Remisión de la dislipemia aterogénica un año después de la cirugía bariátrica

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Introducción

- La dislipemia aterogénica (DA) está compuesta de niveles elevados de triglicéridos, niveles disminuidos de colesterol HDL y partículas pequeñas y densas de colesterol LDL. Es más frecuente en pacientes con **obesidad y síndrome metabólico**.
- Aunque el colesterol LDL se reduce de manera eficaz con estatinas, un riesgo cardiovascular residual persiste en estos pacientes, principalmente debido a la DA.
- La cirugía bariátrica (CB) es el tratamiento más eficaz para la obesidad. Sin embargo, no existen estudios previos que evalúen la remisión de la DA después de la CB.

Objetivos

- Estudiar la remisión de la DA un año después de la CB.
- Conocer la prevalencia de DA en pacientes con obesidad mórbida tributarios de CB. Estudiar las características diferenciales con respecto a los pacientes sin DA.

Material y métodos

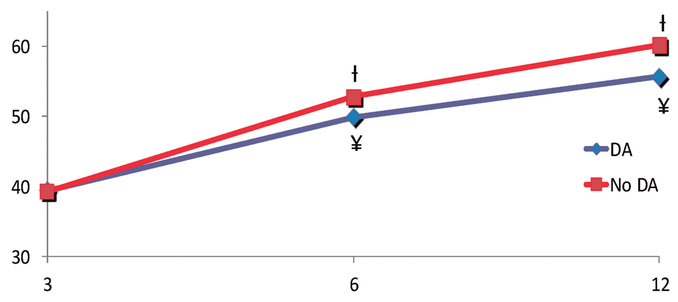
- Estudio de cohortes prospectivo de pacientes intervenidos de CB con seguimiento posterior de un año.
- Los pacientes fueron intervenidos de bypass gástrico en Y de Roux laparoscópico (BGYRL) o gastrectomía tubular laparoscópica (GTL). La elección de la técnica quirúrgica se realizó basándose en criterios clínicos.
- Todos los pacientes fueron visitados antes de la CB, y a los 3, 6 y 12 meses después de la intervención.
- Se definió **DA** por la presencia de hipertrigliceridemia (triglicéridos > 150 mg/dl o tratamiento con fibratos) y niveles disminuidos de colesterol HDL (< 40 mg/dl en los hombres y < 50 mg/dl en las mujeres).
- Se consideró **remisión** la normalización de los niveles de triglicéridos y colesterol HDL, habiendo retirado previamente el tratamiento con fibratos.
- El índice de resistencia a la Insulina HOMA-IR se calculó utilizando la siguiente fórmula: HOMA-IR = insulina (mU/ml) x glicemia plasmática (mmol/l) / 22,5.
- El índice aterogénico plasmático se calculó con la siguiente fórmula: log [triglicéridos (mmol/l) / colesterol HDL (mmol/l)].
- El porcentaje de pérdida de exceso de peso se calculó basándose en el exceso de peso respecto al peso ideal (peso correspondiente a un índice de masa corporal de 25 kg/m^2).
- Se utilizó el test de Fisher o chi-cuadrado para estudiar el grado de asociación entre variables categóricas.
- Se utilizó un modelo ANOVA para estudiar la evolución de las variables contínuas en cada grupo y analizar las diferencias entre grupos en cada punto respecto el valor basal.
- Se consideró estadísticamente significativo un valor p < 0,05

Resultados

Características basales

	DA n = 81	No DA n = 275	p
Mujeres (%)	57 (70,4)	228 (82,9)	0,012
Edad (años)	44,7 ± 9,3	44,2 ± 8,5	0,624
Índice de masa corporal (kg/m²)	43,9 ± 5,3	44,1 ± 5,0	0,800
Circunferencia abdominal (cm)	130,9 ± 9,6	127,3 ± 12,8	0,032
Tipo de cirugía (% de BGYRL)	37 (45,7)	166 (60,4)	0,013
Colesterol total (mg/dl)	199,4 ± 33,4	190,9 ± 34,2	0,049
Colesterol HDL (mg/dl)	38,9 ± 8,1	52,4 ± 14,0	<0,001
Triglicéridos (mg/dl)	221,7 ± 76,7	104,2 ± 37,3	<0,001
Colesterol no-HDL (mg/dl)	160,9 ± 33,2	138,3 ± 33,4	<0,001
Hipercolesterolemia (%)	35 (43,2)	110 (40,0)	0,381
Diabetes mellitus tipo 2 (%)	35 (43,2)	44 (16,0)	<0,001
Hipertensión arterial (%)	50 (61,7)	97 (35,4)	<0,001
Síndrome metabólico (%)	81 (100,0)	157 (57,1)	<0,001
Fumadores (%)	30 (37,0)	72 (26,4)	0,044

Porcentaje de pérdida de exceso de peso



*Diferencias entre grupos respecto valor basal (p < 0,05)
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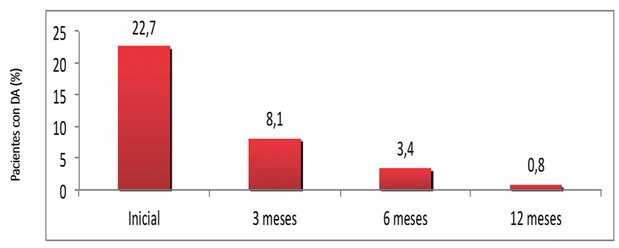
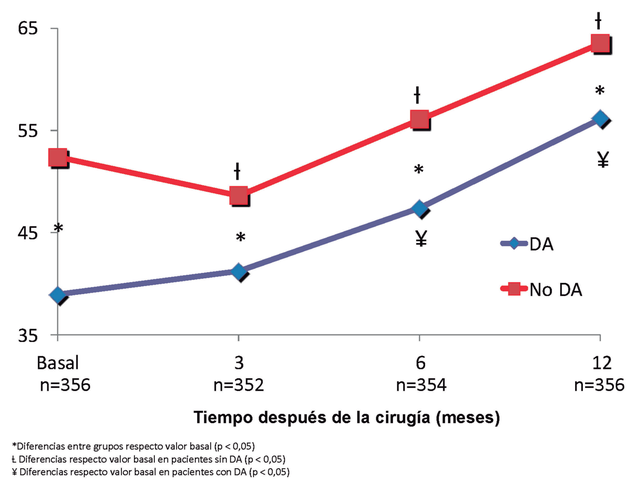
Evolución DA después de la CB



Remisión de la DA a los 3 meses %	74,1 (60/81)
Remisión de la DA a los 6 meses %	90,1 (73/81)
Remisión de la DA a los 12 meses %	96,3 (78/81)

Evolución colesterol HDL (mg/dl)



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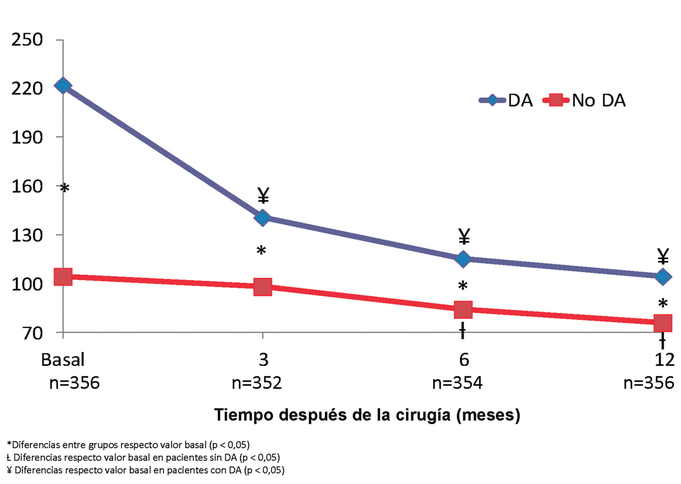
Evolución triglicéridos (mg/dl)



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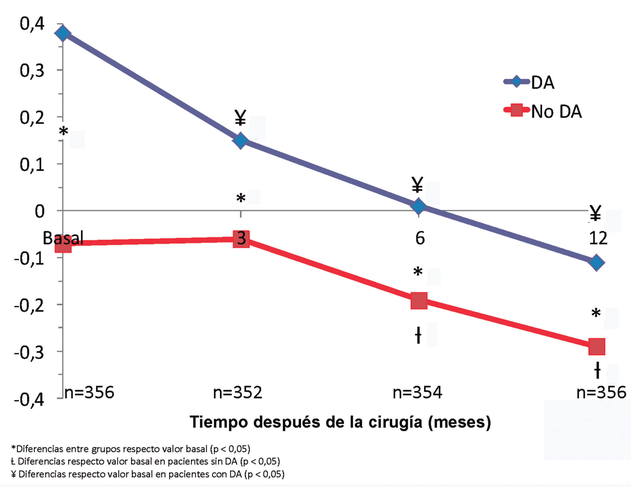
Evolución del índice aterogénico (log)



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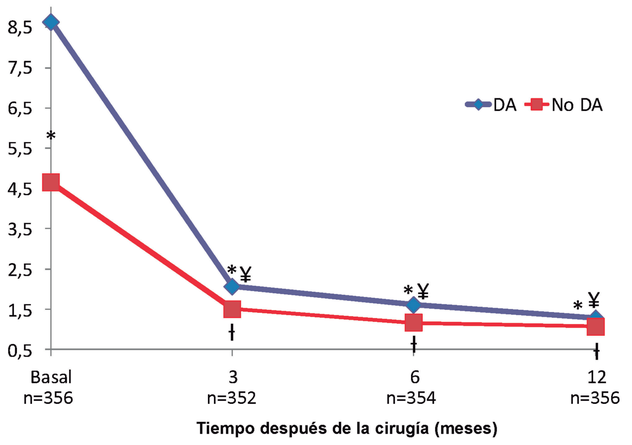
Evolución del HOMA-IR



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Conclusiones

- Prácticamente todos los pacientes obesos presentaron remisión completa de la DA un año después de la CB, independientemente de la técnica quirúrgica utilizada (BGYRL o GTL).
- Dada la refractariedad de la DA a las medidas higiénico-dietéticas y la escasa efectividad clínica de los fibratos, la CB podría ser considerada una opción terapéutica en pacientes con obesidad mórbida y DA, aunque son necesarios estudios a largo plazo.

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Prevalence of malnutrition and sarcopenia in a post-acute care geriatric unit: Applying the new European Society of Clinical Nutrition and Metabolism (ESPEN) definition and European Working Group on Sarcopenia in Older People (EWGSOP) criteria

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Backgrounds & Aims

The European Society of Clinical Nutrition and Metabolism (ESPEN) consensus definition of malnutrition has been applied in hospitalized older diabetics and middle-aged patients, geriatric outpatients, and healthy elderly and young individuals. In a post-acute care setting, our aim was to assess malnutrition (ESPEN definition) and determine its relationship with sarcopenia in older in-patients deconditioned due to an acute process.

Methods

Eighty-eight in-patients aged >70 years with body mass index (BMI) <30 kg/m^2 were included (84.1 years old; 62% women) and screened for malnutrition risk using biochemical markers and Mini-Nutritional Assessment-Short Form (MNA-SF). The ESPEN definition was applied: **1)** BMI <18.5 kg/m^2 or **2)** unintentional weight loss plus a) low BMI or b) low fat-free mass index (FFMI). European Working Group on Sarcopenia in Older People (EWGSOP) criteria were also applied.

Results

Unintentional weight loss occurred in 27 (30.7%) of 88 in-patients considered "at risk" by MNA-SF. Malnutrition prevalence was 4.5%, 7.9%, and 17% using ESPEN definitions 1, 2a, and 2b, respectively; 19.3% were malnourished. Prevalence of sarcopenia was 37.5%, of which 90.9% fulfilled ESPEN malnutrition criteria, a significant association (p = 0.02). No differences in biochemical markers were observed between patients with or without malnutrition or sarcopenia.

Table 1. General characteristics of the study participants.

	Total sample (n= 88)
Age (years)	85.2 (± 6.2)
Sex: - Male - Female	 33 (38%) 55 (62%)
Charlson comorbidity index	**2.4 (± 1.8)**
Short Portable Mental Status Questionnaire	4.4 (± 3.0)
Lawton index	**2.4 (± 2.5)**
Barthel index: - Prior - At admission - At discharge - At 3-month follow-up	 **68 (± 22.5)** **26.4 (± 15.6)** **49.7 (± 27)** **54.5 (± 26.8)**
Length of stay (days): - In referral acute care unit - In post-acute care unit	 **15.2 (± 12.1)** **14.6 (± 6.1)**

(*) Data are given as numbers (percentages) for sex distribution; continuous variables are expressed as mean (± standard deviation).

Figure 1. Overlap of the new ESPEN consensus definition of malnutrition and the individual diagnostic criteria in patients hospitalized in a post-acute care geriatric unit.

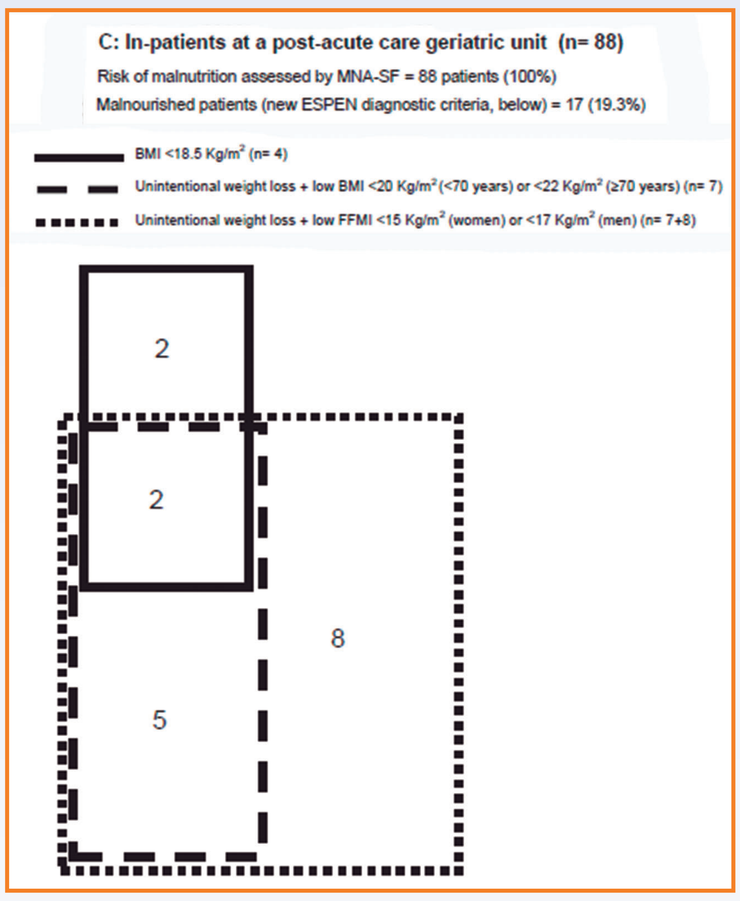

Table 2. Prevalence of malnutrition according to the new ESPEN consensus and the individual diagnostic criteria in a post-acute hospitalized population (n= 88).

First step: Case finding	**Mini-Nutritional Assessment Short Form:** **≤11: At risk of malnutrition** **>11: No risk of malnutrition**	**88 (100%)** **-**
Second step: Diagnosis	First option: Body mass index <18.5 Kg/m^2	4 (4.5%)
	Second option: Unintentional weight loss + low body mass index Unintentional weight loss + low fat-free mass index	7 (8%) 15 (17%)
Total number of patients meeting the new ESPEN criteria		17 (19.3%)

Table 3. Sample distribution according to ESPEN malnutrition definition and EWGSOP sarcopenia criteria (n= 88).

		Malnutrition definition (ESPEN)			
		Yes	No	Total	p-value
Sarcopenia criteria	**Yes**	**13**	32	**45****	p<0.03
(EWGSOP)	**No**	4	39	43	
Total		**17***	71	**88**	

(*) Patients fulfilling ESPEN malnutrition definition.
(**) Patients fulfilling EWGSOP sarcopenia criteria.

Conclusions

ESPEN criteria constitute an appropriate tool to establish a malnutrition diagnosis in postacute care. Sarcopenia, as defined by EWGSOP, was present in 37.5% of patients, of which 90.9% fulfilled ESPEN criteria; therefore, malnutrition was significantly related to sarcopenia. Additional work is needed to determine further implications of the ESPEN consensus definition.

Centre Fòrum — Parc de Salut MAR Barcelona

Usefulness of NT-proBNP levels and FRESCO cardiovascular risk scale for prediction of myocardiotoxicity induced by anthracyclines in patients with diffuse large B-cell lymphoma

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- Anthracyclines: gold-standard for DLBCL treatment
- Cardiomiotoxicity:
  - Continuous phenomenon
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- Incidence depends on method for detection:
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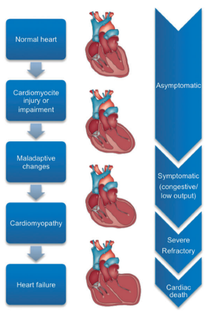
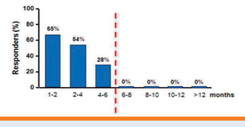
- Reversibility if early cardiologic treatment





Sawyer D et al. NEJM 2013;368:1154-6
Cardinale D et al. Circulation 2015;131:1981-8
Cardinale D et al. Circulation 2006;114:2474-81

Objectives

- To analyze the incidence of anthracycline-induced cardiomyotoxicity (AIC) and its time of onset in patients with DLBCL treated with anthracyclines
- To determine the usefulness in the prediction of anthracycline-induced cardiomyotoxicity prior to initiation of treatment of the following factors:
  - FRESCO function
  - NT-proBNP levels
- To explore the above factors as predictors of mortality from any cause

Patients and methods

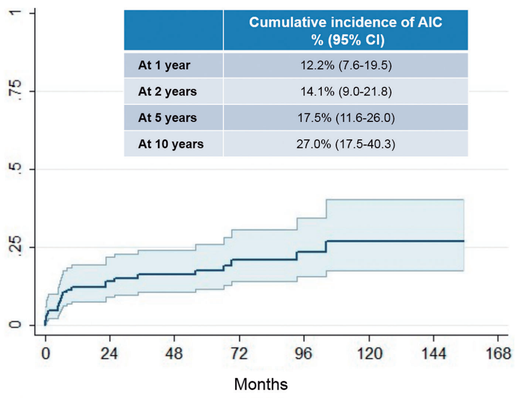
- Prospective: May 2004 – May 2014
- DLBCL treated with anthracyclines (R-CHOP/R-CHOP-like)
- Echocardiography 2D y NT-proBNP levels (Elecsys 2010 System):
  - At diagnosis
  - Post-treatment
  - Follow-up: every 12 months x 2 years, then every 2 years
  - When clinically indicated
- Cardiomyotoxicity definition:
  - Decline in LVEF <55%
  - >15% drop of baseline LVEF, if baseline LVEF <55%
  - Heart failure (HF)
- Statistical analysis: descriptive, competitive risks, discrimination, reclassificacition and bayesian network

Baseline characteristics and CV risk factors

	N=130	Conventional doxorubicin N=96	Liposomal doxorubicin N=34	p
Age years, median (IQR)	68 (54-75)	62 (50-73)	76 (71-77)	<0.0001
Sex: female	64 (49%)	48 (50%)	16 (47%)	0.843
Hypertension	54 (42%)	32 (33%)	22 (65%)	0.002
Dyslipidemia	34 (26%)	22 (23%)	12 (35%)	0.177
Diabetes	24 (19%)	18 (19%)	6 (18%)	1
Enolism	7 (5%)	4 (4%)	3 (9%)	0.377
Smoker	46 (35%)	34 (35%)	12 (35%)	1
Chronic obstructive pulmonary disease	9 (7%)	6 (6%)	3 (9%)	0.696
Cardiac disease	25 (17%)	9 (9%)	16 (47%)	<0.0001
Body mass index ≥30 kg/m²	29 (27%)	34 (35%)	12 (35%)	1
Liver disease	15 (14%)	8 (8%)	10 (29%)	0.004
FRESCO (%), median (IQR)	4.5 (2.1-7.2)	3.7 (1.7-6.6)	6.7 (5.5-8.7)	<0.0001
NT-proBNP (pg/ml), median (IQR)	252 (76-560)	163 (57-405)	449 (261-1795)	<0.0001
NT-proBNP > 600 pg/ml*	28 (22%)	14 (16%)	14 (41%)	0.004
LVEF (%), median (IQR)	64 (60-69)	64 (60-69)	63 (58-70)	0.436
IPI Intermediate-high/High	65 (50%)	40 (42%)	25 (74%)	0.002

Incidence of anthracycline-induced cardiomyotoxicity

	Cumulative incidence of AIC % (95% CI)
At 1 year	12.2% (7.6-19.5)
At 2 years	14.1% (9.0-21.8)
At 5 years	17.5% (11.6-26.0)
At 10 years	27.0% (17.5-40.3)



Event for competitive risk analysis

	n (%)
No cardiomyotoxicity nor death	**78 (60.0)**
Cardiomyotoxicity	**24 (18.5)**
HF with normal LVEF	5 (3.8)
HF with LVEF <55%	7 (5.4)
Decline LVEF <55% without HF	11 (8.5)
Decline >15% of LVEF if baseline LVEF <55%	1 (0.8)
Death	**28 (21.5)**
Death due to cardiomyotoxicity	3 (2.3)
Death due to other causes	25 (19.2)

Baseline characteristics according to competitive risk event

	None N=78	Cardiomyotoxicity N=24	Death N=28	p
Age years, median (IQR)	62 (50-74)	73 (68-76)	72 (64-76)	0.001
Sex: female	41 (53%)	8 (33%)	15 (54%)	0.225
Hypertension	25 (32%)	16 (67%)	13 (46%)	0.009
Dyslipidemia	12 (15%)	15 (63%)	7 (25%)	<0.001
Diabetes	10 (13%)	6 (25%)	8 (29%)	0.105
Enolism	3 (4%)	3 (13%)	1 (4%)	0.206
Smoker	26 (33%)	10 (42%)	10 (36%)	0.756
Chronic obstructive pulmonary disease	1 (1%)	4 (17%)	4 (14%)	0.004
Cardiac disease	5 (6%)	12 (50%)	8 (32%)	<0.0001
Body mass index ≥30 kg/m²	15 (19%)	6 (25%)	7 (25%)	0.735
Liver disease	8 (10%)	2 (8%)	8 (29%)	0.057
FRESCO (%), median (IQR)	3.7 (1.5-6.5)	7.1 (4.4-8.8)	5.3 (3.9-8.2)	<0.0001
NT-proBNP (pg/ml), median (IQR)	107 (50-342)	589 (290-1916)	329 (196-1117)	<0.0001
NT-proBNP > 600 pg/ml*	7 (10%)	12 (50%)	9 (33%)	<0.0001
LVEF (%), median (IQR)	64 (60-70)	64 (58-70)	65 (60-68)	0.563
IPI Intermediate-high/High	28 (36%)	17 (71%)	20 (71%)	<0.0001

Risk of cardiomyotoxicity or death (competitive risk)

Cardiomyotoxicity

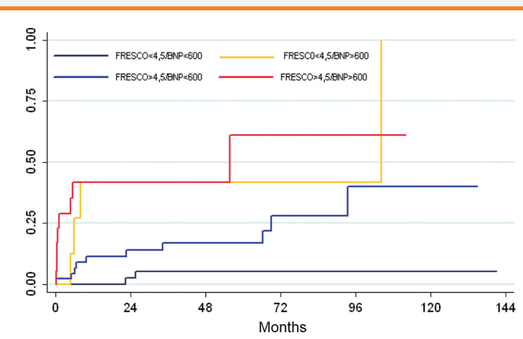
	HR (95% CI)	p
Log_2 NT-proBNP	1.44 [1.17-1.77]	0.001
FRESCO	1.15 [1.01-1.30]	0.030

Death

	HR (95% CI)	p
Log_2 NT-proBNP	1.26 [1.04-1.52]	0.020
FRESCO	1.01 [0.89-1.14]	0.888

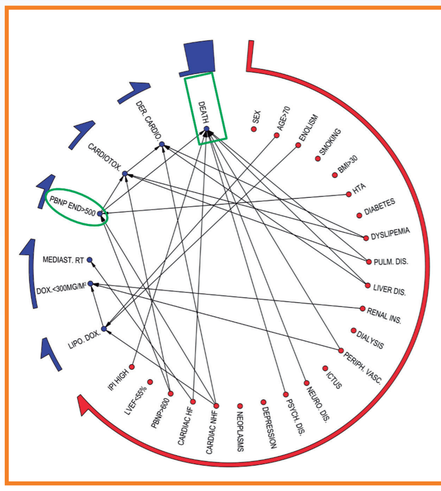
Adding doxorubicin type (conventional vs liposomal) to both models did not significantly modify the results (p = 0.648 and 0.153, respectively)

Cardiotoxicity incidence according to NT-proBNP and FRESCO



FRESCO/NT-proBNP	N (%)	1 year	2 years	4 years	7 years
<4.5% + <600	47 (39%)	0	2.22	4.50	4.50
≥4.5% + <600	47 (39%)	10.64	12.83	15.09	23.42
<4.5% + ≥600	10 (8%)	33.33	33.33	33.33	33.33
≥4.5% + ≥600	18 (15%)	38.89	38.89	38.89	45.83

Bayesian network - 1



No risk factor:
2% death probability

IPI high:
44% death probability

End-of-treatment NT-proBNP>500:
25% death probability

Conclusions

- Anthracycline-induced cardiomyopathy is a common problem in adults with DLBCL and has a cumulative incidence of 12% in the first year and 18% at five years
- NT-proBNP improves FRESCO discrimination for cardiomyotoxicity
- NT-proBNP and FRESCO are factors that independently predict an increased risk of cardiomyotoxicity, in particular NT-proBNP levels ≥ 600 pg/ml and FRESCO ≥ 4.5%

These results have given rise in our institution to set up a pilot program for early cardiologic assessment in patients with lymphoma, based on FRESCO / NT-proBNP risk

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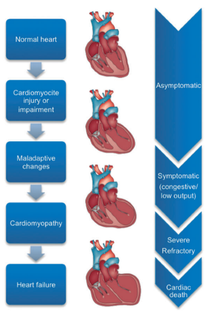

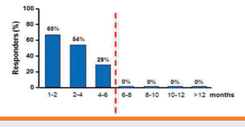

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Cardinale D et al. Circulation 2015;131:1981-8
Cardinale D et al. Circulation 2006;114:2474-81

Objectives

- To analyze the incidence of anthracycline-induced cardiomyotoxicity (AIC) and its time of onset in patients with DLBCL treated with anthracyclines
- To determine the usefulness in the prediction of anthracycline-induced cardiomyotoxicity prior to initiation of treatment of the following factors:
  - FRESCO function
  - NT-proBNP levels
- To explore the above factors as predictors of mortality from any cause

Patients and methods

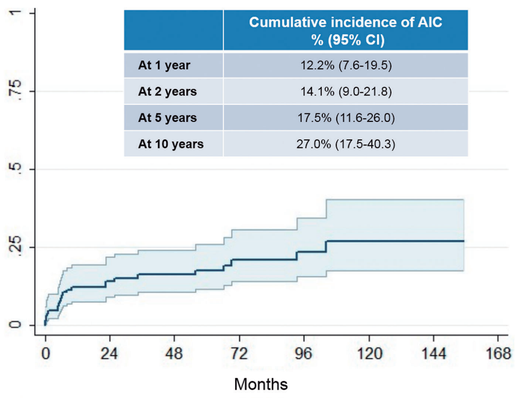
- Prospective: May 2004 – May 2014
- DLBCL treated with anthracyclines (R-CHOP/R-CHOP-like)
- Echocardiography 2D y NT-proBNP levels (Elecsys 2010 System):
  - At diagnosis
  - Post-treatment
  - Follow-up: every 12 months x 2 years, then every 2 years
  - When clinically indicated
- Cardiomyotoxicity definition:
  - Decline in LVEF <55%
  - >15% drop of baseline LVEF, if baseline LVEF <55%
  - Heart failure (HF)
- Statistical analysis: descriptive, competitive risks, discrimination, reclassificacition and bayesian network

Baseline characteristics and CV risk factors

	N=130	Conventional doxorubicin N=96	Liposomal doxorubicin N=34	p
Age years, median (IQR)	68 (54-75)	62 (50-73)	76 (71-77)	<0.0001
Sex: female	64 (49%)	48 (50%)	16 (47%)	0.843
Hypertension	54 (42%)	32 (33%)	22 (65%)	0.002
Dyslipidemia	34 (26%)	22 (23%)	12 (35%)	0.177
Diabetes	24 (19%)	18 (19%)	6 (18%)	1
Enolism	7 (5%)	4 (4%)	3 (9%)	0.377
Smoker	46 (35%)	34 (35%)	12 (35%)	1
Chronic obstructive pulmonary disease	9 (7%)	6 (6%)	3 (9%)	0.696
Cardiac disease	25 (17%)	9 (9%)	16 (47%)	<0.0001
Body mass index ≥30 kg/m²	29 (27%)	34 (35%)	12 (35%)	1
Liver disease	15 (14%)	8 (8%)	10 (29%)	0.004
FRESCO (%), median (IQR)	4.5 (2.1-7.2)	3.7 (1.7-6.6)	6.7 (5.5-8.7)	<0.0001
NT-proBNP (pg/ml), median (IQR)	252 (76-560)	163 (57-405)	449 (261-1795)	<0.0001
NT-proBNP > 600 pg/ml*	28 (22%)	14 (16%)	14 (41%)	0.004
LVEF (%), median (IQR)	64 (60-69)	64 (60-69)	63 (58-70)	0.436
IPI Intermediate-high/High	65 (50%)	40 (42%)	25 (74%)	0.002

Incidence of anthracycline-induced cardiomyotoxicity

	Cumulative incidence of AIC % (95% CI)
At 1 year	12.2% (7.6-19.5)
At 2 years	14.1% (9.0-21.8)
At 5 years	17.5% (11.6-26.0)
At 10 years	27.0% (17.5-40.3)



Event for competitive risk analysis

	n (%)
No cardiomyotoxicity nor death	**78 (60.0)**
Cardiomyotoxicity	**24 (18.5)**
HF with normal LVEF	5 (3.8)
HF with LVEF <55%	7 (5.4)
Decline LVEF <55% without HF	11 (8.5)
Decline >15% of LVEF if baseline LVEF <55%	1 (0.8)
Death	**28 (21.5)**
Death due to cardiomyotoxicity	3 (2.3)
Death due to other causes	25 (19.2)

Baseline characteristics according to competitive risk event

	None N=78	Cardiomyotoxicity N=24	Death N=28	p
Age years, median (IQR)	62 (50-74)	73 (68-76)	72 (64-76)	0.001
Sex: female	41 (53%)	8 (33%)	15 (54%)	0.225
Hypertension	25 (32%)	16 (67%)	13 (46%)	0.009
Dyslipidemia	12 (15%)	15 (63%)	7 (25%)	<0.001
Diabetes	10 (13%)	6 (25%)	8 (29%)	0.105
Enolism	3 (4%)	3 (13%)	1 (4%)	0.206
Smoker	26 (33%)	10 (42%)	10 (36%)	0.756
Chronic obstructive pulmonary disease	1 (1%)	4 (17%)	4 (14%)	0.004
Cardiac disease	5 (6%)	12 (50%)	8 (32%)	<0.0001
Body mass index ≥30 kg/m²	15 (19%)	6 (25%)	7 (25%)	0.735
Liver disease	8 (10%)	2 (8%)	8 (29%)	0.057
FRESCO (%), median (IQR)	3.7 (1.5-6.5)	7.1 (4.4-8.8)	5.3 (3.9-8.2)	<0.0001
NT-proBNP (pg/ml), median (IQR)	107 (50-342)	589 (290-1916)	329 (196-1117)	<0.0001
NT-proBNP > 600 pg/ml*	7 (10%)	12 (50%)	9 (33%)	<0.0001
LVEF (%), median (IQR)	64 (60-70)	64 (58-70)	65 (60-68)	0.563
IPI Intermediate-high/High	28 (36%)	17 (71%)	20 (71%)	<0.0001

Risk of cardiomyotoxicity or death (competitive risk)

Cardiomyotoxicity

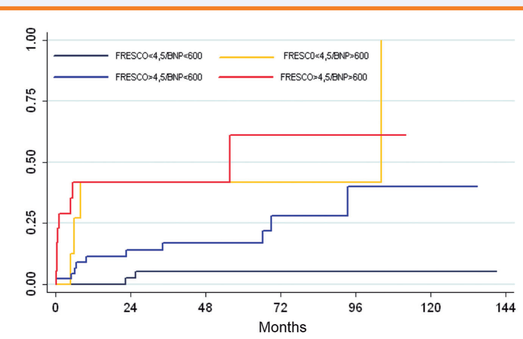
	HR (95% CI)	p
Log_2 NT-proBNP	1.44 [1.17-1.77]	0.001
FRESCO	1.15 [1.01-1.30]	0.030

Death

	HR (95% CI)	p
Log_2 NT-proBNP	1.26 [1.04-1.52]	0.020
FRESCO	1.01 [0.89-1.14]	0.888

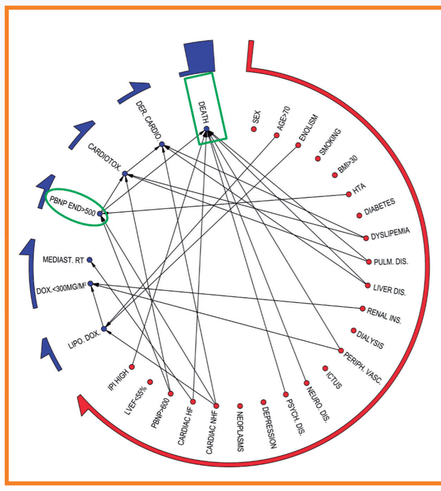
Adding doxorubicin type (conventional vs liposomal) to both models did not significantly modify the results (p = 0.648 and 0.153, respectively)

Cardiotoxicity incidence according to NT-proBNP and FRESCO



FRESCO/NT-proBNP	N (%)	1 year	2 years	4 years	7 years
<4.5% + <600	47 (39%)	0	2.22	4.50	4.50
≥4.5% + <600	47 (39%)	10.64	12.83	15.09	23.42
<4.5% + ≥600	10 (8%)	33.33	33.33	33.33	33.33
≥4.5% + ≥600	18 (15%)	38.89	38.89	38.89	45.83

Bayesian network - 1



No risk factor:
2% death probability

IPI high:
44% death probability

End-of-treatment NT-proBNP>500:
25% death probability

Conclusions

- Anthracycline-induced cardiomyopathy is a common problem in adults with DLBCL and has a cumulative incidence of 12% in the first year and 18% at five years
- NT-proBNP improves FRESCO discrimination for cardiomyotoxicity
- NT-proBNP and FRESCO are factors that independently predict an increased risk of cardiomyotoxicity, in particular NT-proBNP levels ≥ 600 pg/ml and FRESCO ≥ 4.5%

These results have given rise in our institution to set up a pilot program for early cardiologic assessment in patients with lymphoma, based on FRESCO / NT-proBNP risk

Hospital del Mar

Parc de Salut MAR Barcelona

Millora dels resultats assistencials efectuant un seguiment post-alta de UCI

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INTRODUCCIÓ

Els malalts crítics, una vegada donats d'alta de UCI, poden presentar complicacions amb risc de reingrés a UCI i/o mort.

HIPÒTESI

L'aplicació d'un programa de seguiment de malalts post-alta de UCI per part dels intensivistes responsables, pot millorar els resultats assistencials dels pacients crítics.

OBJECTIUS

Conèixer la incidència de reingressos i la mortalitat post-alta de UCI a l'aplicar el seguiment actiu post-alta de UCI.

METODOLOGIA

Estudi prospectiu, efectuat a la UCI de l'Hospital del Mar de Barcelona del 1/02/2013 al 30/09/2015. Es van incloure els malalts donats d'alta de la UCI vius (excloent <18a, trasllats a altres UCIs, Hospitals o a domicili, i els ingressos programats per neuroangiografia). Als pacients se'ls efectuava un seguiment actiu post-alta (presencial o telemàtic), amb contacte amb els facultatius responsables a planta. S'omplia una fitxa de seguiment en cada cas. Les diferències foren analitzades mitjançant xi quadrat per variables categòriques.

RESULTATS

Taula 1. Característiques demogràfiques dels pacients inclosos en l'estudi

Variables	n=1048
Edat, anys (IQRL)	63 (49-74)
Sexe, n (%)	
-Home	660 (63)
-Dona	388 (37)
Procedència, n (%)	
-Urgències	633 (60,4)
-Unitat Hospitalització	218 (20,8)
-Altre Centre	119 (11,4)
Tipus de malalt, n (%)	
-Mèdic	699 (66,7)
-Quirúrgic	202 (19,3)
Comorbiditats, n (%)	
-Diabetes	147 (14)
-MPOC	116 (11,1)
Motiu Ingrés, n (%)	
-Alteració del nivell de consciència	282 (26,9)
-Insuficiència respiratòria	258 (24,6)
Gravetat, (IQRL)	
-APACHE II$_{ingrés}$	15 (9-22)
-SOFA$_{ingrés}$	4 (1-6)
-SOFA$_{alta}$	1 (0-3)
Estada hospital, dies (IQRL)	17 (9-31)
Estada a UCI, dies (±DE)	7,5 (10,1)
Dies fins a reingrés, dies (±DE)	7,5 (9,4)
Evolució, n (%)	
-Amb seguiment post-alta	766 (73,1)
-Reingressats	86 (8,2)
-Mortalitat global	96 (9,2)

Taula 2. Evolució Reingressats/no reingressats

	Reingressats (n=86)	No reingressats (n=962)	P
APACHE II; mitjana (±DE)	18,5 (7,7)	15,5 (8,6)	<0.001
SOFA$_{alta\ UCI}$; mitjana (±DE)	2 (1,9)	1,1 (1,7)	
Ordre no reanima/LTSV, n (%)			
-Si	0 (0)	43 (4,4)	Ns
-No	86 (100)	919 (95,6)	
Estada hospital, mediana (IQRL)	40,5 (24-66)	16 (9-28)	<0.001
Mortalitat, n=96 (9,2%)	34 (39,5%)	62 (6,4%)	
- Planta	11	62	<0.001
- UCI	23	0	

Gràfic 1. Evolució dels reingressos

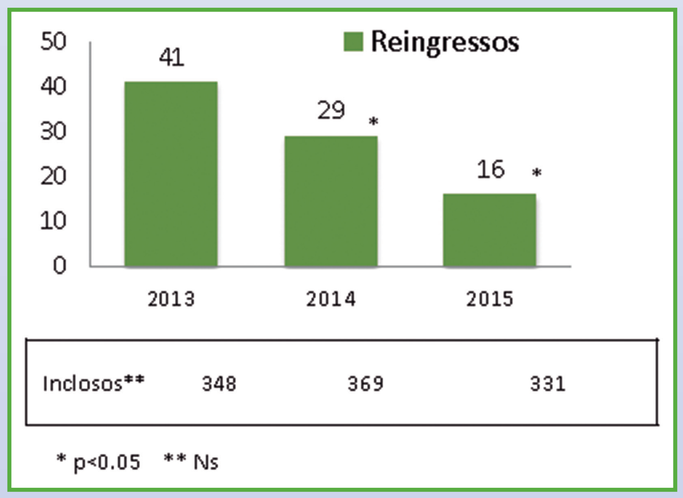
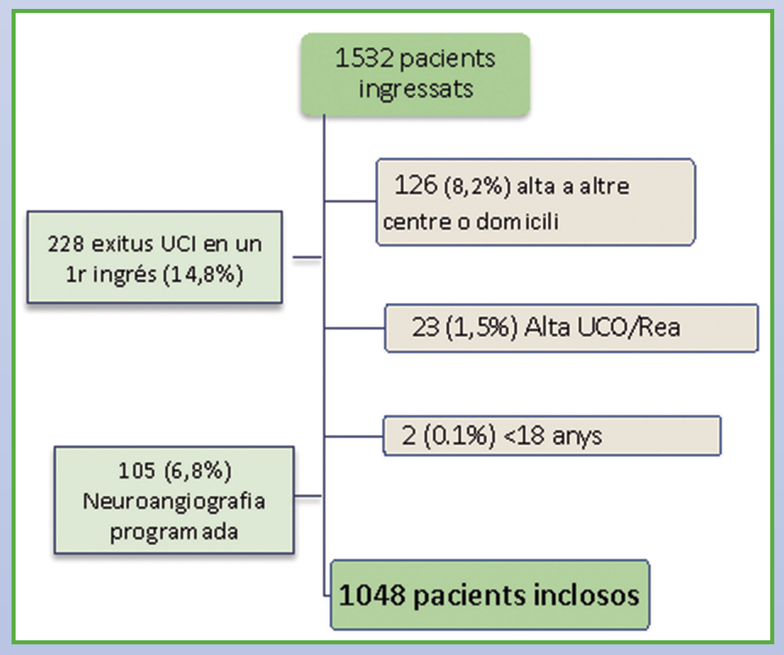
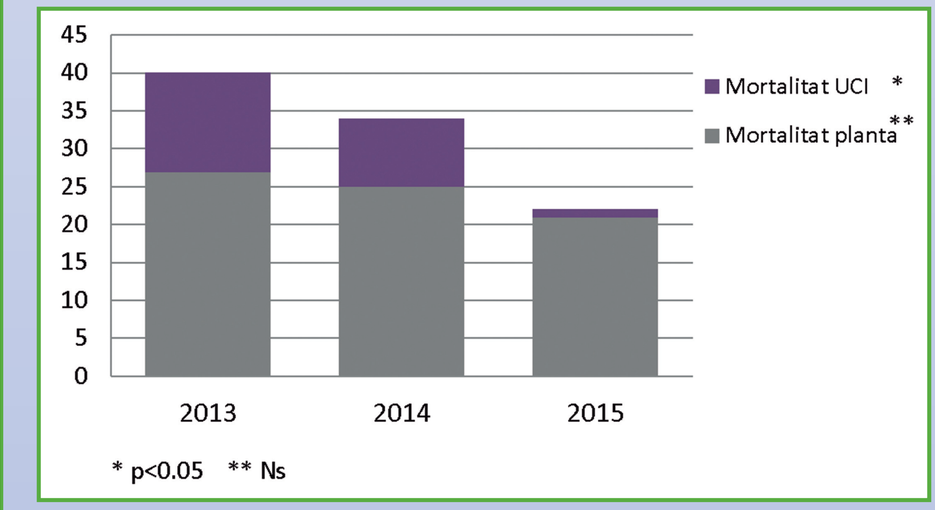


Figura 1. Flux de pacients



Gràfic 2. Evolució mortalitat dels pacients inclosos



CONCLUSIONS

La instauració d'un programa de seguiment a l'alta d'UCI dels pacients crítics, s'associa a una reducció en la taxa de reingressos, a una reducció en la mortalitat intraUCI i al descens de la mortalitat intraUCI associada a reingrés, probablement degut a una millor comunicació amb els responsables a planta d'hospitalització i una anticipació en el tractament dels problemes.

Finançat per el Projecte Estrella PSMAR 2012.

Hospital del Mar

Parc de Salut MAR Barcelona

Meta-Analysis of the Risk of Subsequent Mood Episodes in Bipolar Disorder

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Introduction

Reported relapse and recurrence rates in bipolar disorder (BD) differ significantly between studies. Most data originate from highly selective patients participating in sponsored randomized controlled trials with narrow inclusion criteria. To estimate the true risk of a subsequent mood episode (SME) under real-world conditions, we conducted a meta-analysis of rates of SME as reported in naturalistic BD studies.

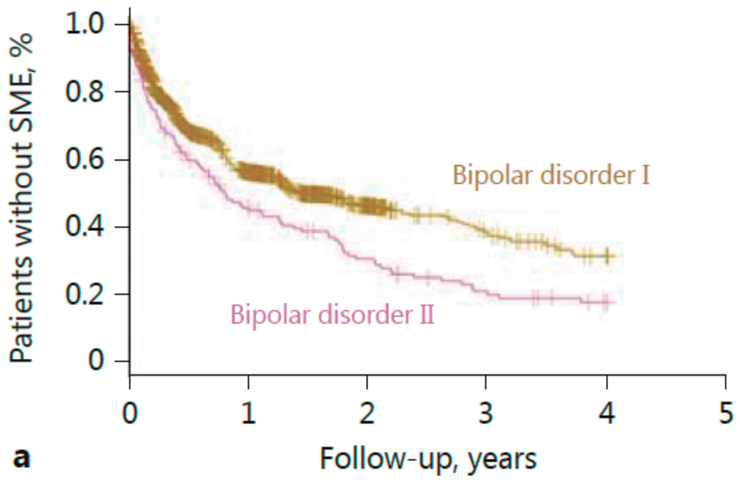
Methods

PubMed, ScienceDirect, Scopus, and Web of Knowledge were searched until July 2015. Studies reporting the time until the emergence of an SME, from which individual data or Kaplan-Meier plots with censors marked could be retrieved, were included.

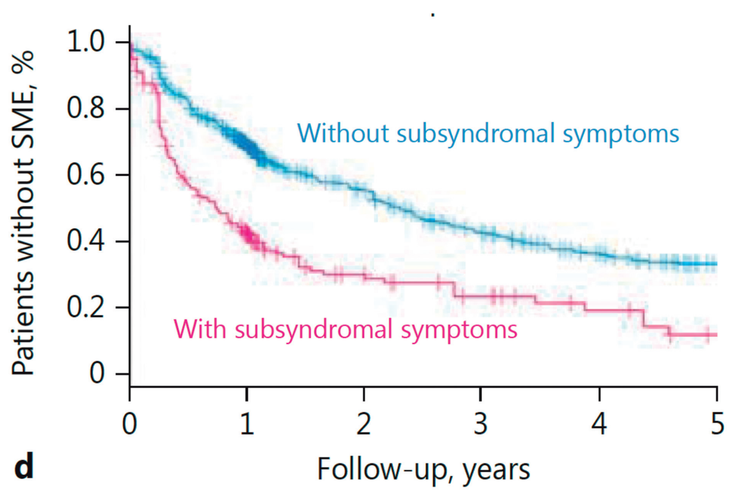
Results

Twelve studies comprising 5,837 patients met the inclusion criteria. The median time to an SME in adults after an index episode was 1.44 years. The risk of an SME was 44% during the first year. Not having a SME during this first year lowered this risk to 19% in the second year. The risk was higher in bipolar II disorder (BD-II) than in bipolar I disorder (BD-I; HR = 1.5). In BD-I, the risk of a subsequent manic, mixed, or depressive mood episode was higher after an index episode of the same polarity (HR = 1.89–5.14). The overall risk of an SME was higher in patients with persisting subsyndromal symptoms (HR = 2.17) but lower in adolescent patients (HR 0.62), when compared to adult subjects.

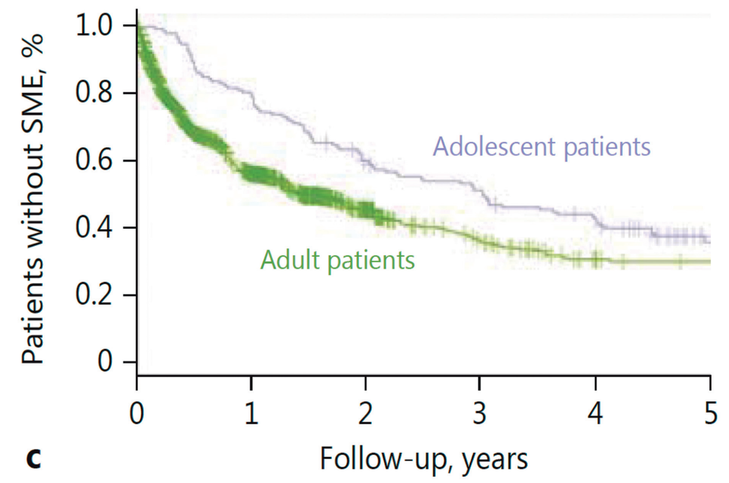
All adult patients recruited during an episode



All adult patients



All adult patients recruited during an episode



Conclusions

The data from this study provide a more reliable estimate of a pronounced risk of an SME in BD in real-world settings. Subsyndromal symptoms cause more SME whereas more research into the longitudinal course of BD-II and adolescent patients is warranted to confirm its role as a risk factor for SME.

Reference

Radua J, Grunze H, Amann BL: Meta-analysis of the risk of relapse in bipolar disorder. Psychotherapy and Psychosomatics (2017) 86:90-98.

Population pharmacokinetics of linezolid as it applies to therapeutic drug monitoring: a comparison of ten approaches

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Abstract

Objectives: There are no reports comparing the accuracy and precision of published pharmacokinetic (PK) models of Linezolid (LNZ) Therapeutic Drug Monitoring (TDM). The goal was to compare the bias and precision of ten published population equations at predicting future LNZ concentrations.

Methods: LNZ levels were collected as part of TDM programs. Ten linear and mixed linear and non-linear population equations with one to multiple compartments were coded into Individually Designed Optimum Dosing Strategies (ID-ODS^{TM}) online. Up to fifteen levels were predicted per patient. For models with covariate relationship, a change in PK parameters - as a result of a change in physiologic variables - were allowed to improve the predictive performance of the equations. The mean prediction error (ME) and mean squared prediction error (MSE) and their 95% confidence intervals (95%CI) were calculated to measure absolute, while Δ ME and Δ MSE and their 95% CI to measure relative bias and precision, respectively.

Results: 179 LNZ levels in 54 patients were analyzed. The models studied showed MEs in predicting serum concentrations that ranged from a mean (95% CI) % difference of -5.94 (-7.16, -4.72) mg/L to 6.44 (5.07, 7.82) mg/L, while MSEs that ranged from 62.61 (40.25, 84.97) mg/L^2 to 127.92 (92.63, 163.21) mg/L^2. The one compartment model by Tsuji et al. was found to be numerically most accurate and precise. When compared to the model by Tsuji et al., the formulas by Polk and Abe et al. showed non-significantly different Δ MEs for bias, while the equations by Matsumoto, Boak and Abe et al. resulted in non-significantly different Δ MSEs for precision. The comparison of the rest of the approaches relative to the Tsuji method showed mostly negative values of Δ MEs and Δ MSEs that ranged from 13.51 (2.05, 24.97) mg/L^2 to 65.30 (26.55, 104.05) mg/L^2.

Conclusion: Eight of the ten equations are likely to under-predict total LNZ concentrations. Thee model by Tsuji et al. ranked the highest at accurately and precisely predicting LNZ concentrations. The best performed model may be adapted into a TDM program focusing on the optimal dosing of LNZ.

Methods

Simulation and data analysis

- The ID – ODS^{TM} (Individually Designed Optimum Dosing Strategies) program was used to predict total plasma LNZ concentrations taking into account patient demographic and laboratory information[4].
- The linear and mixed linear and non-linear population equations with one to multiple compartments with IV infusion and oral administration were coded using the R® language into ID - ODS^{TM} where LNZ concentration-time profiles were calculated using the published mean population pharmacokinetic parameter estimates.
- Protein binding of 15% was assumed to calculate the total LNZ concentrations for models established based on free measured concentrations.
- Change in calculated pharmacokinetic parameters were allowed from dose to dose to allow for the incorporation of changing physiologic variables during the time course of therapy to grant the way for better predictions of observed concentrations.
- Analysis of prediction errors was based on evaluating measures of absolute and relative bias and precision.
  - Agreement between observed and predicted concentrations were described with the Bland-Altman method using the calculated percentage mean difference and 95% limits of agreement and their 95% confidence intervals. Mean prediction errors (ME) and mean squared prediction errors (MSE) were also calculated.
  - Relative bias and precision were established by calculating delta mean prediction errors (ΔME) and delta mean squared prediction errors (ΔMSE) against the model with the best absolute performance and their 95% confidence intervals, respectively.
- The R® software environment for statistical computing and graphics was used for statistical analysis and to generate plots[5].

Results

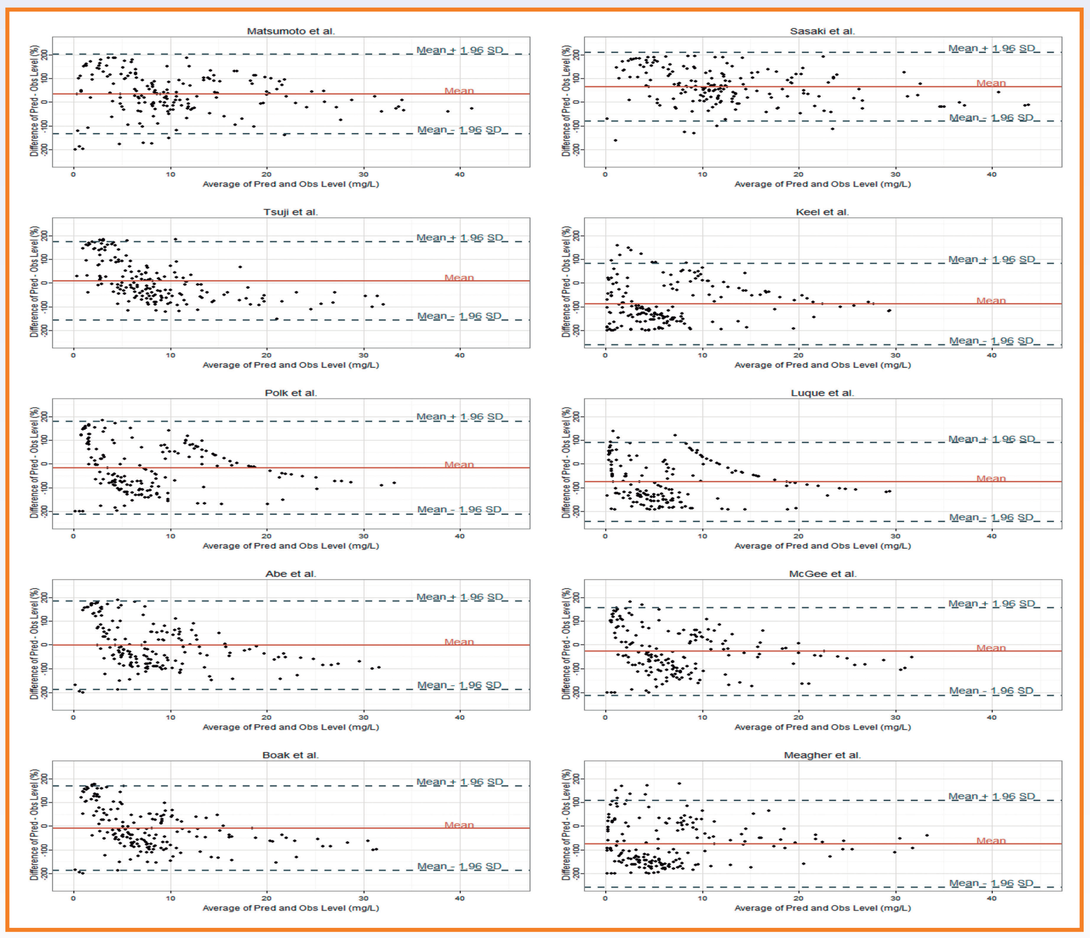
Table 1. Summary statistics of absolute performance indicators

Model	ME		MSE	
	Mean	95% CI	Mean	95% CI
Matsumoto	2.42	1.17 to 3.68	78.14	58.50 to 97.77
Sasaki	6.44	5.07 to 7.82	127.92	92.63 to 163.21
Tsuji	-2.23	-3.35 to -1.11	62.61	40.25 to 84.97
Keel	-5.71	-6.88 to -4.54	95.55	64.38 to 126.71
Polk	-2.84	-4.10 to -1.58	80.49	54.77 to 106.21
Luque	-5.94	-7.16 to -4.72	103.83	69.37 to 138.29
Abe	-2.58	-3.76 to -1.40	70.31	46.27 to 94.35
McGee	-3.83	-4.99 to -2.67	76.12	49.11 to 103.13
Boak	-3.23	-4.35 to -2.11	67.63	43.26 to 92.00
Meagher	-5.36	-6.48 to -4.24	85.80	60.00 to 111.60

Table 2. Summary statistics of relative performance indicators against the Tsuji model

Model	Δ ME		Δ MSE	
	Mean	95% CI	Mean	95% CI
Matsumoto	4.66	3.75 to 5.57	15.52	-6.72 to 37.78
Sasaki	8.68	7.71 to 9.65	65.30	26.55 to 104.05
Keel	-3.47	-4.03 to -2.91	32.93	18.28 to 47.59
Polk	-0.60	-1.32 to 0.10	17.88	4.67 to 31.08
Luque	-3.70	-4.27 to -3.14	41.21	24.00 to 58.43
Abe	-0.34	-0.85 to 0.15	7.69	-1.53 to 16.93
McGee	-1.59	-2.17 to -1.01	13.51	2.05 to 24.97
Boak	-0.99	-1.38 to -0.60	5.01	-2.88 to 12.91
Meagher	-3.12	-3.58 to -2.67	23.18	13.29 to 32.78

Figure 1. Percent difference Bland – Altman plots of observed versus predicted concentrations for the ten equations evaluated



Conclusion

- Eight out of the ten equations evaluated in our work slightly under-predict LNZ concentrations accompanied by variable magnitudes of precision.
- When compared to the Tsuji model, the model by Abe et al. ranked very similar in accuracy and precision at predicting LNZ concentrations.
- Based on these predictive performance indicators, the two best performed models by Tsuji and Abe et al. may be consider for adaptation into a TDM program focusing on the optimal dosing of LNZ.

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Hospital del Mar

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A phase IIb trial of docetaxel concurrent with radiotherapy plus hormotherapy versus radio hormonotherapy in high-risk localized prostate cancer (QRT SOGUG trial): Preliminary report for design, tolerance, and toxicity

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OBJECTIVE

To assess the toxicity and feasibility of concomitant radiotherapy with low doses of docetaxel plus standard hormonal treatment in patients with high risk localized CaP.

MATERIAL AND METHODS

Patients were randomly assigned to either arm A (LH-RH analogs every 3 months for 3 years and radiotherapy 74 Gy [2Gy x 37 fractions]) or arm B (LH-RH analogs every 3 months for 3 years, radiotherapy 73.8 Gy [1.8 Gy x 41 fractions] and concurrent weekly docetaxel at 20 mg/m^2 for 9 weeks). Chemotherapy was started one week before of radiotherapy (**Figure 1**). Primary endpoint was PSA relapse according to the Phoenix definition. The planned number of pts was 130 to detect a 15% difference with a power of 80% and an alpha of 0.05 (two-sided).

Figure 1

RESULTS

From 12/2008 to 9/2012, 130 pts were accrued (Arm A: 64, Arm B: 66). Median age was 68 years (61-73). Patients had T3-T4 (82.6%), GS ? 8 (76.3%), PSA > 20 ng/mL (26.9%) and pN+ (18.9%). All characteristics were well-balanced between arms. (**Table 1**). Median dose of radiotherapy was 74 Gy (72–74.8) in arm A, and 73.8 Gy (72-75.6) in arm B. 75.7% of pts received the planned 9 treatments of docetaxel and median number of cycles delivered per patient was 9. After a median follow-up of 29.6 months (9.6-40.2) over 95 % of patients reported at least one AE wich was considered treatment related in 90.3% of patients. Twenty three (18.6%) patients experienced at least one grade ≥3 treatment related AE. One serious related AE was reported in Arm B. (**Table 2**). The most common grade ≥2 toxicities (arm A and arm B) were: cystitis (12.5% vs 8.3%), diarrhea (3.3% vs 65%), proctitis (9.4% vs 13.3%), rectal tenesmus (3.1% vs 23.3%), asthenia (17.2% vs 56.7%) and dysuria (26.6% vs 23.3%). Toxicity G3/G4 diarrhea was reported in 8.3% of pts in arm B and 0% in arm A. G3/G4 lymphopenia occurred in arm A in 23.3% and 0% in arm B. There was no toxicity-related death. (**Figure 2-3**)

Figure 2. Most common treatment-related grade ≥2 AEs reported

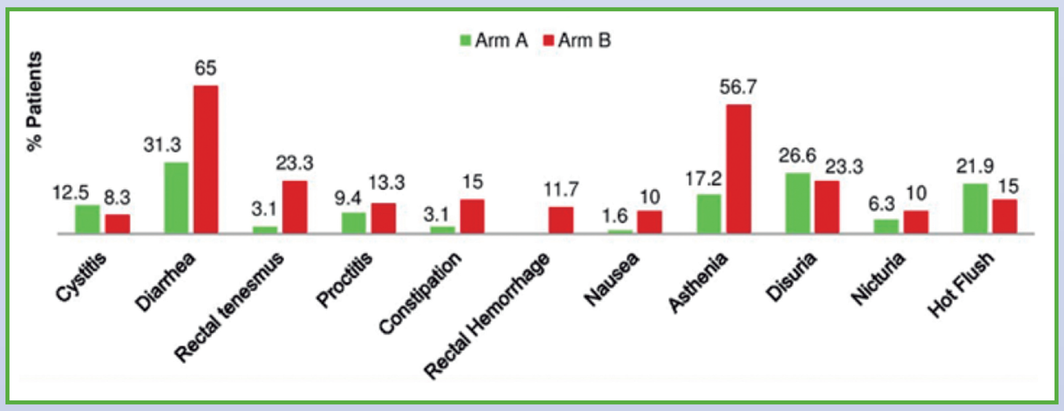
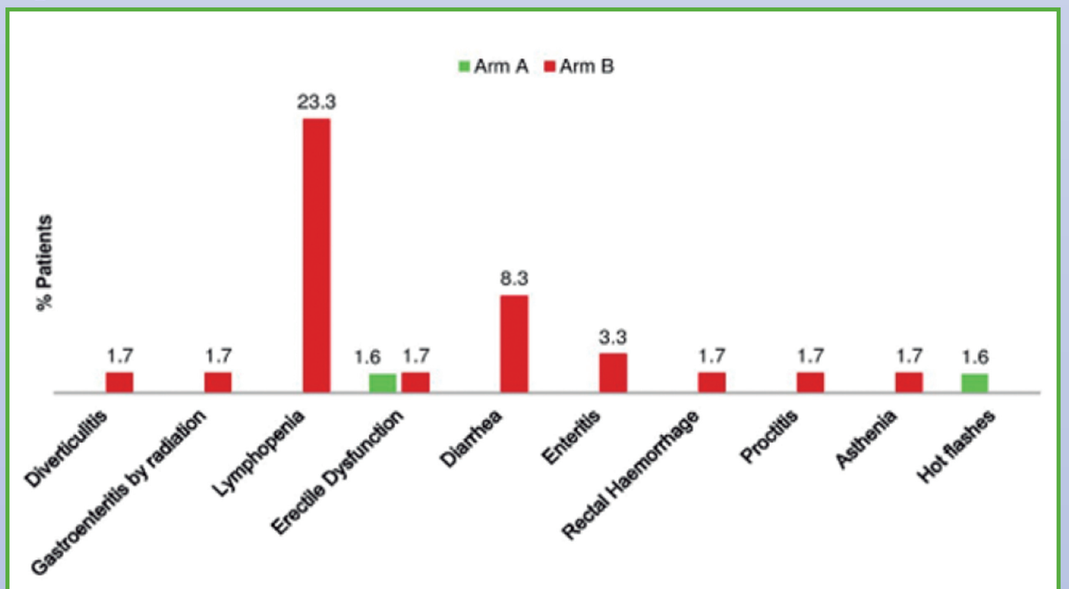


Figure 3. Grade 3-4 AEs



Grade ≥3 treatment-related AEs were more frequent in Arm B than Arm A: 35.0% (n=27) vs. 3.1% (n=2)

Table 1. Baseline characteristics

PATIENT CHARACTERISTICS	Arm A (n=64)	Arm B (n=66)	Overall population (n= 130)
Age (years), median (IQR)	68.0 (63.0-73.0)	67.5 (59.0-74.0)	68.0 (61.0-73.0)
ECOG PS as per Karnosfky scale, n (%)*[a]	54	53	107
0	49 (90.7)	46 (86.8)	95 (88.8)
1	5 (9.3)	7 (13.2)	12 (11.2)
Stage at diagnosis, n (%)*[b]	64	63	127
Tx, T1, T2	9 (14.1)	13 (20.6)	22 (17.3)
T3, T4	55 (85.9)	50 (79.4)	105 (82.7)
pN+, n (%)*[b]	15 (23.4)	9 (14.3)	24 (18.9)
Gleason score, n (%)*[b]	64	63	127
2-6 (well-differentiated)	2 (3.1)	2 (3.2)	4 (3.2)
7 (moderately differentiated)	14 (21.9)	12 (19.1)	26 (20.5)
8-10 (poor differentiated)	48 (75.0)	49 (77.8)	97 (76.4)
Baseline PSA, n (%)[c]			
≥20 ng/mL	15 (23.4)	20 (30.3)	35 (26.9)
<20 ng/mL	48 (75.0)	42 (63.6)	90 (69.2)

ECOG PS = Eastern Cooperative Oncology Group performance status; *Percentage calculated on the evaluable data (missing data are excluded).
aMissing data: 10 patients in arm A and 13 patients in arm B; bMissing data 3 patients in arm B; cMissing data: 1 arm A and B in arm B.

Table 2. Patients reporting at least one AE

Patients reporting at least one, n (%)	Arm A (N=64)	Arm B (N=60)	Overall Safety Population (N= 124)	P value*
AE	59 (92.2)	59 (98.3)	118 (95.16)	>0.05
Related AE	54 (84.4)	58 (96.7)	112 (90.3)	<0.05
Grade ≥3 related AE	2 (3.1)	21 (35.0)	23 (18.6)	<0.0001
Serious related AE	-	1 (1.7)	1 (0.8)	>0.05

CONCLUSIONS

The QRT SOGUG phase IIb trial shows that standard doses of radiotherapy and concurrent weekly docetaxel can be administered without increasing toxicity profile. Clinical trial information: 2008-003554-14.

LOW INCIDENCE OF PROPIONIBACTERIUM ACNES IN THE SKIN OF PATIENTS UNDERGOING PRIMARY SHOULDER ARTHROPLASTY

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INTRODUCTION

In shoulder surgery it is commonly believed that the P. acnes is inoculated into the deep dermal layers after surgical incision. On the contrary, some authors defend the existence of the saprophyte organism in deeper tissues.

OBJECTIVES

The aim of this study is to determine the number of positive cultures in skin and subcutaneous tissue cultures for P. acnes in prosthetic shoulder surgery.

METHODS

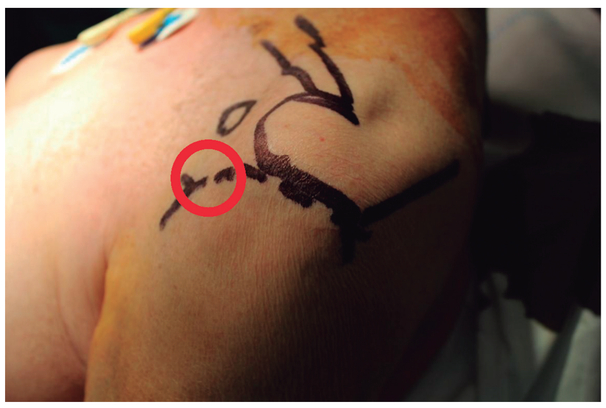
We designed a prospective observational study involving 30 patients undergoing primary shoulder arthroplasty. In all patients we obtained two skin biopsies with a 3 mm dermal punch and one subcutaneous tissue simple after surgical incision. Skin biopsies were obtained at the most anterior part of the surgical wound in case of superior approach and at the upper part in the deltopectoral approach. All patients underwent preoperative antibiotic prophylaxis with cefazolin 2g ev and skin preparation with 2% chlorhexidine alcoholic tinted before the start of surgery twice. Each tissue sample was individually homogenized and was initially inoculated in PoliVitex agar plate and thioglycolate broth. After 5 days, the thioglycolate broth culture was reseeded to a new plate of PoliVitex agar and another to a Laked blood agar plate (anaerobic specific plate). The aerobic cultures were incubated at 37ºC for 7 days whereas the anaerobic ones incubated for 14 days.

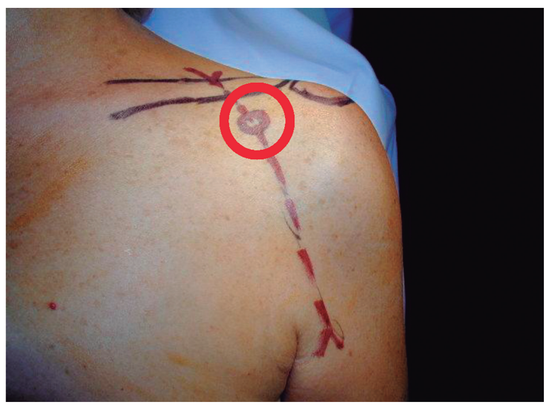
- The skin was prepared **twice** with 2% chlorhexidine gluconate and 70% isopropyl alcohol.

- All patients had:
  - **Two skin biopsies** for culture (3mm skin-punch)

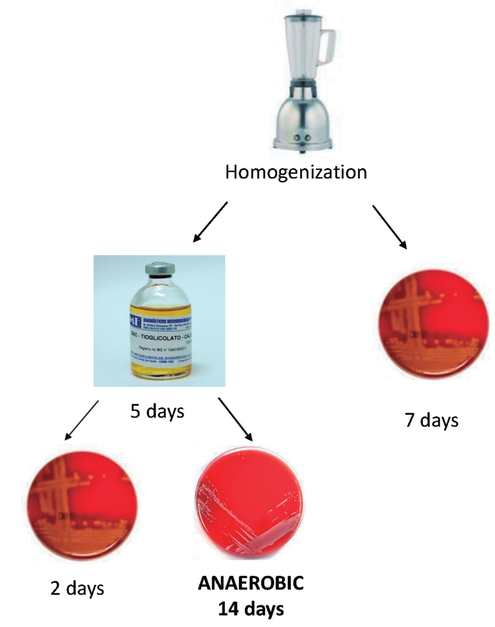
  - After the skin incision, we obtained a **subcutaneous tissue** biopsy for culture

- Skin biopsies were taken from:
  - The **anterior edge** of the wound → **supero-lateral approach**
  - The **upper edge** of the wound → **delto-pectoral approach**





- Tissue samples procedure:
  - Sample homogenization
    - ❍ PoliVitex agar plate (7 days)
    - ❍ Thioglycolate broth (5 days)
      - PoliVitex agar plate (2 days)
      - Laked blood agar plate (anaerobic specific plate). 14 days



RESULTS

A total of 30 consecutive patients who underwent shoulder arthroplasty (20 reverse shoulder arthroplasty and 10 anatomical) were analysed. 28 women and 2 men, mean age of 73.02 (SD 7.2). The indication for arthroplasty was a secondary arthropathy cuff injury in 16 cases, primary osteoarthritis in 2, acute fracture in 8 and fracture sequelae in 4. We obtained 90 tissue cultures (60 skin cultures and 30 subcutaneous) and only 3 cultures were positive (3.33%) for P. acnes in 2 different patients. A patient (female) had both positive skin cultures, while the second patient (male) only had positive the subcutaneous tissue cultures. This 2 patients underwent reverse shoulder arthroplasty. The time to grow was 15 days in first patient and 14 days in the second patient (mean 14.66 days).

CONCLUSIONS

In a real setting of patients undergoing shoulder arthroplasty using antibiotic prophylaxis and standard preoperative skin preparation with chlorhexidine we found a low rate of positive cultures for P. acnes (3.33%).
The higher rate of P. acnes positive cultures in skin reported in previous studies may be caused by a different population study group (healthy and younger volunteers without antibiotic prophylaxis) or suboptimal culture technique (use of swaps).