Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

UN'ANALISI MULTIVARIATA DEI MARKERS SISTEMICI DI INFIAMMAZIONE NEL TUMORE DELLA CERVICE SOTTOPOSTO A CHEMIORADIOTERAPIA DEFINITIVA

(A COMPREHENSIVE MULTIVARIATE ANALYSIS OF MULTIPLE SYSTEMIC INFLAMMATION MARKERS IN CERVICAL CANCERS UNDERGOING DEFINITIVE CHEMORADIATION)

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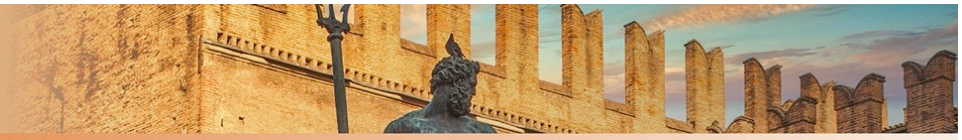


DICHIARAZIONE

Relatore: DR.SSA LUDOVICA FORLANI

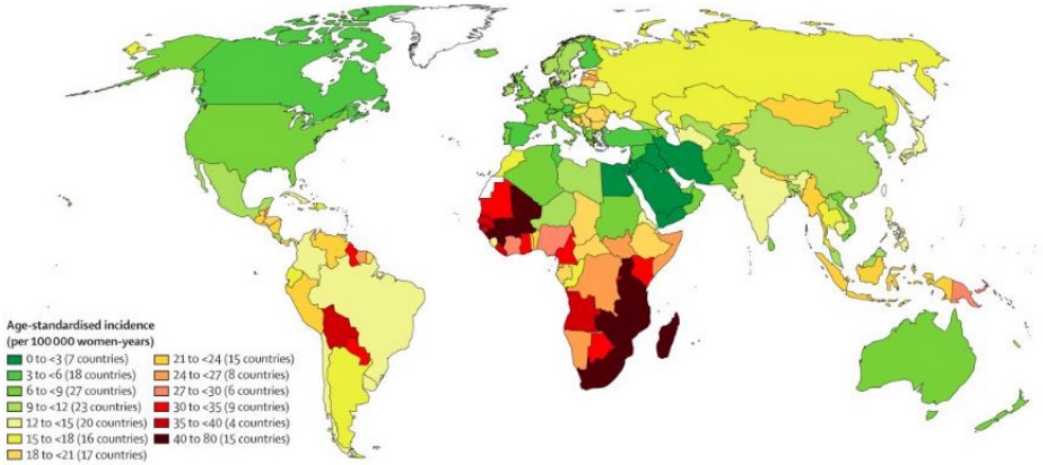
Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

CERVICAL CANCER EPIDEMIOLOGY

Cervical cancer is:

- the 4th most common cancer, with more than 85% of cases occurring in developing countries where cervical cancer is a leading cause of cancer death in women.
- In several Western Countries, where screening programs have long been established, cervical cancer rates have decreased by as much as 65% over the past 40 years



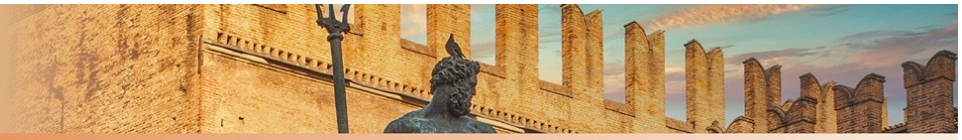
CERVICAL CANCER TREATMENT

Surgery and chemoradiation are widely utilized treatments for cervical cancer.

RT is often used in the management of patients with cervical cancer either:

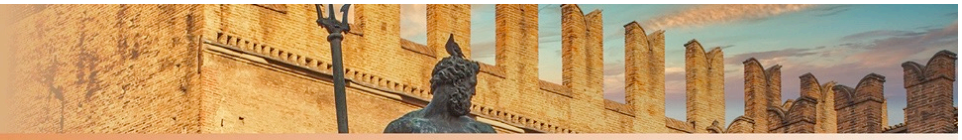
- as definitive therapy, with concurrent chemotherapy, for those with locally advanced disease or for those who are poor surgical candidates

According to international guidelines advanced-stage disease, including FIGO stage IIB and above, is not usually treated with hysterectomy.



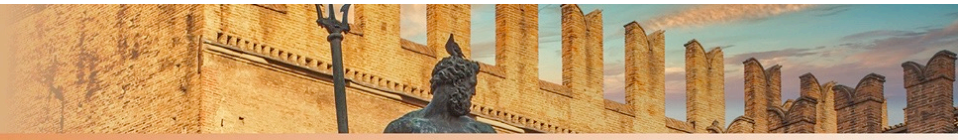
SYSTEMIC INFLAMMATORY MARKERS

Author/year	Type of study	Evaluated index	Cut-off	Outcome predictions	Type of analysis	Considered confounders
Lee et al. 2012	retrospective	NLR	1.9	higher NLR associated with poor survival	univariate multivariate	age histology FIGO stage type of treatment
Mizunuma et al. 2015	retrospective	NLR	2.5	<OS and <PFS if NLR>2.5	univariate multivariate	age histology FIGO stage tumor size lymph node metastases type of treatment
Li et al. 2016	retrospective	LMR	5.28	>PFS and >OS if LMR high	univariate multivariate	age histology lymph node metastases HPV +
Onal et al. 2016	retrospective	NLR PLR	3.03 133.02	NLR and PLR associated to larger tumors, lymph node metastases and poorer therapeutic response <OS and <PFS if higher NLR or PLR	univariate multivariate	age histology FIGO stage tumor size lymph node metastases
Wang et al. 2016	retrospective	NLR	2	<OS if NLR>2	univariate multivariate	age histology FIGO stage tumor size lymph node metastases
Koulis et al. 2017	retrospective	NLR Hb	5 11.5	<PFS and <OS if NLR>5 <PFS and <OS if Hb<11.5	univariate multivariate	age histology FIGO stage tumor size lymph node metastases type of treatment
Holub et al. 2018	retrospective	NLR PLR SII ELR	3.8 210 1000 0.07	<OS if NLR>3.8 or PLR>210 or SII>1000 or ELR>0.07 <PFS if PLR>210 or SII>1000	univariate multivariate	age histology FIGO stage HPV +



SYSTEMIC INFLAMMATORY MARKERS

Author/year	Type of study	Evaluated index	Cut-off	Outcome predictions	Type of analysis	Considered confounders
Jonska-Gymrec et al./2018	retrospective	NLR PLR MLR	1.6 158 0.33	<OS if NLR>1.6 <OS if PLR>158 in pts FIGO IIb-IV	univariate multivariate	age histology FIGO stage tumor grade Lymph node metastases
Jeong et al. 2019	retrospective	NLR	2.8	<PFS if NLR>2.8	univariate multivariate	age histology tumor size FIGO stage type of treatment
Kim et al. 2020	retrospective	NLR PLR LMR Hb	2.33 136.6 4.17 11.5	ΔNLR strongest predictor of survival	univariate multivariate	age histology FIGO stage
Lee et al. 2020	retrospective	NLR MLR PLR	3.04 174.30 3.85	ΔNLR and ΔPLR prognostic factors for DFS	univariate multivariate	age histology FIGO stage tumor size lymph node metastases
Lee et al. 2021	retrospective	NLR PLR	2.34 148.89	<DFS and <OS if combination of high NLR and PLR	univariate multivariate	age histology FIGO stage tumor size lymph node metastases
Chauan et al. 2022	retrospective	NLR PLR Hb	3 70 11	NLR <3 e PLR <70 associated to CR	univariate multivariate	age histology FIGO stage
Liang et al. 2022	retrospective	NLR	3.87	<OS and <PFS if NLR>3.87	univariate multivariate	age BMI histology FIGO stage tumor size lymph node metastases type of treatment



AIMS

Analyze a wide range of inflammation indices

- ELR - eosinophil to lymphocyte ratio
- LMR - lymphocyte to monocyte ratio
- MLR - monocyte to lymphocyte ratio
- NLR - neutrophil to lymphocyte ratio
- PLR - platelet to lymphocyte ratio
- SII - systemic immune-inflammation index
- SIRI - systemic inflammatory response index

including also other known prognostic factors:

- AGE
- BMI
- FIGO STAGE
- HB

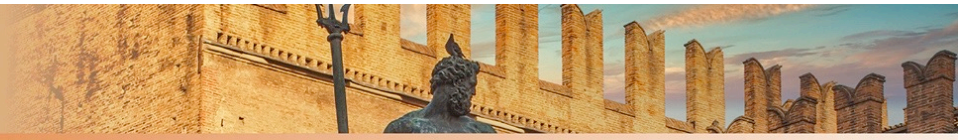
METHODS

Retrospective analysis:

- 173 patients
- Staged according to FIGO 2018
- Underwent a radical chemoradiation treatment
- from July 2007 to July 2021
- Median age: 56 yo (range 27-85)
- Pretreatment values of inflammatory indices

METHODS

- Univariate analysis (logrank test) on the impact of individual parameter:
  - LC - local control
  - DMFS - distant metastasis free survival
  - DFS - disease free survival
  - OS - overall survival
- Multivariate Cox analysis on the same endpoints performed including parameters significantly correlated with outcomes at univariate analysis.



RESULTS: UNIVARIATE

Variable	Value	Patients N (%)	2-year LC(%)	5-year LC (%)	*p*-Values	2-year DMFS (%)	5-year DMFS (%)	*p*-Values	2-year DFS (%)	5-year DFS (%)	*p*-Values	2-year OS (%)	5-year OS (%)	*p*-Values
Age (years)	< 55	72 (44%)	84.2	82.3	0.99	84.7	83	**0.026**	74.6	63.2	0.353	88.8	78.1	**0.004**
	55 ≥ age < 70	62 (36%)	83.1	81.1		84.2	72.6		73	58		82.4	63.3	
	≥70	34 (20%)	83.7	83.7		64.8	60.5		55.2	55.2		77.2	48.2	
BMI	< 18.5	7 (4%)	85.7	85.7	0.228	71.4	71.4	**0.004**	71.4	71.4	**0.003**	85.7	42.9	**0.002**
	18.5≧BMI<25	84 (49%)	90.4	88.7		88.5	87		79.9	76.5		90	80.9	
	25 ≧ BMI <30	51 (29%)	80	77.7		76.6	67.6		66.2	58.4		85.5	65	
	≥ 30	31 (18%)	71.6	71.6		67.8	52.8		48.4	39.1		74.9	44.2	
cT stage	1-2	133 (77%)	87.5	85.4	**0.008**	82.3	76	0.271	75.2	66.4	**0.013**	88.9	72.3	0.102
	3	18 (10%)	81.9	81.9		78.4	62.7		76	60.8		77.4	40.6	
	4	22 (13%)	62.9	62.9		71.9	71.9		48.1	48.1		70.7	64.8	
cN stage	0	102 (59%)	86.9	85.3	0.236	86.1	81.6	**0.023**	75	68.9	0.058	87.2	75.4	0.102
	1-2	71 (41%)	79.3	72.4		72.6	64.7		62.6	57.1		83.5	61.6	
FIGO	I-II	77 (45%)	93.4	91.5	**0.002**	90.3	85.1	**0.008**	82.2	74.8	**<0.001**	93.3	85.0	**0.014**
	III	73 (42%)	9.6	79.6		72.9	63.8		62.8	56.6		81.8	57.0	
	IV	23 (13%)	64.2	64.2		72.8	72.8		49.7	49.7		65.2	65.2	
HB	<10	16 (9%)	49.2	49.2	**<0.001**	72.3	72.3	0.271	48.1	48.1	**0.002**	51.6	51.6	**<0.001**
	≧10-<12	42 (24%)	73.3	69.7		79.5	79.5		63.4	60.1		79.5	66.8	
	≧12	115 (67%)	92.5	91.4		82.4	73.8		75.3	67.7		92.5	72.5	
NLR	≤3.59	122 (71%)	88.6	86.2	**0.004**	81.6	74.6	0.698	74.5	65.5	0.117	90.3	69.5	0.164
	>3.59	51 (29%)	72.3	72.3		78.5	75.1		63.4	60.4		74.8	68.2	
PLR	≤210.00	127 (73%)	88.3	85.9	**0.005**	83.1	77.3	0.147	73.6	66.7	**0.048**	88.8	73.6	0.080
	>210.00	46 (27%)	71.4	71.4		73.6	67.5		59.2	56.4		77.4	63.3	
SII	≤1000.00	106 (61%)	87.8	86.1	**0.039**	80.3	74.3	0.864	70.8	63.3	0.430	87.6	67.9	0.734
	>1000.00	67 (39%)	77.4	75.6		81.2	75.0		68.1	64.2		82.8	70.7	
ELR	≤0.07	79 (46%)	86.8	86.8	0.230	83.5	79.7	0.222	75.8	71.8	0.056	89.4	73.8	0.371
	>0.07	94 (54%)	81.3	78.1		78.3	70.3		64.9	57.6		82.6	65.1	
LMR	≤5.28	120 (69%)	78.8	76.5	**0.007**	80.6	74.7	0.687	67.6	60.9	0.259	83.4	68.4	0.259
	>5.28	53 (31%)	95.9	95.9		80.7	74.3		75.3	71.7		91.4	71.7	
MLR	≤0.26	103 (60%)	88.4	85.5	**0.036**	79.7	72.8	0.347	69.2	63.9	0.779	88.2	66.1	0.791
	>0.26	70 (40%)	77.0	77.0		82.0	77.4		70.6	64.2		82.2	74.1	

RESULTS: MULTIVARIATE

Higher LC rates were significantly correlated only to higher hemoglobin levels

(HR 0.57; 95% CI: 0.46-0.71, p<0.001)

CONCLUSION

- Limited role of systemic inflammation markers in predicting prognosis in patients undergoing ChRT

- Dramatically negative impact of anemia in this setting

CONCLUSION

However, further studies are underway to evaluate:

I. the impact of inflammation markers assessed after ChRT

II. the possible correlation between inflammation markers, radiomics features and sarcopenia and the predictive role of their combination in this setting.

GRAZIE PER L'ATTENZIONE

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