Visceral Fat Area and Bioelectrical Impedance Phase Angle as a Prognosticator in Advanced Gastric Cancer Patients Receiving Second-line Chemotherapy

Submission ID : 2012
Contact information:
hso102@yuhs.ac

Sang Uk Han[1], Se Eung Oh[1], Seo Young Lee[2], Ji Hyung Kim[2], Hei-Cheul Jeung[2]

[1]Department of Medicine, Graduate School, Yonsei University, Seoul, Korea, [2]Division of Medical Oncology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

BACKGROUND

- Gastric cancer (GC) is common in East Asian countries, accounting for more than 70% of the total global GC cases. The prognosis for patients with metastatic/recurrent gastric cancer remains dismal and 5-year survival rates do not exceed 25%.
- **Weekly paclitaxel plus ramucirumab (VEGFR-2 specific mAb)** therapy [PACL(W) + RAMU] is recommended as a second-line treatment, and it is widely used in Korea. However, no common prognostic index exists for the treatment.
- Advanced GC are **at high risk of malnutrition (>80%)**. Patients often present stricture of the gastric outlet, leading to early satiety, anorexia, and emesis. Moreover, these patients present **maldigestion and malabsorption**, dietary restrictions lead to loss of appetite and a low-protein diet and, eventually, malnutrition.
- **Phase angle (PhA)** reflects cell size, membrane integrity, and/or the distribution of water in the extra-/intra-cellular compartment
- It can be calculated directly as it arctangent: (Xc/R)x180º/π, and thus does not depend on equations and their inherent assumptions, in contrast to BIA-derived body compositions
- PhA indeed correlates with various indices of functional and nutritional indices, and it has been shown to be predictive of impaired clinical outcome and mortality.

PATIENTS and METHODS

- **Patients population:** Patients (N=189) undergoing PACL(W)+RAMU (Oct.2019~Nov.2022) at a single center
- **Inclusion criteria:** (1) age >18 years, (2) histologically confirmed GC, (3) metastatic disease or systemic recurrence, and (4) electronic medical records available
- **Exclusion criteria:** (1) CNS metastasis, (2) localized disease for which local therapy is preferred, (3) other synchronous malignancies, (4) uncontrolled infection, active GI bleeding, and severe concurrent disease, (5) lack of follow-up or transfer to a other hospital before a decision had been made.
- **Data collection**
  - **Demography**: age, sex, anthropometry, disease status, ECOG-PS, gastrectomy, and metastasis site
  - **Bioelectrical impedance analysis (BIA)**: body PhA, obesity, extracellular/intracellular water mass Index, body fat mass Index, body fat PER, visceral fat area, extracellular water PER, body water mass index)
  - **Laboratory data:** complete blood count, serum protein, albumin, SGOT/SGPT, ALP, CEA, and CA 19-9
- **Statistical analysis**
  - Laboratory values: transformed to categorical variables according to the upper normal ranges (WBC, Hb, Hct, platelet, serum protein, albumin, AST, ALT, ALP, cholesterol) or the best cutoff point (NLR, BIA parameters) by **Contal and O'Quigley method**
  - **Overall survival (OS), and Progression-free survival (PFS):** Kaplan-Meier and the log-rank test.
  - **Univariate analysis and stepwise multivariate analysis:** Cox's proportional hazard model.
  - Statistical analyses were performed using PASW Statistics ver. 18.0 (SPSS Inc., Chicago, IL).

STUDY OBJECTIVES

- The aim of this retrospective analysis is to determine whether **bioelectrical impedance analysis (BIA)** could be a predictor of survival outcomes in the patients with AGC who received second-line PACL(W) + RAMU therapy.
- Our hypothesis is whether **bioelectrical impedance phase angle** and **Visceral Fat Area (VFA)** could be utilized to identify patients who are likely to benefit from PACL(W)+RAMU therapy, which will lead to enhanced clinical decision-making and improved patient outcome.

RESULTS

Table 1. Comparison of baseline demographic and clinical parameters by VFA & Body PhA group in the patients with advanced gastric cancer

Characteristics		Low VFA + High PhA (Group 1)	High VFA & PhA or Low VFA & PhA (Group 2)	High VFA + Low PhA (Group 3)	P value
		(n=70, 37.0%)	(n=106, 56.1%)	(n=13, 6.9%)	
Sex	Male	62(88.6)	49(46.2)	5(38.5)	0.000
	Female	8(11.4)	57(53.8)	8(61.5)	
Age (median)		59(35-78)	59(23-81)	61(27-78)	0.937
Disease status	Recurrent	19(27.1)	39(36.8)	2(15.4)	0.171
	Metastasis	51(72.9)	67(63.2)	11(84.6)	
Gastrectomy	Not Done	38(54.3)	45(42.5)	11(84.6)	0.010
	Total, Subtotal	32(45.7)	61(57.5)	2(15.4)	
BMI (median)		21.8(16.4-26.6)	20.3(13.6-29.5)	26.4(22.1-29.2)	0.000
Tumor marker (median)	CEA(ng/ml)	3.4(0.8-1430)	3.1(0.3-1290)	4.1(1.1-22.5)	0.471
	CA19-9(IU/ml)	15.2(0.8-20000)	18.9(0.8-20000)	33.4(6.9-3400)	0.827
Complete blood count (median)	WBC (10^3/uL)	5310(2500-12630)	5770(2690-31810)	5490(2750-15290)	0.075
	Hb (g/dL)	11.6(7.0-14.9)	10.5(6.5-15.4)	10.3(7.7-13.2)	0.002
	Hct (%)	35.5(24.1-45.4)	32.7(11.8-45.7)	32.2(24.3-41.5)	0.005
	Platelet (10^3 /uL)	195.5(80.0-706.0)	211.5(35.1-491.0)	199(61.0-466.0)	0.643
	Neutrophil (10^3 /uL)	3165(990-6960)	3390(730-28560)	2680(1470-13150)	0.042
	Lymphocyte (10^3 /uL)	1500(640-3460)	1385(280-5600)	1850(560-2660)	0.700
Biochemistry (median)	Total Cholesterol (mg/dL)	163(100-286)	157(72-331)	146(73-253)	0.306
	Protein (g/dL)	6.9(5.2-8.0)	6.6(4.3-8.6)	6.5(5.4-8.2)	0.007
	Albumin (g/dL)	3.9(2.8-4.9)	3.6(2.3-4.6)	3.1(2.7-4.8)	0.001
	ALP (IU/L)	97(34-288)	103(24-2043)	95(48-437)	0.169
	AST (IU/L)	32(12-86)	30(11-165)	31(18-52)	0.985
	ALT (IU/L)	22(4-116)	19(5-233)	18(6-60)	0.824
	CRP (mg/L)	2.3(0.4-137.3)	5.0(0.1-133.1)	37.5(0.7-208.5)	0.003
Bioelectrical Impedance analysis (median)	Body PhA (°)	5.1(4.6-6.4)	3.9(2.3-5.3)	4.0(3.3-4.3)	0.000
	VFA (cm^2)	51.1(7.6-104.3)	59.1(15.6-159.8)	126.9(105.0-195.0)	0.000
	Extracellular Water Mass Index	5.1(3.5-6.0)	4.6(3.8-7.0)	4.8(3.9-6.2)	0.000
	Intracellular Water Mass Index	8.2(5.7-9.2)	6.9(5.5-9.0)	7.2(6.1-8.8)	0.000
	Limb Skeletal Muscle Mass Index	7.5(4.7-8.8)	6.3(4.4-10.8)	6.5(5.4-8.7)	0.000
	Body fat (%)	19.0(4.2-33.8)	20.5(3.0-40.3)	35.4(26.2-48.6)	0.000
	Obesity (%)	99(78-121)	93(65-140)	123(105-139)	0.000
	Extracellular Water(%)	0.386(0.375-0.405)	0.398(0.384-0.436)	0.401(0.389-0.416)	0.000
	Body Water Mass Index	13.3(9.2-15.0)	11.5(9.6-16.0)	12.0(9.9-15.0)	0.000
NLR (median)		1.93(0.59-6.23)	2.34(0.34-23.42)	2.55(0.56-12.18)	0.040

*All data are present as median (range); otherwise are shown as n (%), The meaning of index is the item divided by the square of the height
CEA: carcinoembryonic antigen, CA19-9: carbohydrate antigen 19-9, WBC: white blood cell, Hb: hemoglobin, Hct: hematocrit, ALP: alkaline phosphatase. AST: aspartate aminotransferase ALT: Alanine aminotransferase, CRP: C-reactive protein, BMI: body mass index

Table 2. Multivariate analysis of PFS

Progression Free Survival					
Category	Characteristics	Variables	Multivariate analysis		
			HR	95% CI	p-value
Bioelectrical Impedance analysis	VFA & Body PhA	Group 2 / Group 1	1.546	1.060~2.257	0.024
		Group 3 / Group 1	2.391	1.213~4.715	0.012
	Intracellular Water Mass Index	≥8 / <8	1.672	1.150~2.431	0.007

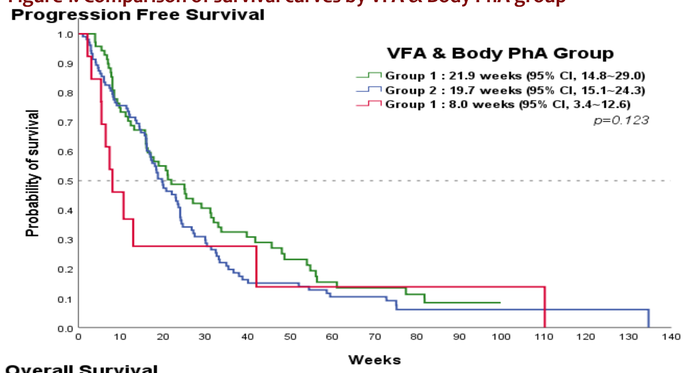
Unselected : Extracellular Water Mass Index, Limb Skeletal Muscle Mass Index
Number of Metastasis, Body Water Mass Index, Extracellular Water PER

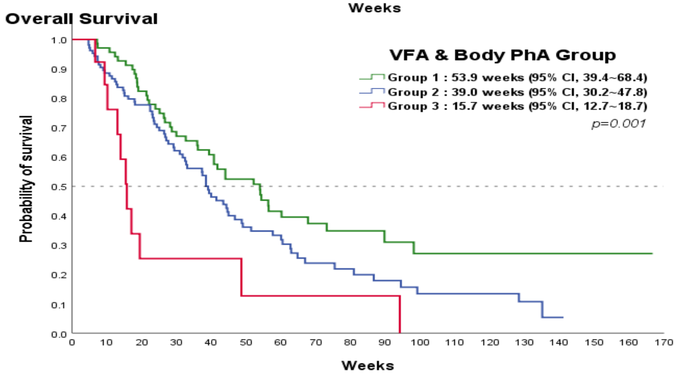
Table 3. Multivariate analysis of OS

Overall Survival					
Category	Characteristics	Variables	Multivariate analysis		
			HR	95% CI	p-value
Bioelectrical Impedance analysis	VFA & Body PhA	Group 2 / Group 1	1.594	1.036~2.453	0.034
		Group 3 / Group 1	4.151	2.033~8.476	0.000
	Body Water Mass Index	≥12.4 / <12.4	1.634	1.096~2.434	0.016
NLR	NLR	≥2.39 / <2.39	2.002	1.378~2.909	0.000
Biochemistry	CRP	≥5.1 / <5.1	2.302	1.572~3.372	0.000

Unselected : Extracellular Water Mass Index, Extracellular Water PER, Number of Metastasis
Limb Skeletal Muscle Mass Index, Intracellular Water Mass Index

Figure 1. Comparison of survival curves by VFA & Body PhA group





CONCLUSION

- **Combination of VFA & Body PhA is an independent prognostic indicator of poor clinical outcomes for patients with advanced GC undergoing 2L PACL(W) plus RAMU therapy.**
- **Limitation: Retrospective design from single institute, Confounding factor from different nutritional support**