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CANCER RESEARCH FOR PERSONALIZED MEDICINE
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Personalized prognostic factors of resectable Lung Cancer

Facteurs Pronostiques Personnalisés du Cancer Pulmonaire Opéré

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PROGNOSTIC FACTORS OF OPERATED LUNG CANCER: AHEAD OF TNM

TNM CLASSIFICATION

1. PROGNOSIS IS BASED ON TUMOR EXTENSION
2. TUMOR IS A DISEASE WHICH PROGRESS FIRST LOCALLY (T), THEN REGIONALLY (N) AND LATELY SYSTEMIC (M).

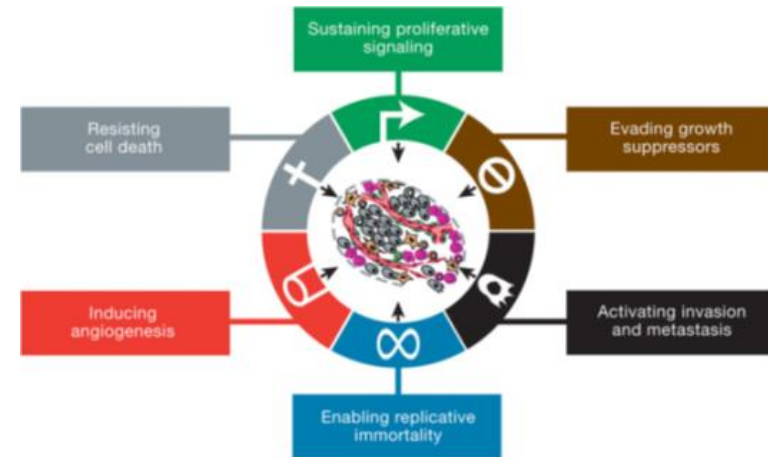
Each stage progression is associated to a worst prognosis

The Hallmarks of Cancer 2000

Hanahan D and Weinberg RA.



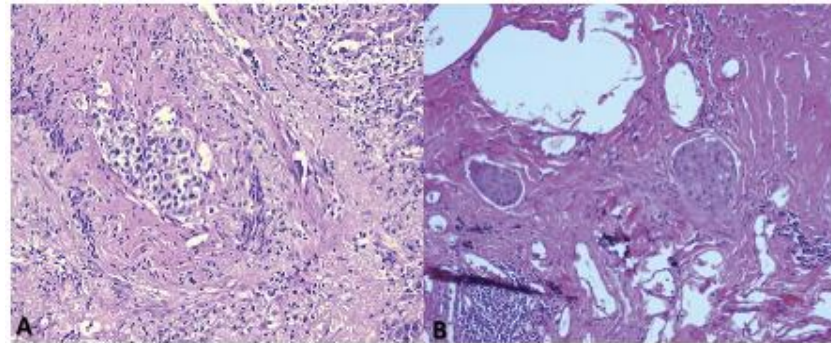
In 2000 from a biological point of view the determinants of cancer were almost exclusively intrinsic to cancer cells.



Prognostic Significance of Vascular and Lymphatic Emboli in Resected Pulmonary Adenocarcinoma

Salvatore Strano, MD, Audrey Lupo, MD, Filippo Lococo, MD, Olivier Schussler, MD, PhD, Mauro Loi, MD, Mohamad Younes, MD, PhD, Antonio Bobbio, MD, PhD, Diane Damotte, MD, PhD, Jean-François Regnard, MD,* and Marco Alifano, MD, PhD*

Departments of Thoracic Surgery and of Pathology, Hôtel-Dieu Hospital, Paris Descartes University, Paris, France; and Department of Thoracic Surgery, Catholic University of Rome, Rome, Italy

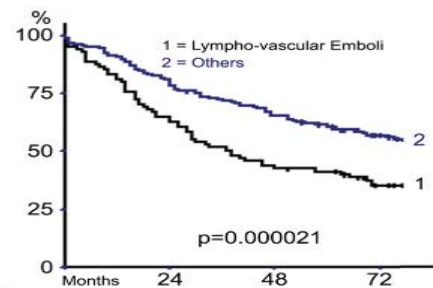


Multivariate Analysis (Model 1)	Odds Ratio (CI)	p Value
Age, >65 years	1.5 (1.13–1.98)	0.0047
Extent of resection		
Lobectomy	1	0.17
Pneumonectomy	1.35 (0.88–2.07)	
Pathologic stage		
I	1	0.00000032
II	1.43 (1.25–1.64)	
III	2.05 (1.55–2.69)	
IV	2.92 (1.94–4.42)	
Vascular emboli	1.07 (0.8–1.44)	0.65
Lymphatic emboli	1.34 (1–1.81)	0.05

Multivariate Analysis (Model 2)	Odds Ratio (CI)	p Value
Age, >65 years	1.5 (1.12–2.02)	0.007
Extent of resection		
Lobectomy	1	0.57
Pneumonectomy	1.15 (0.71–1.85)	
Pathologic stage	...	
T size		
<2 cm	1	0.032
2–3 cm	1.17 (1.01–1.35)	
3–5 cm	1.37 (1.03–1.83)	
5–7 cm	1.61 (1.04–2.48)	
>7 cm	1.88 (1.06–3.36)	
pN		
N0	1	0.0000096
N1	1.46 (1.23–1.72)	
N2	2.13 (1.52–2.97)	
Vascular emboli	1.07 (0.79–1.45)	0.67
Lymphatic emboli	1.39 (1.02–1.90)	0.036

CI = confidence interval; COPD = chronic obstructive pulmonary disease.

Ann Thorac Surg
2013;95:1204–11



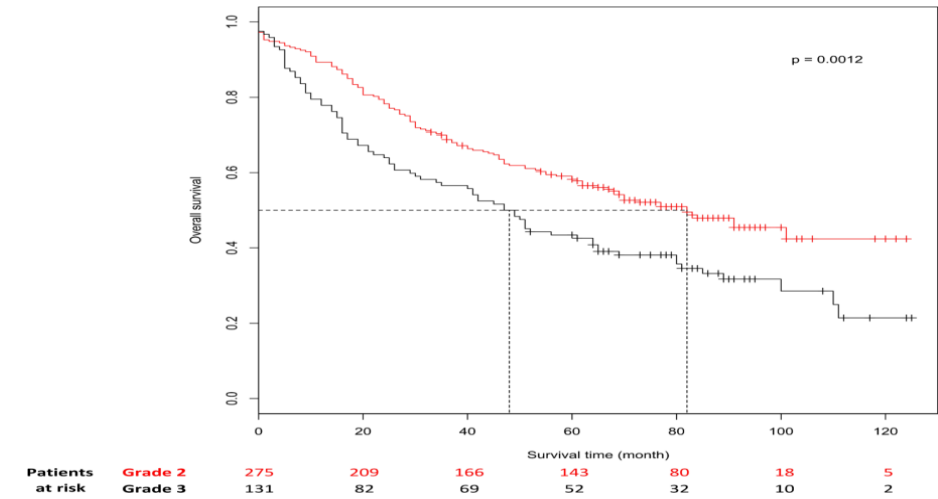
	Patients at Risk			
Months	0	24	48	72
Group 1	96	62	38	20
Group 2	267	207	140	77

Fig 4. Survival according with the simultaneous presence of both lymphatic and vascular emboli.

The New Histologic Classification of Lung Primary Adenocarcinoma Subtypes Is a Reliable Prognostic Marker and Identifies Tumors With Different Mutation Status

The Experience of a French Cohort

Audrey Mansuet-Lupo, MD; Antonio Bobbio, MD, PhD; H el ene Blons, PharmD, PhD; Etienne Becht; Hanane Ouakrim; Audrey Didelot; Marie-Christine Charpentier, MD; Serge Bain; B eatrice Marmey; Patricia Bonjour; J er ome Biton, PhD; Isabelle Cremer, PhD; Marie-Caroline Dieu-Nosjean, PhD; Catherine Saut es-Fridman, PhD; Jean-Fran ois R egnard, MD; Pierre Laurent-Puig, MD, PhD; Marco Alifano, MD, PhD, FCCP; and Diane Damotte, MD, PhD



– Kaplan-Meier survival curves (log-rank test) for histologic grade. The tumors were divided into two histologic grades according to International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society. Classification: intermediate-grade group (lepidic-, acinar-, and papillary-predominant pattern) and high-grade group (solid-, mucinous-, micropapillary-, and solid with signet ring cells-predominant pattern).

ORIGINAL ARTICLE

Intratumoral Immune Cell Densities Are Associated with Lung Adenocarcinoma Gene Alterations

Audrey Mansuet-Lupo^{1,2,3,4}, Marco Alifano^{3,5}, Nicolas Pécuchet^{6*}, Jérôme Biton^{1,2,3*}, Etienne Becht^{1,2,3}, Jeremy Goc^{1,2,3}, Claire Germain^{1,2,3}, Hanane Ouakrim^{1,2,3}, Jean-François Régnard^{3,5}, Isabelle Cremer^{1,2,3}, Pierre Laurent-Puig^{3,6,7}, Marie-Caroline Dieu-Nosjean^{1,2,3}, Hélène Blons^{3,6,7†}, and Diane Damotte^{1,2,3,4†}

¹INSERM UMRS 1138, Centre de Recherche des Cordeliers, Paris, France; ²Université Pierre et Marie Curie-Paris 6, Paris, France; ³Université Paris Descartes-Paris 5, Paris, France; ⁴Service de Pathologie and ⁵Service de Chirurgie Thoracique, Hôpital Cochin, and ⁶Service de Biochimie, Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris, Paris, France; and ⁷INSERM UMRS 1147, Paris, France

282 (89%) ADKs with \geq 1 mutation

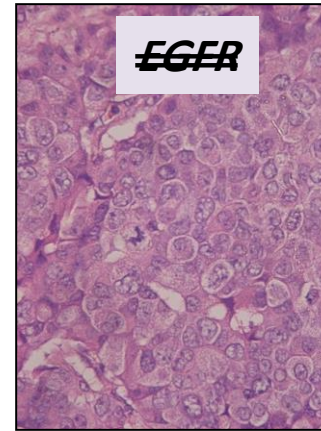
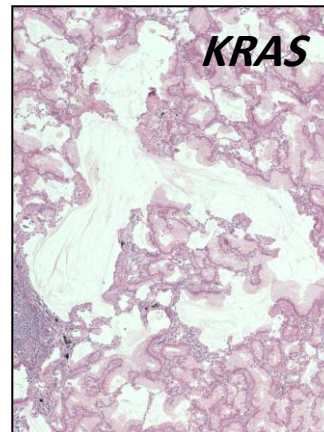
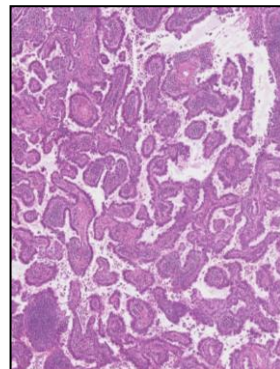
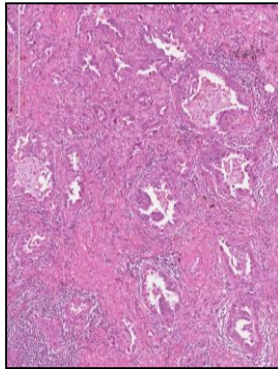
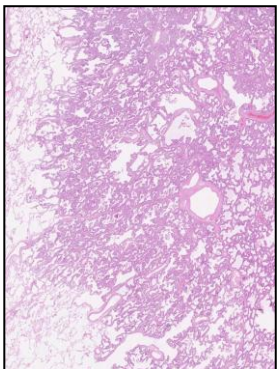
<i>TP53</i> : 58,9%	<i>BRAF</i> :4%
<i>KRAS</i> : 40%	<i>HER2</i> : 2%
<i>STK11</i> : 24,3 %	<i>NRAS</i> : 1,5%
<i>EGFR</i> : 14%	

Associations between molecular alterations and ADK subtype :

Mucinous ADK / *KRAS* mutation (p=0,003)

Intermediate grade/ *EGFR* mutation (p=0,01)

Solid ADK : inverse correlation with mutation *EGFR* mutation (p=0,003)



Intermediate grade : *EGFR* mutation

High density of intratumoral CD8+ T cells

associated with

- smoking (P = 0.02)
- TP53 mutation (P = 0.02)

Low density of intratumoral CD8+ T cells associated with

- BRAF mutation (P = 0.005).

High density of mDCs associated with

- small tumors (P = 0.009),
- low stage (P = 0.01)
- no pleural invasion (P = 0.01)

Low density of mDCs associated with

- STK11 mutation (P = 0.004)

PROGNOSTIC FACTORS OF OPERATED LUNG CANCER: AHEAD OF TNM

- **Hallmarks of Cancer: The Next Generation.**

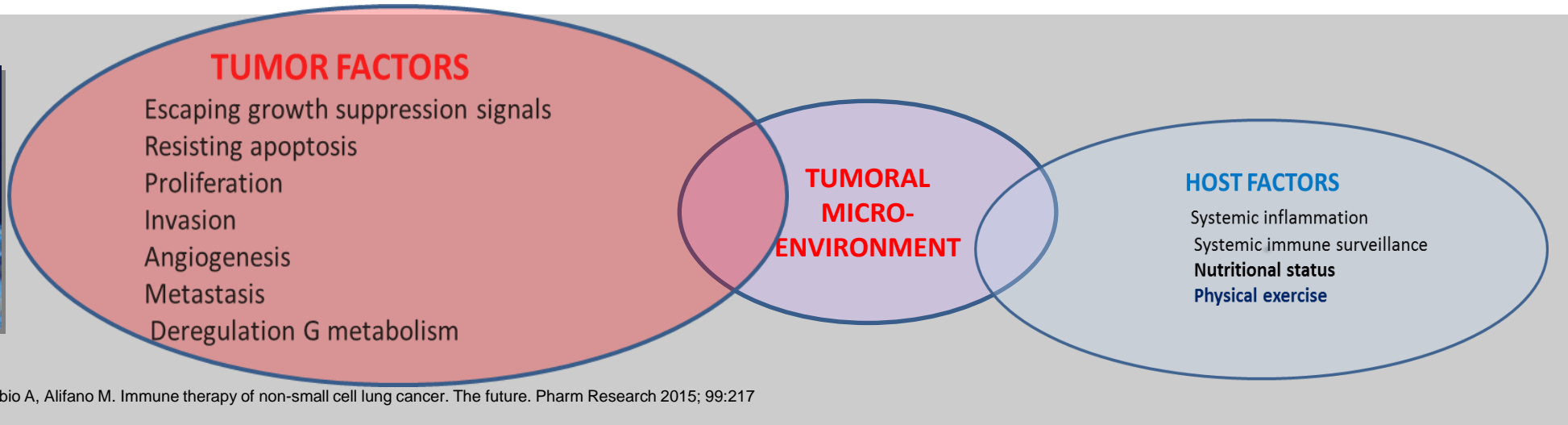
Hanahan D and Weinberg RA. 2011

- *Tumors are more than insular masses of proliferating cancer cells!!*
- *They are complex tissues composed of multiple distinct cell types that participate in heterotypic interactions with one another.*



- Two emerging hallmarks of cancer:
 - Reprogramming of energy metabolism
 - **EVADING IMMUNE DESTRUCTION**
- Two enabling characteristics:
 - **INFLAMMATION**
 - Genome instability.
- Recognition of «**tumoral micro environment**»

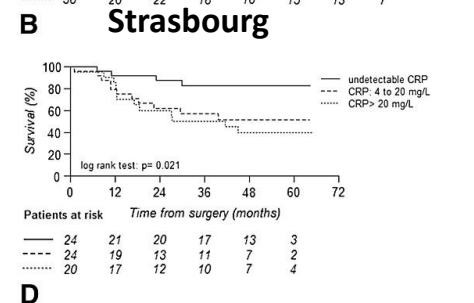
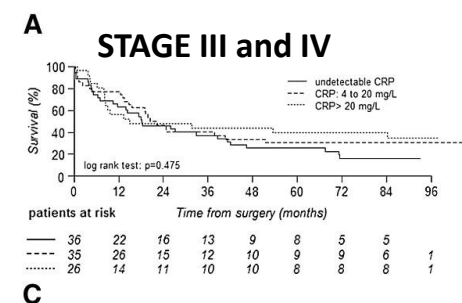
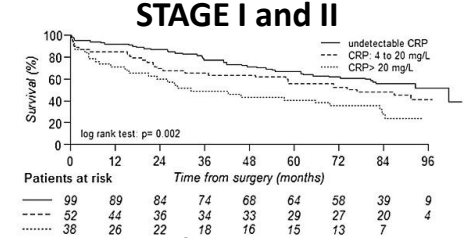
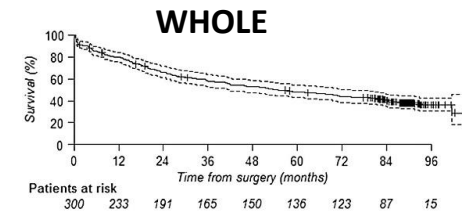
Our approach: Host and tumor factors interact through tumoral immune environment



Alifano et al **General Thoracic Surgery**

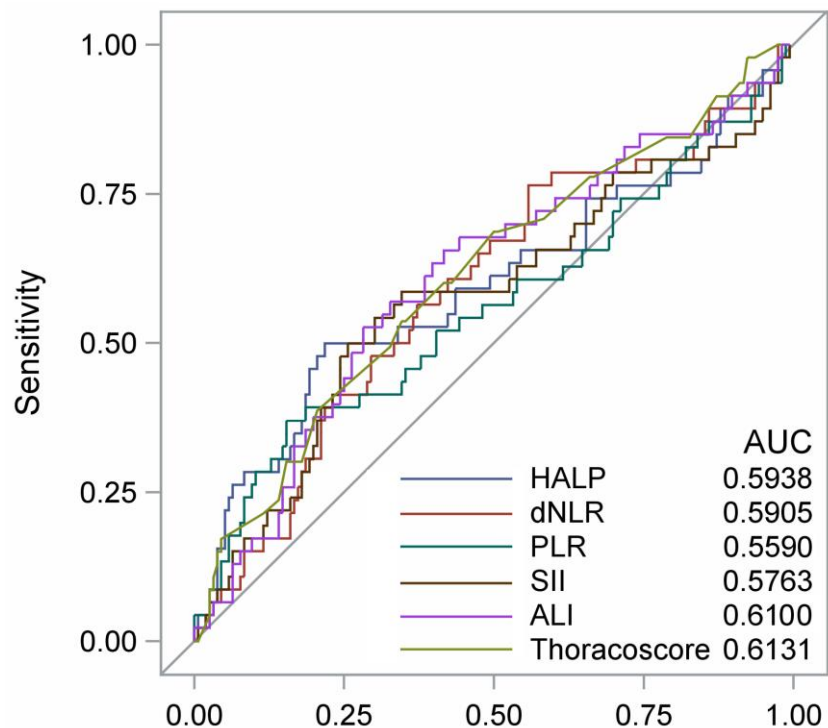
Preresection serum C-reactive protein measurement and survival among patients with resectable non-small cell lung cancer

Marco Alifano, MD, PhD,^{a,e} Pierre E. Falcoz, MD, PhD,^f Valérie Seegers, MD,^b Nicolas Roche, MD, PhD,^c Olivier Schussler, MD, PhD,^a Mohamad Younes, MD,^e Filippo Antonacci, MD,^f Patricia Forgez, PhD,^e Agnes Dechartres, MD,^b Gilbert Massard, MD,^f Diane Damotte, MD, PhD,^{d,g,h,i} and Jean-François Régnard, MD^a

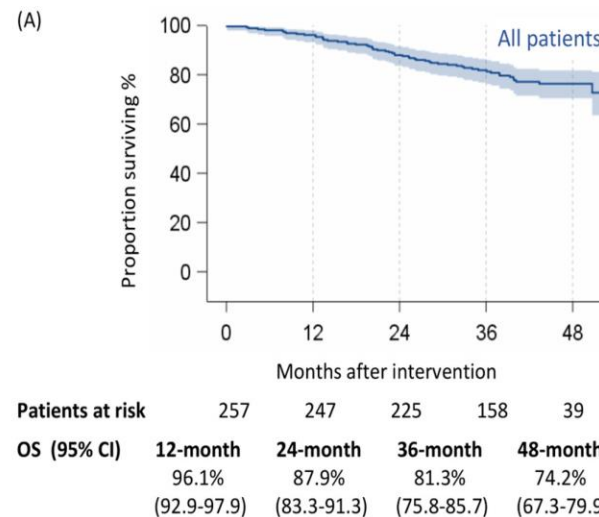


Systemic Inflammation and Lung Cancer: Is It a Real Paradigm? Prognostic Value of Inflammatory Indexes in Patients with Resected Non-Small-Cell Lung Cancer

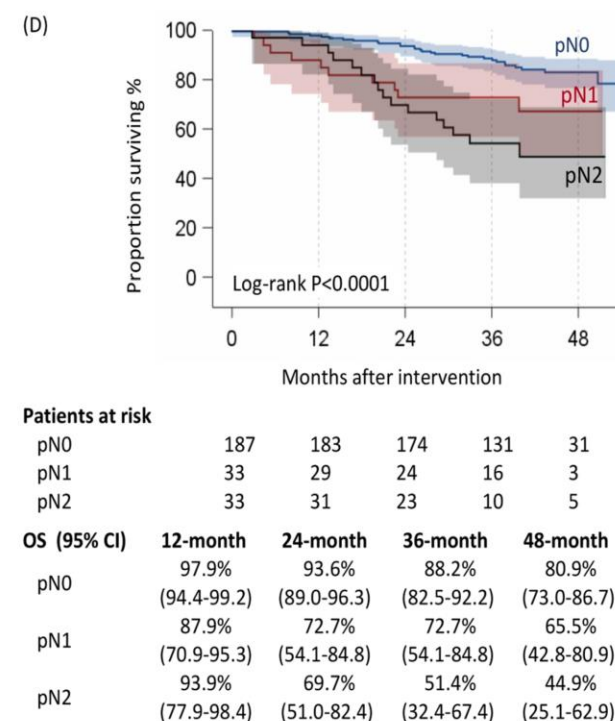
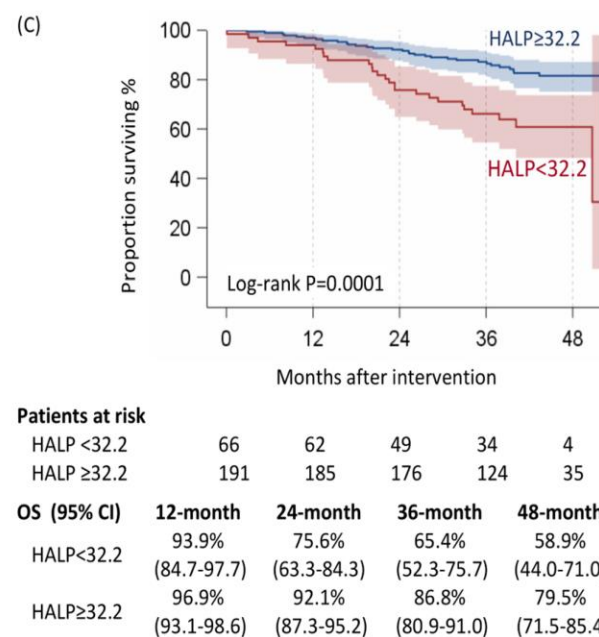
by Antonio Mazzella ^{1,†,‡} Elena Maiolino ^{1,†}, Patrick Maisonneuve ² Mauro Loi ¹ and Marco Alifano ¹










PLR=platelet-to-lymphocyte ratio
 PNI= albumin multiplying lymphocytes
 NLR=neutrophil-to-lymphocyte ratio
 SII= serum platelets * neutrophil/lymphocytes
 ALI= serum albumin * BMI/NLR



HALP=hemoglobin x
 albumin x lymphocytes/
 platelets



**Systemic Inflammation and Lung Cancer: Is It a Real Paradigm?
Prognostic Value of Inflammatory Indexes in Patients with Resected
Non-Small-Cell Lung Cancer**

by  Antonio Mazzella ^{1,†,‡}   Elena Maiolino ^{1,†},  Patrick Maisonneuve ²  Mauro Loi ¹ and  Marco Alifano ¹ 

Correlations between inflammatory markers and tumor characteristics

	pN				Stage			
	pN0 N (%)	pN1 N (%)	pN2 N (%)	p-Value *	I N (%)	II N (%)	III N (%)	p-Value *
HALP								
<32.16	44 (67.7)	13 (20.0)	8 (12.3)		27 (40.9)	20 (30.3)	19 (28.8)	
≥32.16	143 (76.1)	20 (10.6)	25 (13.3)	0.47	118 (61.8)	37 (19.4)	36 (18.8)	0.008
dNLR								
<2.67	75 (75.8)	12 (12.1)	12 (12.1)		63 (62.4)	21 (20.8)	17 (16.8)	
≥2.67	112 (72.7)	21 (13.6)	21 (13.6)	0.62	82 (52.6)	36 (23.1)	38 (24.4)	0.09
PLR								
<196.1	158 (76.7)	23 (11.2)	25 (12.1)		126 (60.3)	45 (21.5)	38 (18.2)	
≥196.1	29 (61.7)	10 (21.3)	8 (17.0)	0.08	19 (39.6)	12 (25.0)	17 (35.4)	0.004
SII								
<723.3	134 (77.9)	18 (10.5)	20 (11.6)		113 (64.6)	34 (19.4)	28 (16.0)	
≥723.3	53 (65.4)	15 (18.5)	13 (16.0)	0.08	32 (39.0)	23 (28.0)	27 (32.9)	<0.0001
ALI								
<34.86	57 (67.9)	14 (16.7)	13 (15.5)		38 (44.7)	24 (28.2)	23 (27.1)	
≥34.86	130 (76.9)	19 (11.2)	20 (11.8)	0.18	107 (62.2)	33 (19.2)	32 (18.6)	0.02

Multivariate analysis.

Parameter	HR (95% CI)	p Value
Thoracoscore		
Histology	1.43 (0.73–2.79)	0.30
	3.57 (1.51–8.41)	0.004
Pathological N	2.10 (0.98–4.48)	0.06
	4.77 (2.53–8.98)	<0.0001
HALP	2.30 (1.30–4.05)	0.004

Cancers **2023**, *15*(6), 1854;

<https://doi.org/10.3390/cancers15061854>

Associations between the biomarkers related to systemic inflammation, nutrition and tumoral immune microenvironment with clinical and pathological variables.

	Prealbumin	CRP	CD8	mDC
Age	0.835	NS	0.0062	0.0061
Sex	NS	NS	NS	0.0011
Usual body weight	0.0231	NS	0.0825	0.0055
Actual body weight	0.0001	NS	NS	0.0374
BMI	0.0002	NS	NS	0.0294
Smoking status	NS	0.0055	NS	0.0087
Pack/year	NS	NS	0.0725	0.0813
Alcohol abuse	NS	NS	NS	NS
Chronic bronchitis	NS	NS	NS	0.0621
COPD	NS	NS	NS	0.0272
Atheroma	NS	NS	NS	NS
Diabetes	0.0333	NS	NS	0.0581
Angor	NS	NS	NS	0.0991
Stroke	NS	0.0432	NS	0.0432
Karnofsky	NS	NS	NS	NS
ASA	0.0153	0.063	NS	0.0004
Extent resection	NS	0.0003	0.0081	0.0947
Pathologic stage	NS	0.0006	NS	NS
pT	0.0011	≤0.0001	NS	0.0551
pN	NS	NS	NS	NS
Histological type	0.0497	0.0572	0.0414	0.0008
Vascular emboli	0.0192	0.0773	NS	NS
Lymphatic emboli	NS	NS	NS	NS
Albumin	≤0.0001	≤0.0001	NS	<0.0001
Nutritional risk index	≤0.0001	≤0.0001	NS	0.0123
Prealbumin	NA	≤0.0001	NS	0.0003
CRP	≤0.0001	NA	NS	≤0.0001
CD8	NS	NS	NA	≤0.0001
mDC	0.0003	≤0.0001	0.0001	NA

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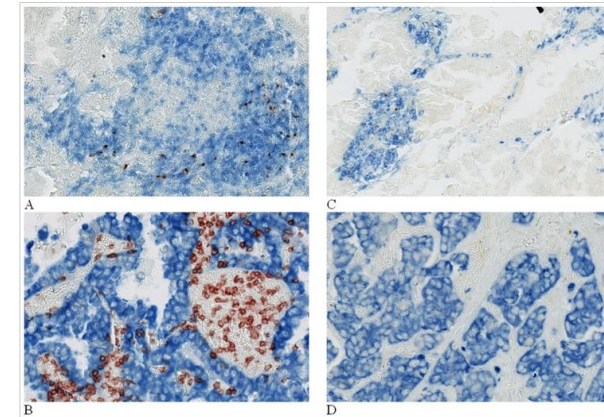
PLOS ONE



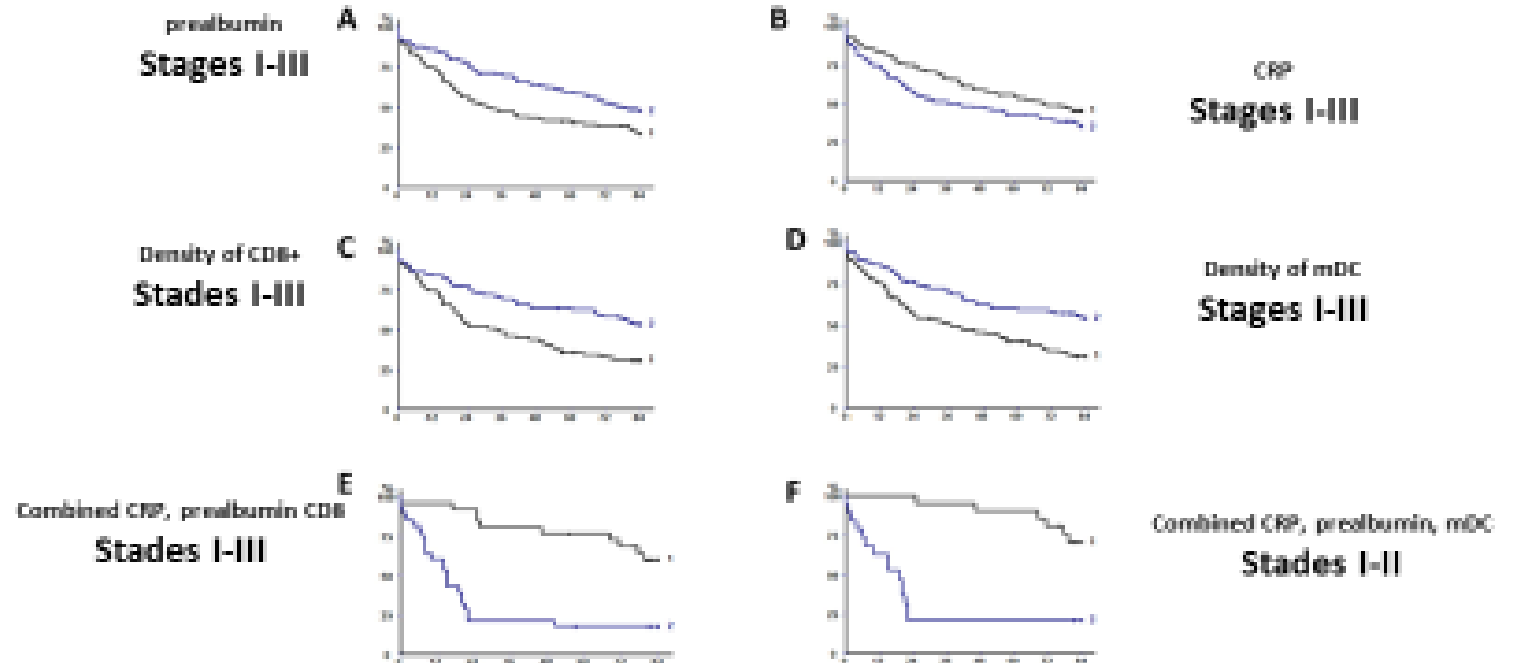
Systemic Inflammation, Nutritional Status and Tumor Immune Microenvironment Determine Outcome of Resected Non-Small Cell Lung Cancer

Marco Alifano^{1,2*}, Audrey Mansuet-Lupo^{2,3,4,5}, Filippo Lococo⁶, Nicolas Roche^{2,7}, Antonio Bobbio¹, Emelyne Canny¹, Olivier Schussler¹, Hervé Dermine⁶, Jean-François Régnard^{1,2}, Barbara Burroni³, Jérémy Goc^{2,4,5}, Jérôme Biton^{2,4,5}, Hanane Ouakrim^{2,4,5}, Isabelle Cremer^{2,4,5}, Marie-Caroline Dieu-Nosjean^{2,4,5}, Diane Damotte^{2,3,4,5}

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CD8+ and DC-Lamp+ cell densities are heterogeneous in non-small cell carcinoma.



National perioperative outcomes of pulmonary lobectomy for cancer: the influence of nutritional status[†]

Pascal Alexandre Thomas^{a,*}, Julie Berbis^b, Pierre-Emmanuel Falcoz^c, Françoise Le Pimpec-Barthes^d, Alain Bernard^e, Jacques Jougon^f, Henri Porte^g, Marco Alifano^h and Marcel Dahanⁱ on behalf of the EPITHOR Group

	Operative death		<i>P</i> *	OR a	95% CI
	Yes (<i>N</i> = 490)	No (<i>N</i> = 145)			
BMI, <i>N</i> (%)					
Normal	249 (2.7)	9142 (97.3)	0.002	1	
Underweight	35 (4.1)	822 (95.9)		1.89	[1.30–p2.75]
Overweight	156 (2.3)	6565 (97.7)		0.72	[0.59–0.89]
Obesity	50 (1.9)	2616 (98.1)		0.54	[0.40–0.74]

Table 3:
Pulmonary complications

	Pulmonary complications		<i>P</i> *	OR a	95% CI	<i>P</i> **
	Yes (<i>N</i> = 2865)	No (<i>N</i> = 16 770)				
BMI, <i>N</i> (%)						
Normal	1369 (14.6)	8022 (85.4)	<0.001	1		
Underweight	181 (21.1)	676 (78.9)		1.67	[1.39–2.00]	<0.001
Overweight	913 (13.6)	5808 (86.4)		0.84	[0.77–0.93]	<0.001
Obesity	402 (15.1)	2264 (84.9)		0.95	[0.84–1.08]	0.420

*Unadjusted analysis.

**Adjusted analysis. Co-variables: male gender, age, performance status, ASA score, comorbidities, active smokers, right side, open surgical approach, upper lobectomy, extended lobectomy, histology non-adenocarcinoma, operative time.

Bold values: *P* < 0.05 was significant.

BMI: body mass index; OR a: adjusted odd ratio; CI: confidence interval.

Postoperative complications:
Less in overweight and obese patients:
The end of another dogma

Body Mass Index and Total Psoas Area Affect Outcomes in Patients Undergoing Pneumonectomy for Cancer



Remi Hervochoon, MD, Antonio Bobbio, MD, PhD, Claude Guinet, MD, PhD, Audrey Mansuet-Lupo, MD, PhD, Antoine Rabbat, MD, Jean-François Régnard, MD, Nicolas Roche, MD, PhD, Diane Damotte, MD, PhD, Antonio Iannelli, MD, PhD, and Marco Alifano, MD, PhD

Departments of Thoracic Surgery, Radiology, Pathology, and Chest Disease and Intensive Care, Paris Centre University Hospitals, Paris; University Paris Descartes, Paris; and Department of Surgery, Nice University Hospital, Nice, France

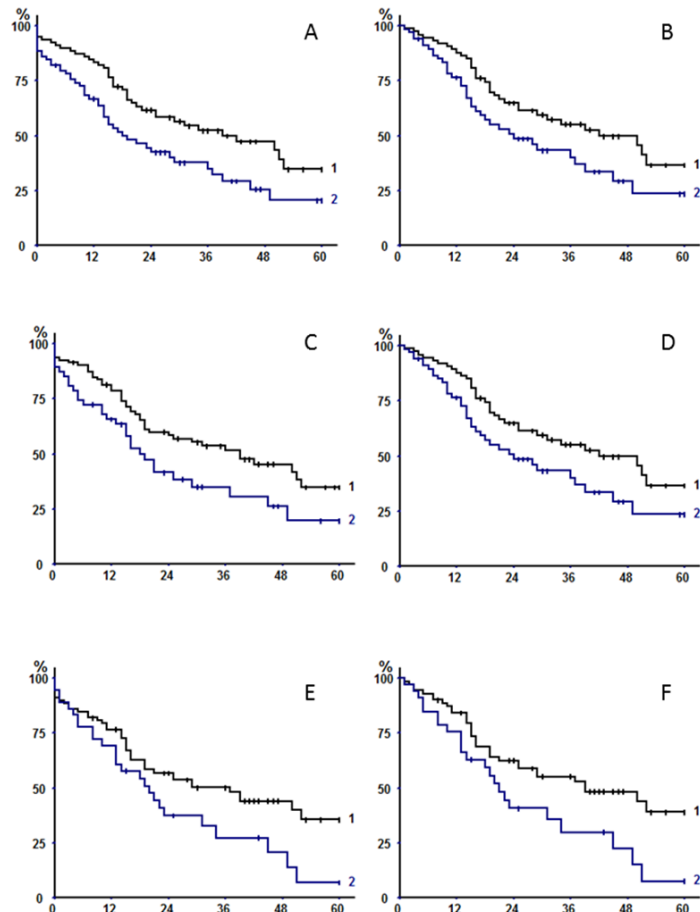


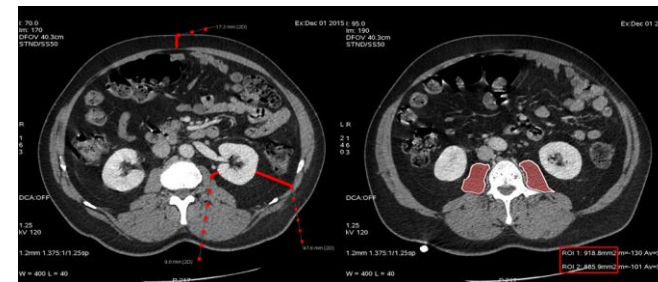
Table 4. Results of the 3 Cox Models^a

Factor	p Value	RR	95% CI
Model 1			
Histologic type	0.57	1.17	0.68–2.02
Pathologic stage	0.077	1.80	0.94–3.45
BMI	0.014	2.07	1.16–3.70
Total psoas area	0.59	1.17	0.66–2.08
CRP	0.035	1.72	1.04–2.85
Model 2			
Histologic type	0.084	1.49	0.95–2.33
Pathologic stage	0.23	1.38	0.82–2.34
BMI	0.042	1.57	1.02–2.42
Model 3			
Histologic type	0.069	1.52	0.97–2.37
Pathologic stage	0.096	1.55	0.93–2.61
Total psoas area	0.045	1.57	1.01–2.45

^a Model 1 includes (histologic type [squamous cell versus nonsquamous cell], pathologic stage [I–IIA versus III–IV], BMI [≤ 25 kg/m² versus > 25 kg/m²], total psoas area [≤ 33 rd percentile versus > 33 rd percentile]), and CRP level [≤ 20 mg/L versus > 20 mg/L]). Model 2 includes histologic type, pathologic stage, and BMI. Model 3 includes histologic type, pathologic stage, and total psoas area.

BMI = body mass index; CI = confidence interval; CRP = C-reactive protein; RR = relative risk.

GENERAL THORACIC



Better survival in overweight and obese patients: The lung cancer paradox

Article

Pre-Disease and Pre-Surgery BMI, Weight Loss and Sarcopenia Impact Survival of Resected Lung Cancer Independently of Tumor Stage

Philippe Icard^{1,2}, Olivier Schussler¹, Mauro Loi³, Antonio Bobbio¹, Audrey Mansuet Lupo^{4,5}, Marie Wislez^{5,6}, Antonio Iannelli^{7,8}, Ludovic Fournel^{1,9}, Diane Damotte^{4,5} and Marco Alifano^{1,5,*}

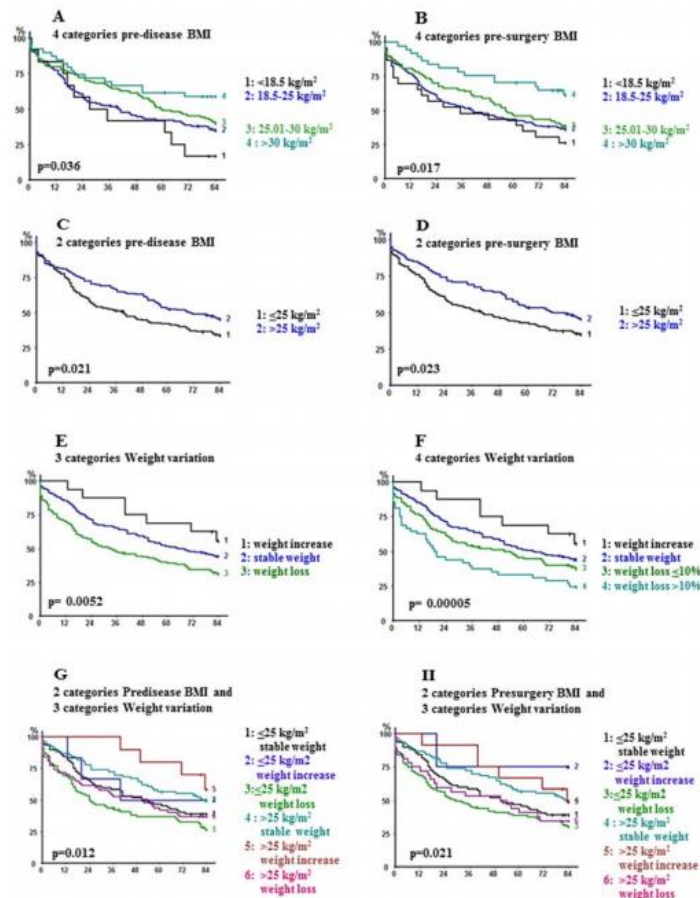


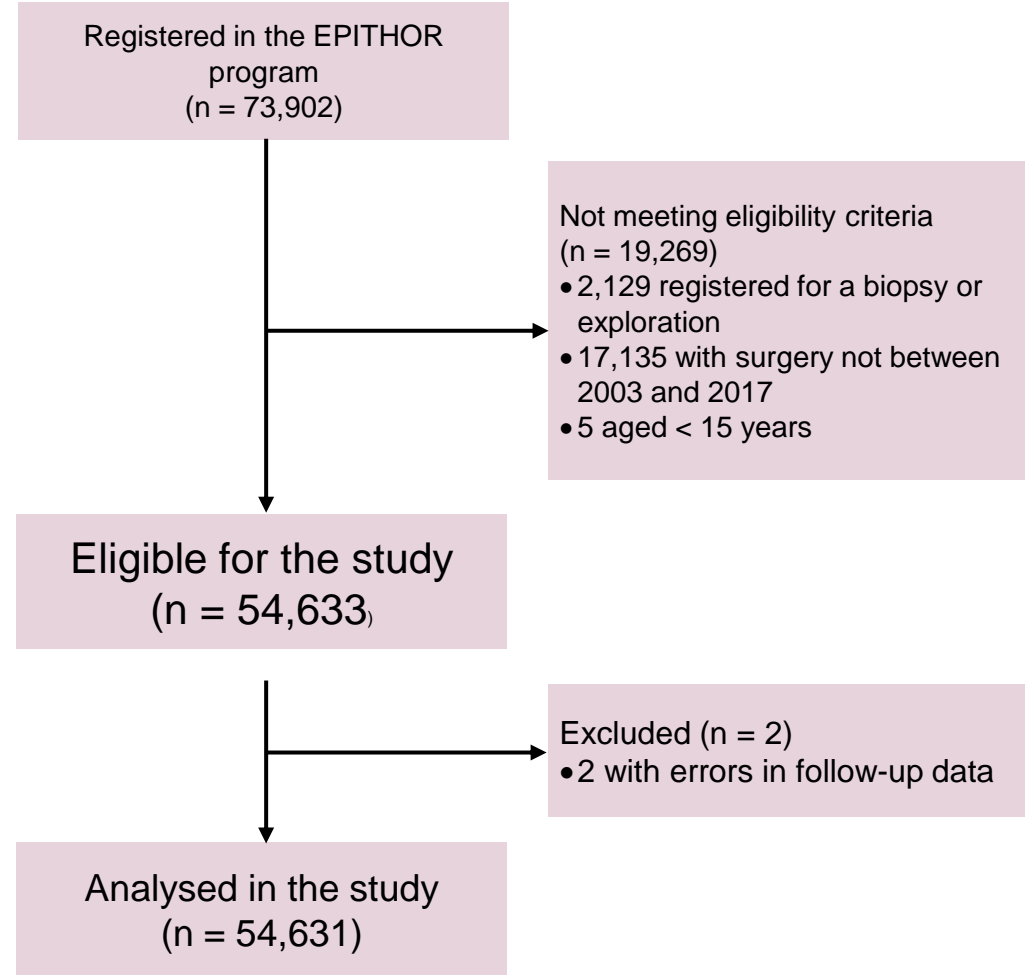
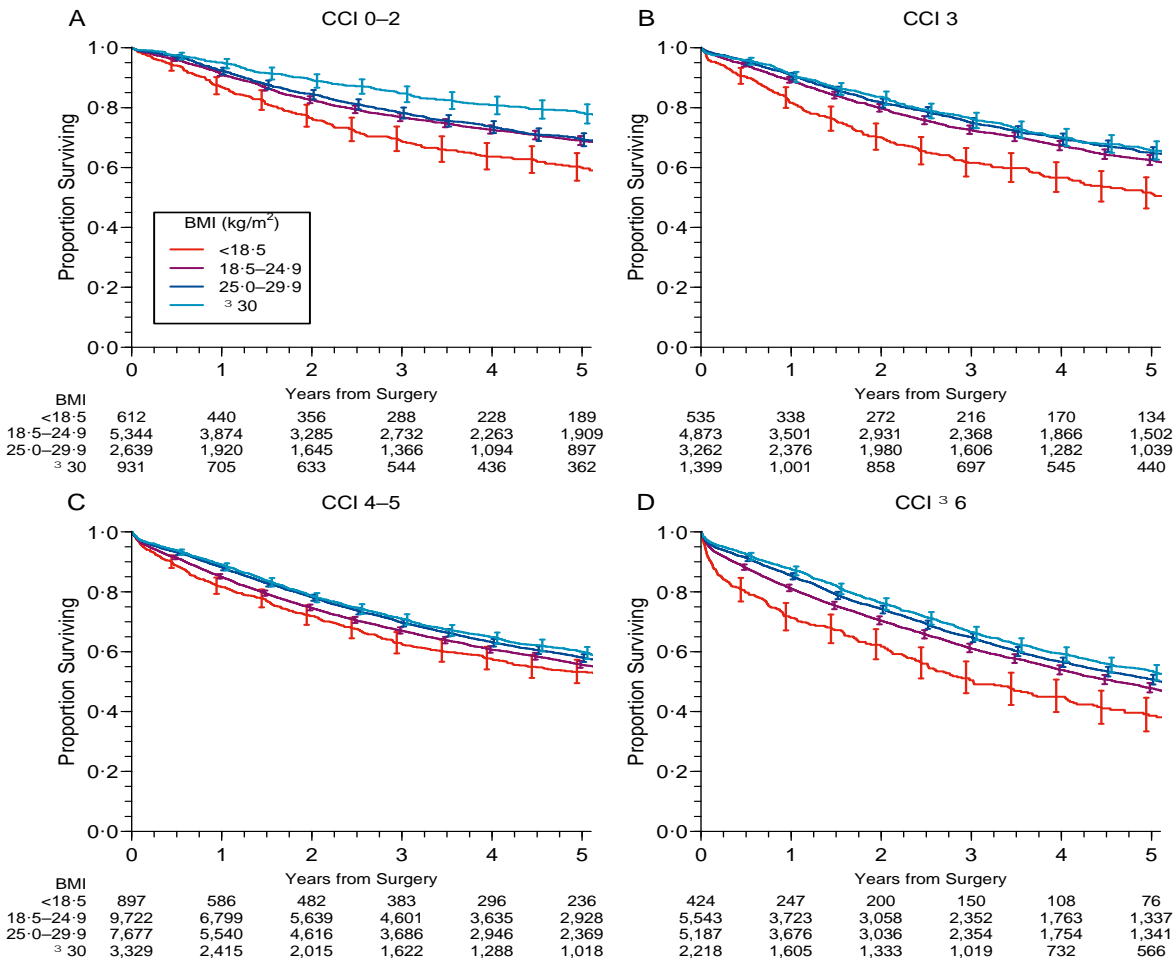
Figure 1. Kaplan–Meier overall survival analyses and log-rank comparisons with respect to: (A) pre-disease BMI (four categories: underweight, normal weight, overweight, obesity); (B) pre-surgery

Table 5. Multivariate analysis of factors influencing survival (four different Cox models). n.s.: non-significant.

Variable	Relative Risk	95% CI	p Value
Model 1			
Age (years)			
≤65	1		
>65	1.45	(1.08–1.94)	0.0014
Resection type			
Lobectomy/bilobectomy	1		
Pneumonectomy	1.77	(1.27–2.47)	0.00083
ASA score			
I–II	1		
III/IV	1.56	(1.15–2.10)	0.0038
Stage			
I	1		
II	1.50	(1.25–1.81)	
III/IV	2.26	(1.56–3.28)	0.000018
Pre-disease BMI (Kg/m ²)			
<25	1		
>25	0.66	(0.49–0.89)	0.006
Weight variation			
Increase	1		
Stable	1.36	(1.06–1.75)	
Decrease	1.86	(1.13–3.06)	0.014

Article
The Reality of Lung Cancer Paradox: The Impact of Body Mass Index on Long-Term Survival of Resected Lung Cancer. A French Nationwide Analysis from the Epithor Database

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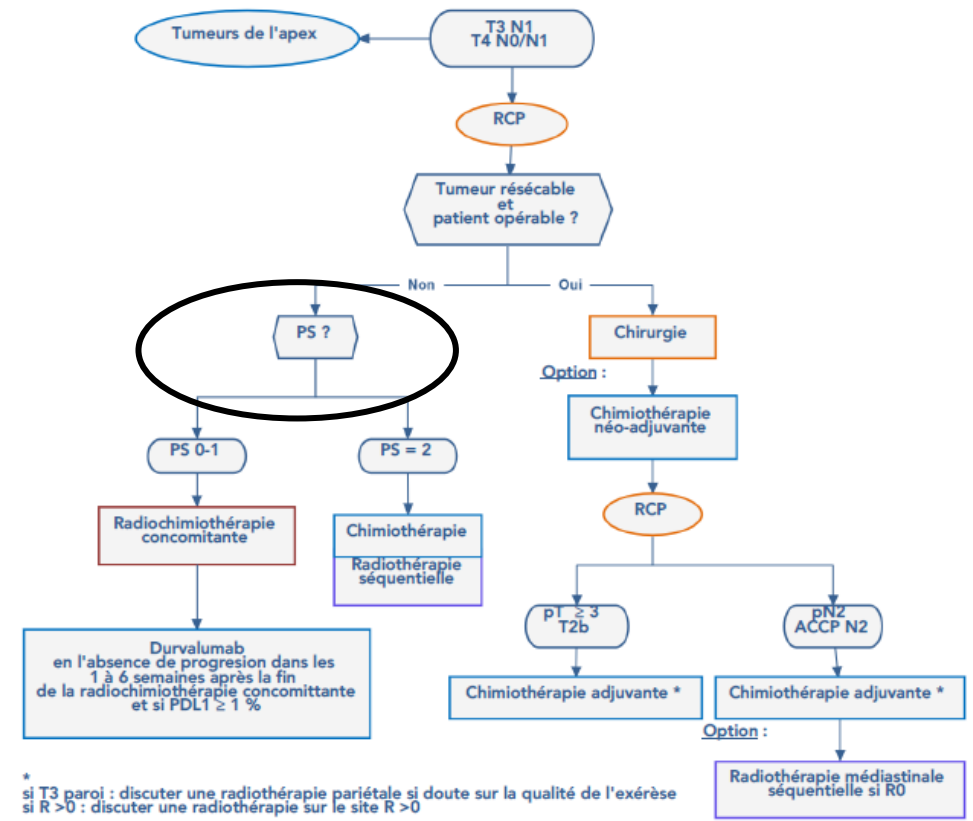
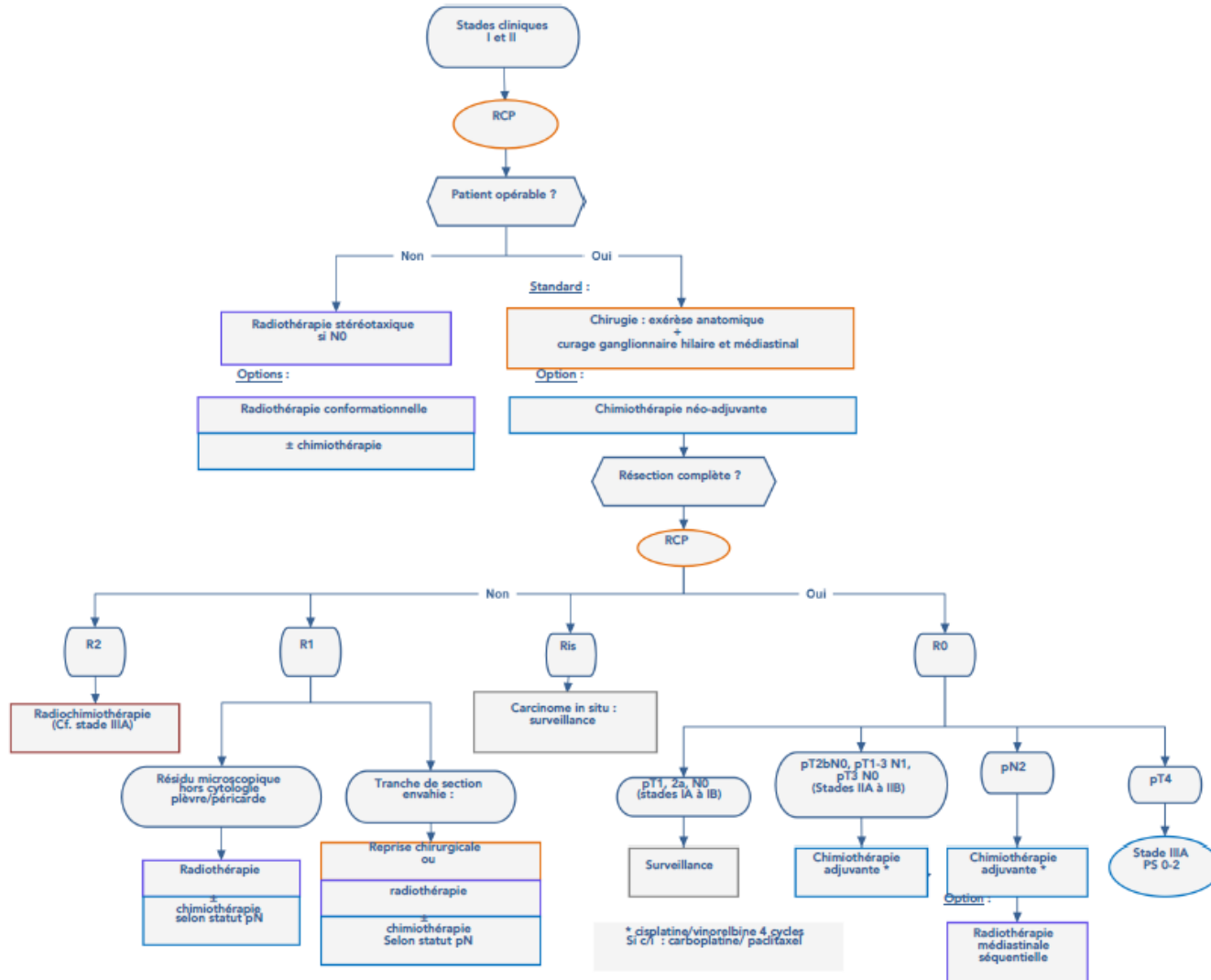
Median follow-up: 5,2 ans (IQR 2,3-9,5).
30 and days mortality : 2,6 % and 4,7 %.
1, 3, et 5 year survival : 87,2 %, 69,5 %, 58,4 %.
Survival differences according to BMI class: p<0,0001

Unadjusted RR :

- **Normal weight:** Ref
- **Underweight:** 1,24 (IC à 95 % 1,16-1,33)
- **Overweight :** 0,95 (IC à 95 % 0,92-0,98)
- **Obesity :** 0,88 (IC à 95 % 0,84-0,92)

To date:

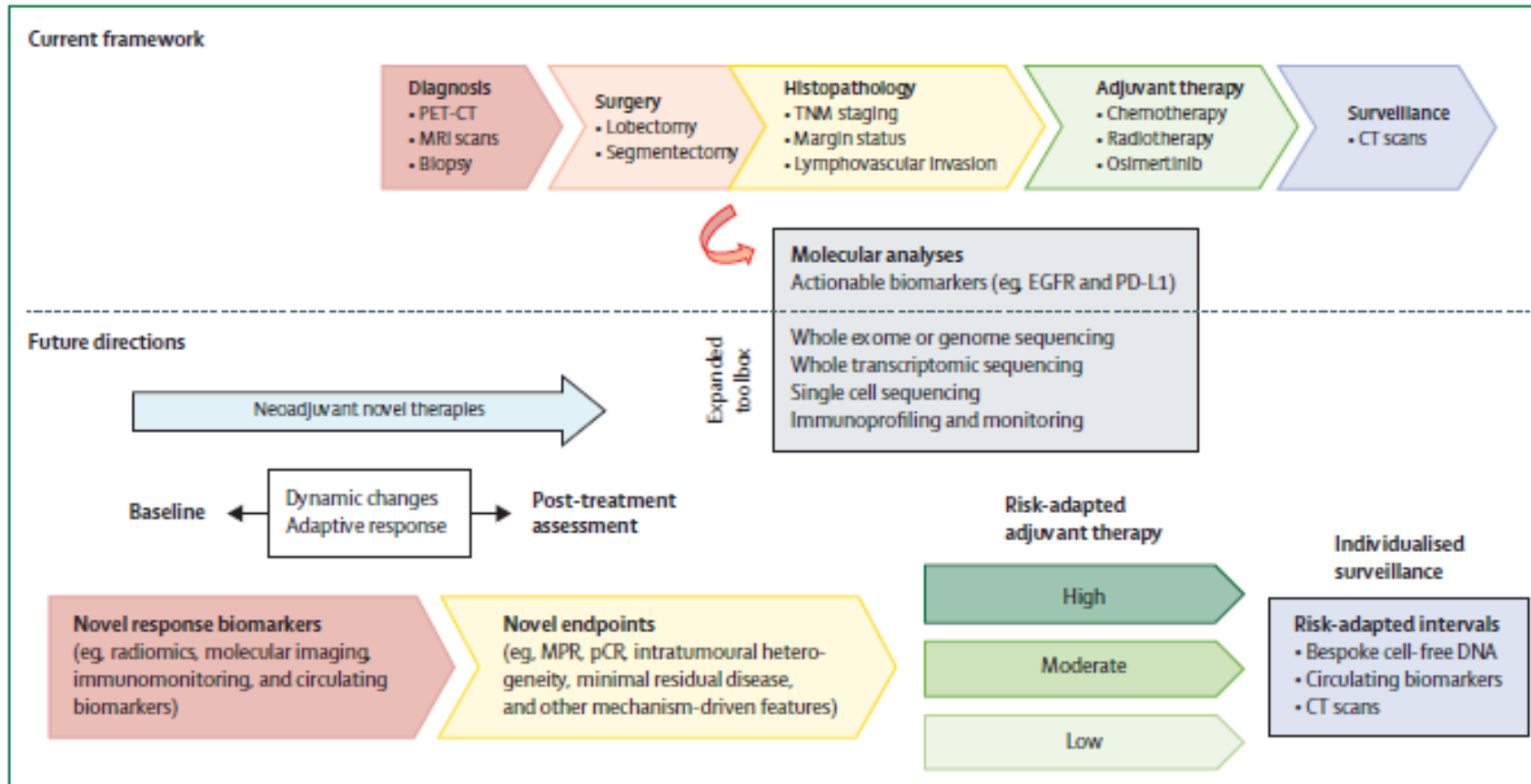
Host characteristics taken into account only to establish is patient is fit enough to undergo a treatment



Résécabilité des tumeurs IIIA N2 (2013)

ACCP	Diagnostic N2	Résécabilité
1	Infiltrant	Pas d'exérèse
2	Lors de la thoracotomie (peropératoire) malgré un bilan préopératoire bien conduit	Continuer l'exérèse si la résection complète est réalisable. Si résection complète non réalisable, se reporter aux modalités de prise en charge des stades "non-résécables".
3	Atteinte N2 évidente au scanner ou à la TEP-TDM, n'entrant pas dans le cadre du groupe 1	Résécabilité à discuter au cas par cas

The adaptation of patients' management is now an objective in therapeutic proposals with the development of numerous perioperative treatment trials



But the approach remains tumor-based

Figure 2: Neoadjuvant treatment of early-stage non-small-cell lung cancer with an adaptive approach
MPR=major pathological response, pCR=pathological complete response.

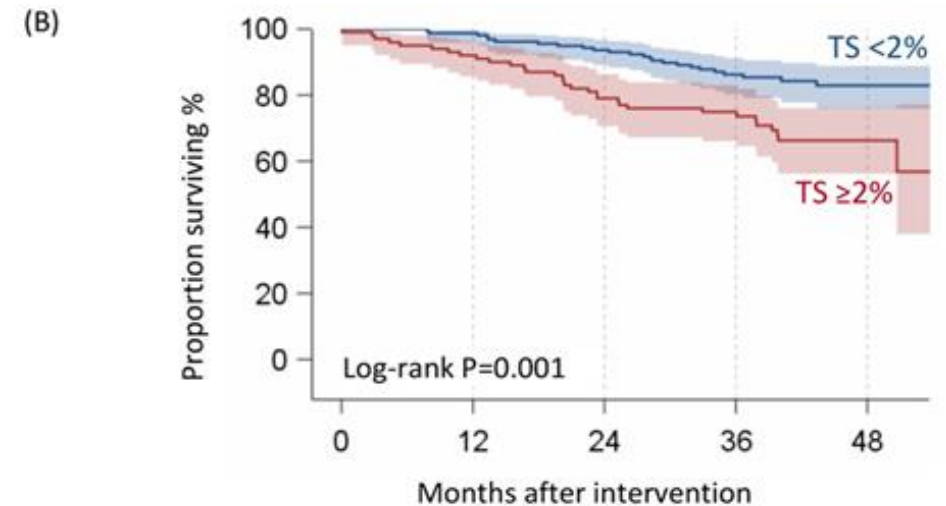
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	Patients (%)	HR (95% CI)	p Value
All patients	257 (100)		
Age			
<55	32 (12.5)	1.00	
55–64	70 (27.2)	2.06 (0.59–7.23)	0.26
65+	155 (60.3)	2.90 (0.90–9.37)	0.08
Sex			
Males	149 (58.0)	1.00	
Females	108 (42.0)	0.91 (0.54–1.56)	0.74
Performance status			
0	162 (63.0)	1.00	
1	75 (29.2)	1.58 (0.90–2.78)	0.11
2	17 (6.6)	2.13 (0.88–5.14)	0.09
ASA score			
1	118 (45.9)	1.00	
2	86 (33.5)	1.58 (0.85–2.94)	0.15
3	48 (18.7)	1.72 (0.85–3.48)	0.13
Comorbidities			
None	11 (4.3)	1.00	
1	37 (14.4)	1.76 (0.39–7.95)	0.46
2	58 (22.6)	0.94 (0.21–4.31)	0.94
3	151 (58.8)	1.31 (0.31–5.47)	0.71
Any (1–3)	246 (95.7)	1.28 (0.31–5.27)	0.73
Cardiovascular	80 (31.1)	0.69 (0.37–1.29)	0.25
BPCO	99 (38.5)	1.09 (0.64–1.87)	0.73
Other malignancy	91 (35.4)	1.34 (0.79–2.29)	0.28
Dyspnea scale			
None	168 (65.4)	1.00	
1	56 (21.8)	1.22 (0.65–2.29)	0.54
2–4	18 (7.0)	2.12 (0.93–4.80)	0.07
Intervention			
Other †	238 (92.6)	1.00	
Pneumonectomy	19 (7.4)	2.99 (1.41–6.34)	0.004
Thoracoscore *			
<2%	155 (60.3)	1.00	
>2%	100 (38.9)	2.33 (1.37–3.95)	0.002

Systemic Inflammation and Lung Cancer: Is It a Real Paradigm? Prognostic Value of Inflammatory Indexes in Patients with Resected Non-Small-Cell Lung Cancer

by Antonio Mazzella ^{1,†,‡}, Elena Maiolino ^{1,†}, Patrick Maisonneuve ², Mauro Loi ¹ and Marco Alifano ¹

SURVIVAL ACCORDING TO THORACOSCORE







Patients at risk					
	0	12	24	36	48
TS <2%	157	155	146	103	25
TS ≥2%	100	92	79	55	14
OS (95% CI)	12-month	24-month	36-month	48-month	
TS <2%	98.7% (95.0–99.7)	93.6% (88.5–96.5)	85.7% (78.9–90.4)	81.8% (73.6–87.6)	
TS ≥2%	92.0% (84.6–95.9)	79.0% (69.6–85.8)	74.4% (64.5–82.0)	62.5% (50.0–72.7)	

Cancers **2023**, *15*(6), 1854;

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Multivariate analysis.

Parameter	HR (95% CI)	p Value
Thoracoscore	1.92 (1.10–3.36)	0.02
Histology	1.43 (0.73–2.79)	0.30
	3.57 (1.51–8.41)	0.004
Pathological N	2.10 (0.98–4.48)	0.06
	4.77 (2.53–8.98)	<0.0001
HALP	2.30 (1.30–4.05)	0.004

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Prognostic score and sex-specific nomograms to predict survival in resectable lung cancer: A French nationwide study from the Epithor cohort database

Marco Alfano,^{1,a} Elisa Daffré,^{1,a} Laurent Brouchet,^{1,b} Pierre Emmanuel Falcoz,^{1,c} Françoise Le Pimpec Barthes,^{1,d} Pierre Benoit Pages,^{1,e} Pascal Alexandre Thomas,^{1,f} Marcel Dahan,^{1,b} and Raphael Porcher^{1,h}

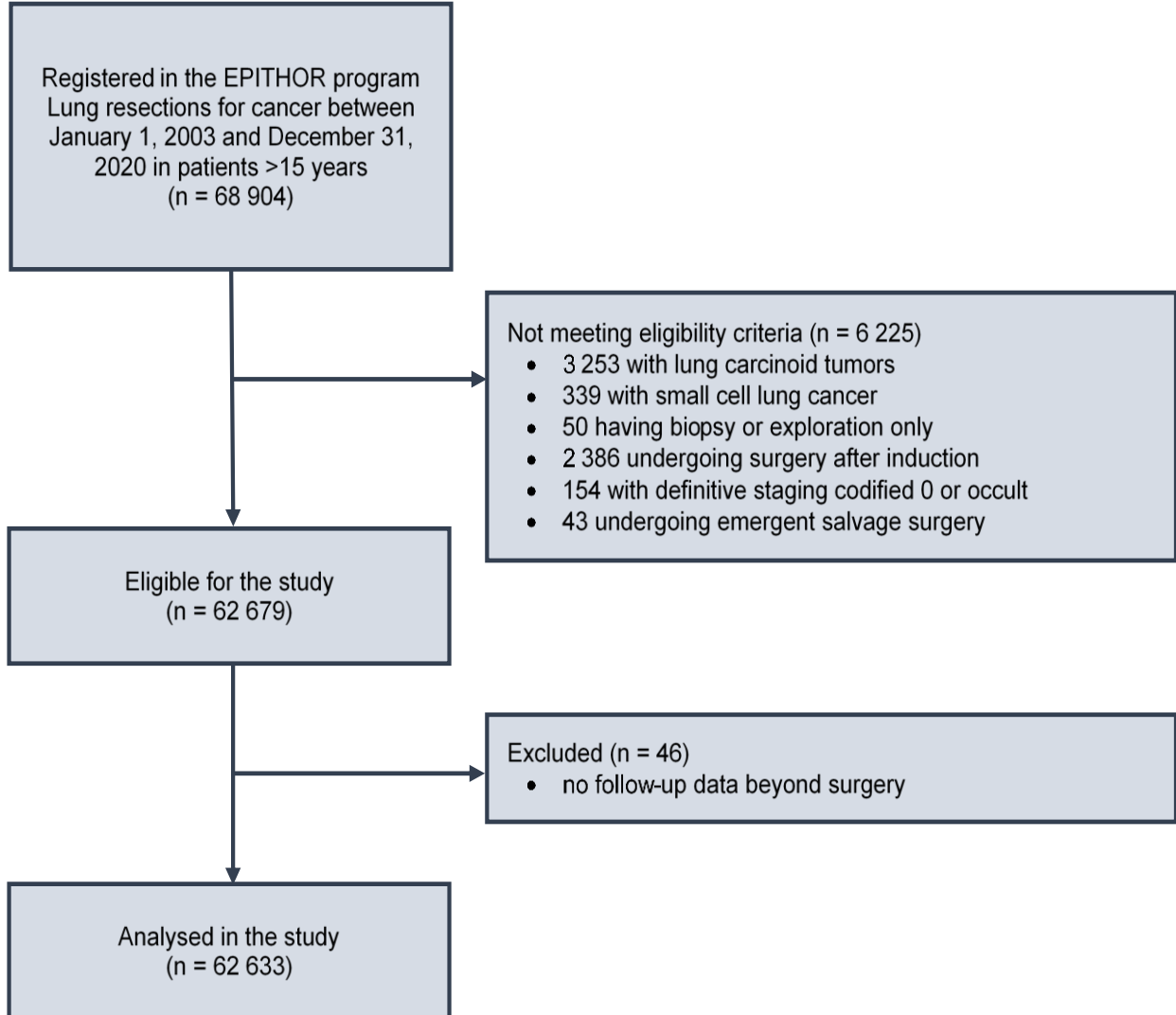
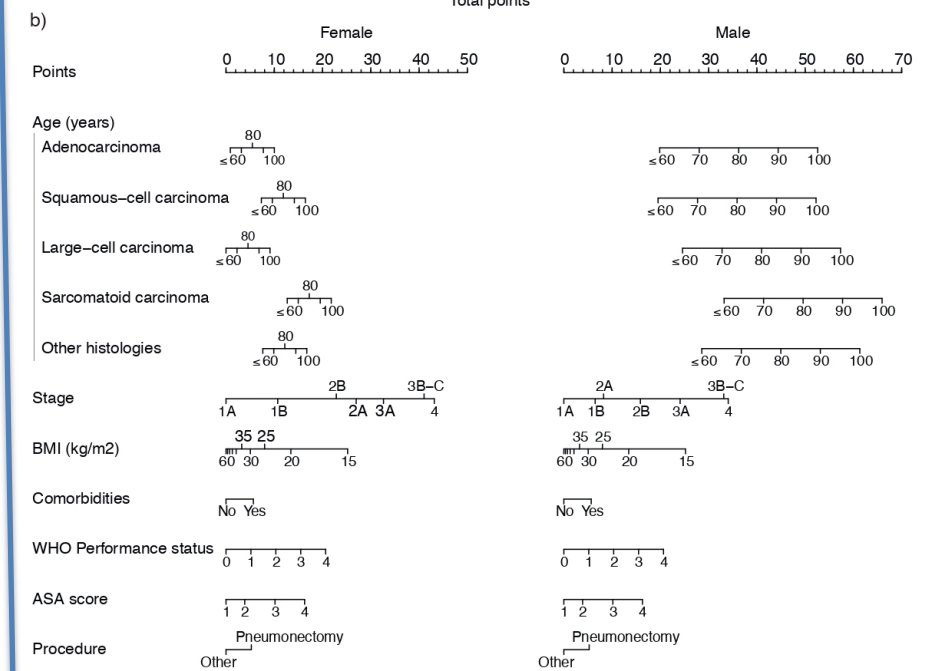
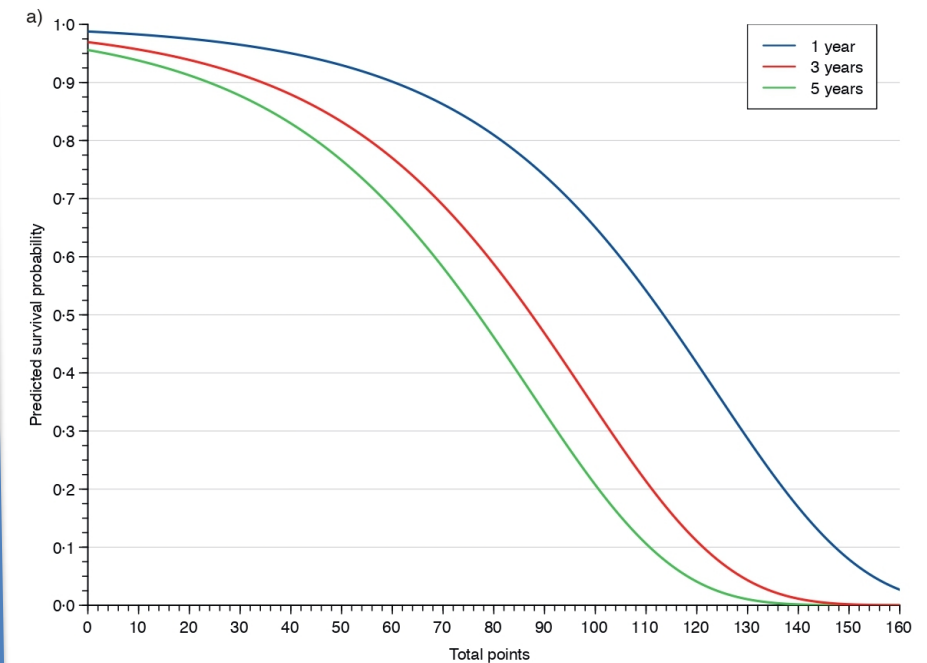


Table 1. Characteristics of patients at time of surgery.

	N missing (%)	Whole sample N = 62 633 NSCLC (%)	Development N = 40 848 NSCLC (%)	Temporal validation N = 21 785 NSCLC (%)
Period	0 (0)			
2003–2008		11 994 (19.1)	11 994 (29.4)	—
2009–2012		13 515 (21.6)	13 515 (33.1)	—
2013–2016		15 339 (24.5)	15 339 (37.6)	—
2017–2020		21 785 (34.8)	—	21 785 (100.0)
Sex	0 (0)			
Female		19 082 (30.5)	11 170 (27.3)	7 912 (36.3)
Male		43 551 (69.5)	29 678 (72.7)	13 873 (63.7)
Age (years)	88 (0.1)	65.0 (9.6)	64.3 (9.7)	66.4 (9.1)
Height (cm)	20 (<0.1)	169.5 (8.4)	169.7 (8.3)	169.1 (8.7)
Body-mass index (kg/m ²)	42 (0.1)	25.3 (4.6)	25.2 (4.5)	25.5 (4.7)
≥ 30.0 kg/m ²		9 021 (14.4)	5 590 (13.7)	3 431 (15.8)
WHO performance status	2 626 (4.2)			
0		29 211 (48.7)	16 591 (43.1)	12 620 (58.7)
1		254 49 (42.4)	17 952 (46.6)	7 497 (34.9)
2		4 859 (8.1)	3 575 (9.3)	1 284 (6.0)
3-4		488 (0.8)	381 (1.0)	107 (0.5)
GOLD score	0 (0)			
0		58 546 (93.5)	39 867 (97.6)	18 679 (85.7)
1		1 634 (2.6)	374 (0.9)	1 260 (5.8)
2		2 216 (3.5)	540 (1.3)	1 676 (7.7)
3-4		237 (0.4)	67 (0.2)	170 (0.8)
ASA class	404 (0.6)			
1		94 05 (15.1)	6 220 (15.3)	3 185 (14.7)
2		32 614 (52.4)	22 237 (54.9)	10 377 (47.8)
3		196 82 (31.6)	11 791 (29.1)	7 891 (36.4)
4		528 (0.8)	293 (0.7)	235 (1.1)
Surgical procedure	0 (0)			
Pneumonectomy		5 328 (8.5)	4 366 (10.7)	962 (4.4)
Other		57 305 (91.5)	36 482 (89.3)	20 823 (95.6)
Stage	270 (0.4)			
IA		20 798 (33.3)	11 571 (28.4)	9 227 (42.6)
IB		13 127 (21.0)	9 663 (23.8)	3 464 (16.0)
IIA		1 176 (1.9)	235 (0.6)	941 (4.3)
IIB		10 663 (17.1)	7 306 (18.0)	3 357 (15.5)
IIIA		10 685 (17.1)	7 437 (18.3)	3 248 (15.0)
IIIB-3C		3 114 (5.0)	2 225 (5.5)	889 (4.1)
IV		2 800 (4.5)	2 243 (5.5)	557 (2.6)
Histology	232 (0.4)			
Adenocarcinoma		41 323 (66.2)	25 285 (62.1)	16 038 (73.9)
Squamous-cell carcinoma		17 028 (27.3)	12 295 (30.2)	4 733 (21.8)
Large-cell carcinoma		3 001 (4.8)	2 327 (5.7)	674 (3.1)
Sarcomatoid carcinoma		489 (0.8)	329 (0.8)	160 (0.7)
Other		560 (0.9)	452 (1.1)	108 (0.5)
Side	268 (0.4)			
Right		36 081 (57.9)	23 353 (57.4)	12 728 (58.6)
Left		26 284 (42.1)	17 301 (42.6)	8 983 (41.4)

Data are mean (SD) or n (%).

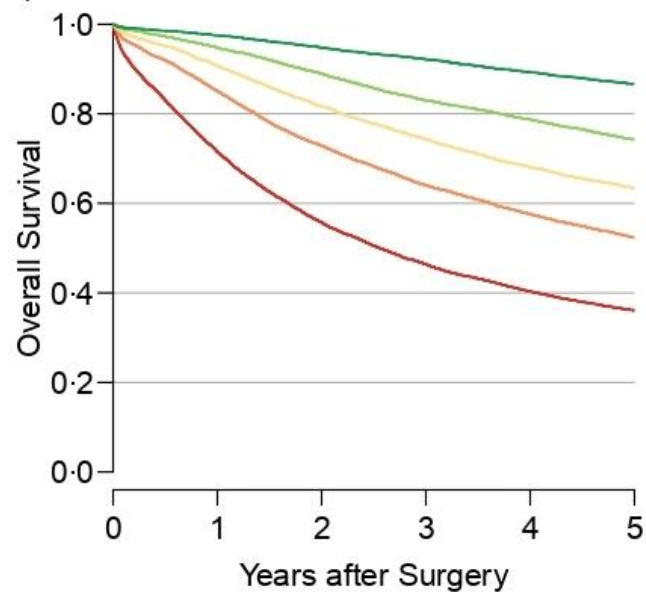
	Full model				Final model
	Female		Male		aHR (95% CI)
	aHR (95% CI)	P	aHR (95% CI)	P	
Male	—	—	—	—	1.96 (1.71 to 2.24)
Age (per 10 yr above 60)	1.08 (1.02 to 1.15)	0.012	1.34 (1.31 to 1.37)	<0.001	1.08 (1.02 to 1.15)
1/(BMI ²)*	5.77 (3.41 to 9.77)	<0.001	9.81 (7.22 to 13.3)	<0.001	8.57 (6.61 to 11.1)
Height (per 10 cm)	0.97 (0.91 to 1.04)	0.40	0.99 (0.96 to 1.02)	0.45	—
Comorbidities	1.25 (1.09 to 1.43)	0.001	1.22 (1.13 to 1.31)	<0.001	1.22 (1.15 to 1.31)
WHO-PS (per unit)	1.13 (1.06 to 1.21)	<0.001	1.22 (1.18 to 1.25)	<0.001	1.20 (1.17 to 1.23)
GOLD score 1	1.48 (1.05 to 2.09)	0.025	0.90 (0.74 to 1.11)	0.33	—
GOLD score 2	1.40 (1.03 to 1.89)	0.031	1.11 (0.95 to 1.29)	0.17	—
GOLD score 3-4	2.31 (0.86 to 6.18)	0.096	1.30 (0.89 to 1.90)	0.17	—
ASA score 2	1.16 (1.03 to 1.31)	0.016	1.14 (1.07 to 1.22)	<0.001	1.15 (1.09 to 1.21)
ASA score 3	1.55 (1.33 to 1.79)	<0.001	1.41 (1.32 to 1.51)	<0.001	1.43 (1.35 to 1.53)
ASA score 4-6	2.29 (1.52 to 3.44)	<0.001	1.71 (1.43 to 2.05)	<0.001	1.78 (1.52 to 2.10)
Pneumonectomy	1.34 (1.18 to 1.52)	<0.001	1.19 (1.13 to 1.25)	<0.001	1.20 (1.15 to 1.26)
Adenocarcinoma	1	—	1	—	1
Squamous-cell carcinoma	1.24 (1.11 to 1.38)	<0.001	0.99 (0.95 to 1.03)	0.61	1.26 (1.13 to 1.39)
Large-cell carcinoma	0.98 (0.82 to 1.17)	0.81	1.18 (1.10 to 1.27)	<0.001	0.97 (0.81 to 1.15)
Sarcomatoid carcinoma	1.54 (1.09 to 2.18)	0.015	1.62 (1.37 to 1.91)	<0.001	1.52 (1.08 to 2.14)
Other histology	1.28 (0.92 to 1.79)	0.14	1.37 (1.17 to 1.61)	<0.001	1.27 (0.91 to 1.76)
Left side	0.96 (0.88 to 1.03)	0.26	1.01 (0.97 to 1.04)	0.78	—
Post-operative stage IA	1	—	1	—	1
Post-operative stage IB	1.47 (1.28 to 1.69)	<0.001	1.26 (1.19 to 1.34)	<0.001	1.46 (1.28 to 1.67)
Post-operative stage IIA	2.63 (1.63 to 4.23)	<0.001	1.34 (1.04 to 1.72)	0.022	2.61 (1.63 to 4.17)
Post-operative stage IIB	2.25 (1.96 to 2.58)	<0.001	1.77 (1.67 to 1.87)	<0.001	2.25 (1.97 to 2.58)
Post-operative stage IIIA	3.18 (2.80 to 3.61)	<0.001	2.38 (2.25 to 2.52)	<0.001	3.19 (2.82 to 3.60)
Post-operative stage IIIB-C	4.31 (3.64 to 5.10)	<0.001	3.30 (3.06 to 3.55)	<0.001	4.29 (3.65 to 5.05)
Post-operative stage IV	4.76 (4.10 to 5.52)	<0.001	3.39 (3.14 to 3.65)	<0.001	4.63 (4.00 to 5.35)
Male x Age (per 10 yr above 60)	—	—	—	—	1.23 (1.16 to 1.31)
Male x Squamous-cell carcinoma	—	—	—	—	0.79 (0.71 to 0.88)
Male x Large-cell carcinoma	—	—	—	—	1.22 (1.01 to 1.48)
Male x Sarcomatoid carcinoma	—	—	—	—	1.06 (0.72 to 1.55)
Male x Other histology	—	—	—	—	1.07 (0.75 to 1.55)
Male x stage IB	—	—	—	—	0.86 (0.74 to 1.00)
Male x stage IIA	—	—	—	—	0.51 (0.30 to 0.87)
Male x stage IIB	—	—	—	—	0.78 (0.67 to 0.90)
Male x stage IIIA	—	—	—	—	0.74 (0.65 to 0.84)
Male x stage IIIB-C	—	—	—	—	0.76 (0.63 to 0.90)
Male x stage IV	—	—	—	—	0.72 (0.62 to 0.85)



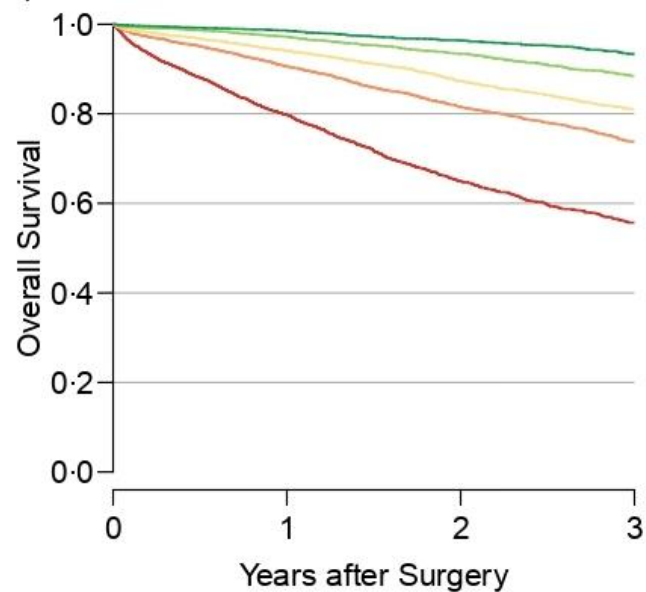
aHR: adjusted hazard ratio.

* BMI had a non-linear effect in the models, and was modeled with a linear effect for 1/(BMI²), BMI units being kg/m²

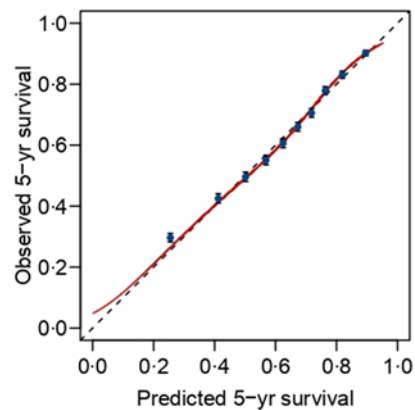
a) Development set



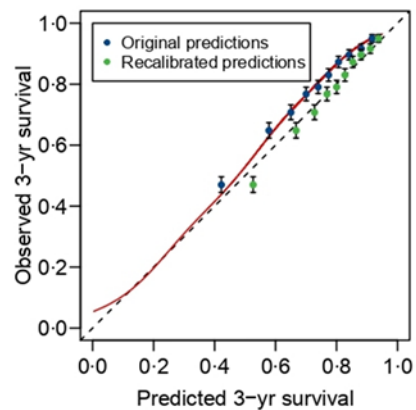
b) Temporal validation set



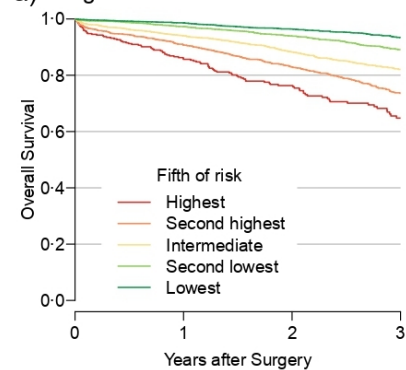
a) Development set



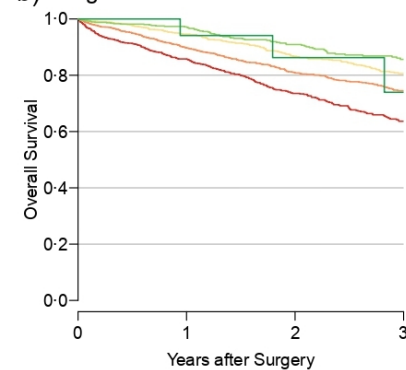
b) Temporal validation set



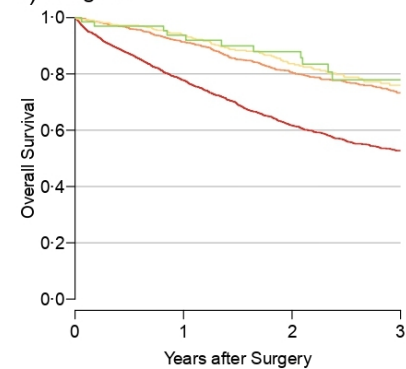
a) Stage I



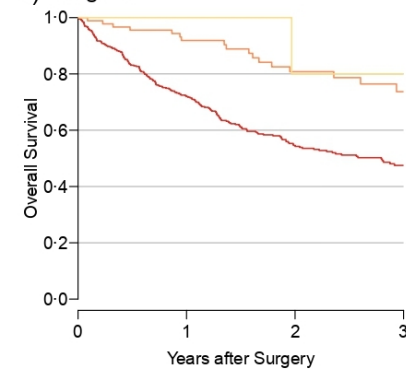
b) Stage II



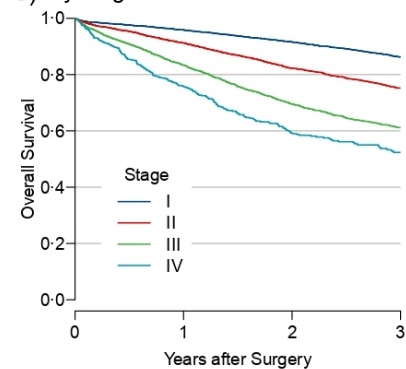
c) Stage III



d) Stage IV



e) By stage



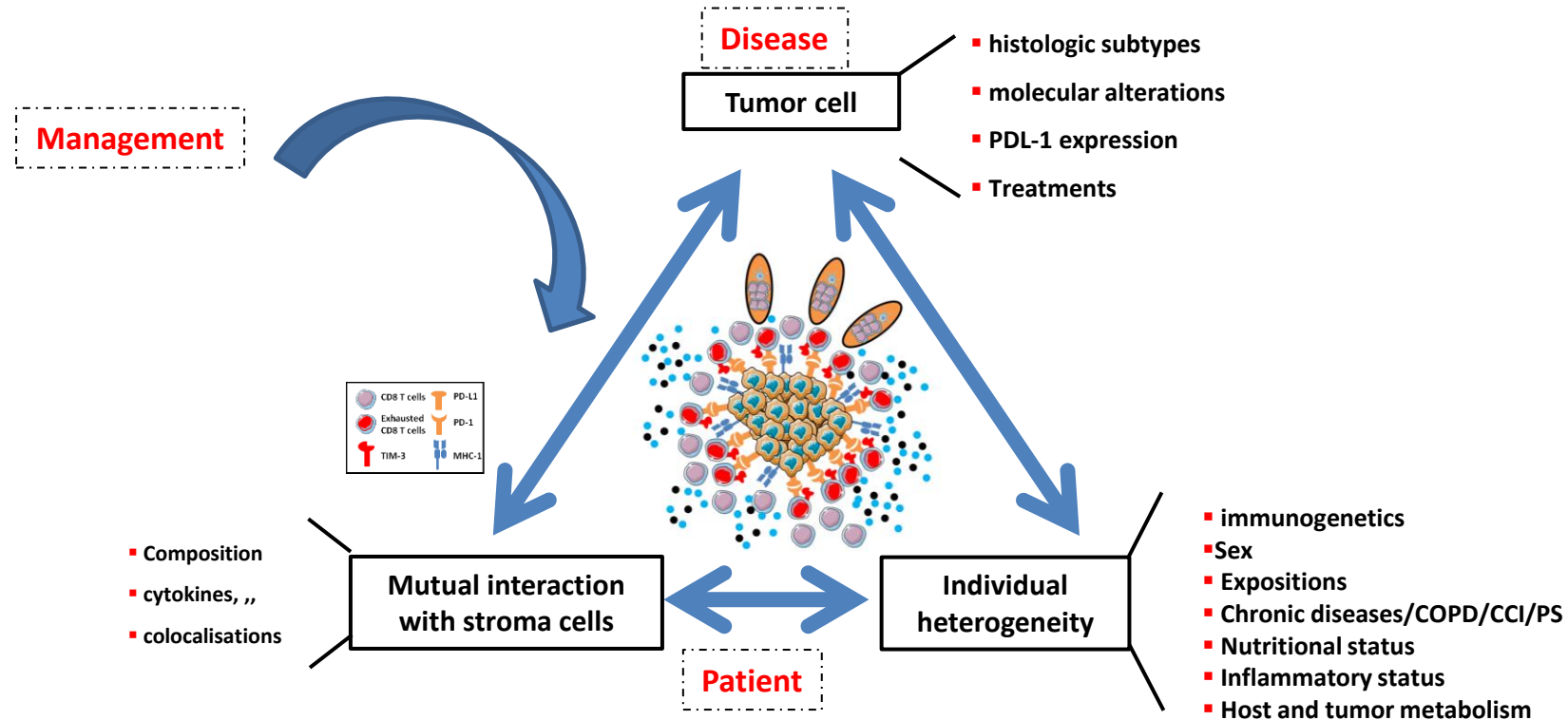
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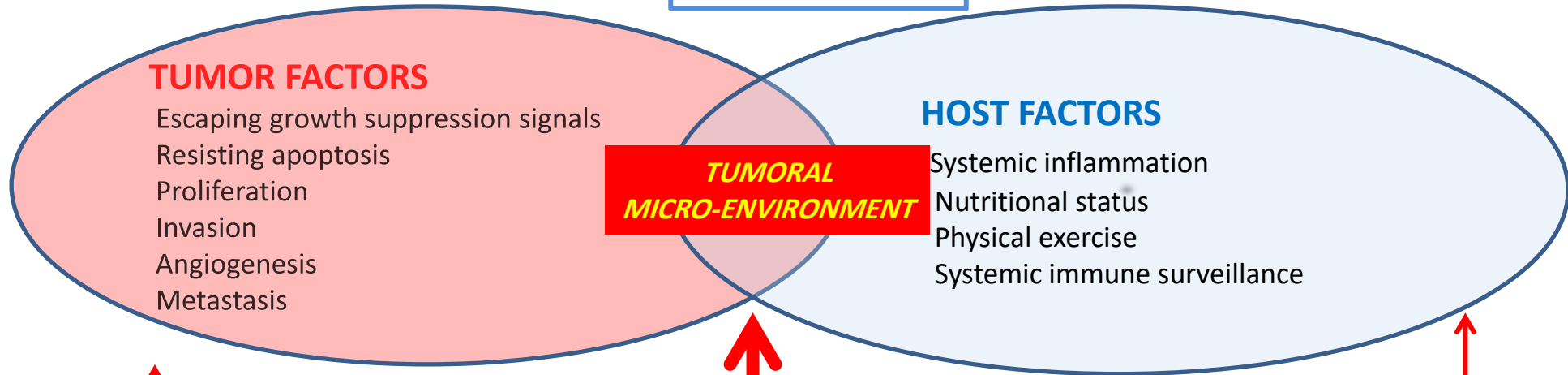


To conclude

Patient-disease interaction determines the initial presentation and the natural or unnatural course of the disease



In Perspective



- *Identify patients likely to benefit from therapies*
- *Increase proportion of patients likely to benefit from therapies*
- *Improve response to classical, targeted and immunotherapies*

- Tumor-related interventions**
- Surgery
 - Chemotherapy
 - Radiation Therapy
 - Antiangiogenic Therapy
 - Tumor-related targeted therapies

- Host related interventions**
- Reduce systemic inflammation
 - Improve nutritional status
 - Increase exercise performance
 - Administer immune-check point receptor blockade

INTERVENTIONS