	1.667 (0.789-3.523)	0.181			1.868 (0.817-4.272)	0.138		
Stage								
Low	1		1		1		1	
High	2.473 (1.270-5.483)	0.009	2.732 (1.246-6.001)	0.012	3.756 (1.077-13.132)	0.037	3.825 (1.250-11.386)	0.013

Conclusion

Sarcopenia is not related to short-term prognoses of g-NENs patients. Sarcopenia is an independent risk factor for patients with gMANEC after radical surgery.

Conflicts of interest

There are no conflicts of interest or financial ties to disclose from any of author.

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