Data Management Education session

Tuesday 5th April 2016

The comorbidity index

Roberto Raimondi

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Vicenza - Italy

The Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI)

- **What is it ?**
- **Why and how was it introduced? Why is it needed ?**
- **What is its clinical utility ?**
- **Where is it inserted into Promise ?**
- **How can you calculate the HCT-CI score ?**

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The HCT-Comorbidity Index is a number, a score, that represents the burden of the incidental comorbidities found in the patient before the transplant.

The specific comorbidities considered are the following:

Arrhythmia	
Cardiac	
Heart valve disease	
Inflammatory bowel disease	
Diabetes	
Cerebrovascular disease	
Psychiatric disturbance	
Obesity	
Infection	

Rheumatologic	
Peptic ulcer	
Renal	
Pulmonary	moderate
	severe
Hepatic	mild
	moderate/severe
Prior solid tumor	

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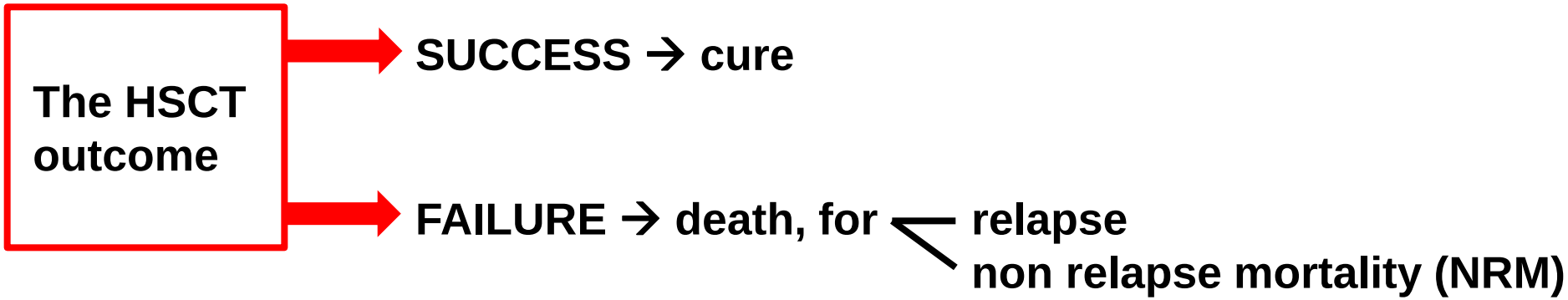


It is obvious that we need to make any effort to reduce the NRM that undermines the potentially curative power of the transplant.

Furthermore we need to estimate as accurately as possible the benefits and the risks of the transplant to calculate in that particular patient the benefit/risk ratio of the procedure.
From this point of view we need a good tool to estimate the NRM risk.

The outcome of the transplant depends on three sets of factors:

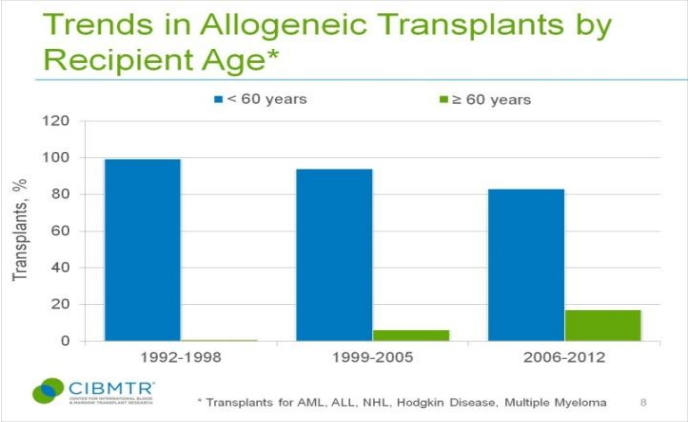
Disease factors	Procedure factors	Patient factors
diagnosis	donor	age
disease stage	source of HSCs	performance status
cytogenetic	conditioning	organ functions
molecular markers	HLA compatibility	comorbidity
MRD	GVHD prophylaxis	etc…
etc…	etc…	

Many studies have evaluated the impact of the disease status or single aspects of the procedure, but little was known about the influence of the patient's characteristics per sé.

Age has been the patient-specific parameter historically used to evaluate the tolerance of the patient, but the "old" limits of 55-60 years are arbitrary and currently in part outdated, especially after the introduction of the reduced-intensity conditionig regimens.

Giorgione, *The three ages of man,* 1507

In the last years the age at transplant has been increasing; 17% of allogeneic transplant recipients in 2006-2012 were older than 60.
In this age group, one would expect a greater presence of comorbidities.



Furthermore, the chronological age not always corresponds to the biological age.

Patient factors

- **Age**
- **Performance status**
- **Single organ functions**

➢ **None of them alone is predictive for NRM or overall survival (OS)**

➢ **How to proceed in case of more than one disfunction?**

Use a scoring system

blood 2005;106: 2912-2919

Hematopoietic cell transplantation (HCT)–specific comorbidity index: a new tool for risk assessment before allogeneic HCT

Mohamed Sorror, Michael Maris, Rainer Storb, Frederic Baron, Brenda Sandmaier, David Maloney, Barry Storer

Sorror and Coll. analized retrospectively all comorbidities encountered in 1055 patients transplanted in Seattle from 1997 to 2003.

Patients were randomly divided into 2 cohorts, a training set (n. 708) to develop the scoring weights and a validation set (n. 347).

For each comorbid condition the hazard ratios (HRs) for NRM at 2 years were calculated.

The adjusted HRs were converted to integer weights according to the following:

comorbidities with HR ≤ 1.2	were dropped from consideration
comorbidities with HR of 1.3 to 2.0	were assigned a weight of 1
comorbidities with HR of 2.1 to 3.0	were assigned a weight of 2
comorbidities with HR ≥ 3.1	were assigned a weight of 3

blood 2005;106: 2912-2919

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At the end, 17 comorbidities (15 + 2 splitted in relation to the severity: hepatic and pulmonary) have been recognized as relevant.

The final HCT-CI score was the sum of these integer weights.

Comorbidity	HCT-CI weighted scores
Arrhythmia	1
Cardiac	1
Inflammatory bowel disease	1
Diabetes	1
Cerebrovascular disease	1
Psychiatric disturbance	1
Hepatic, mild	1
Obesity	1
Infection	1
Rheumatologic	2
Peptic ulcer	2
Moderate/severe renal	2
Moderate pulmonary	2
Prior solid tumor	3
Heart valve disease	3
Severe pulmonary	3
Moderate/severe hepatic	3

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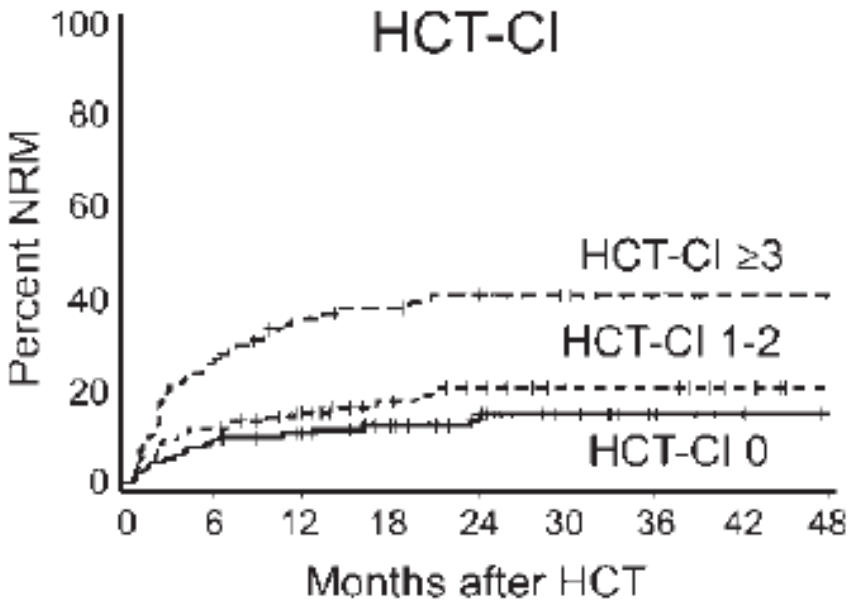
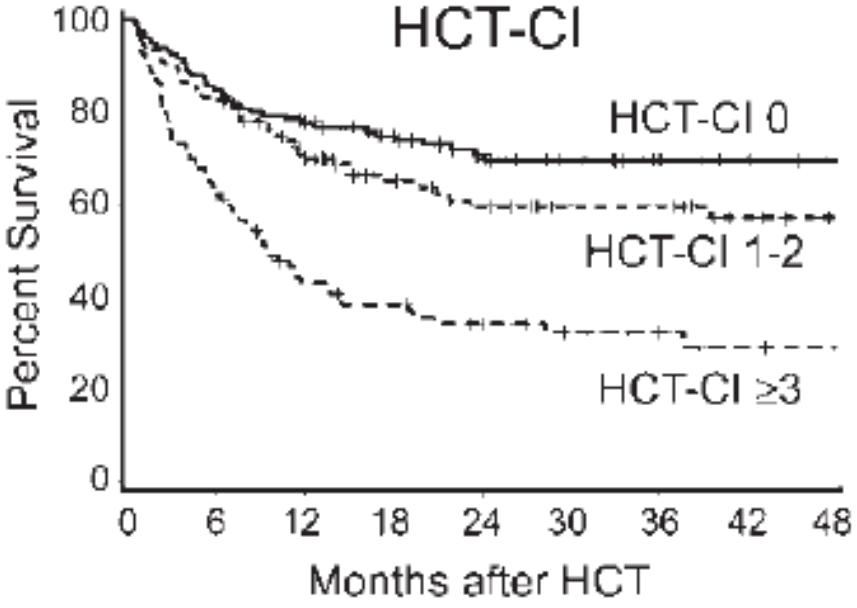
The HCT-CI scores were collapsed into 3 risk groups:

- **score 0 (low risk)**
- **score 1 to 2 (intermediate risk)**
- **score ≥ 3 (high risk)**

According to this, Sorror and Coll. demonstrated that the HCT-CI can stratify the patients for the risk of NRM and also for OS.





After its publication the HCT-CI has been tested in many studies and the majority of them have confirmed its usefulness, but often they were retrospective, from a single center, with a small number of patients and with transplants performed in the past.

Two studies have tested, and validated, the HCT-CI in a prospective manner, with a large multicenter population transplanted in recent years.

blood 2012;120(6): 1327-1333

Validation of the Hematopoietic Cell Transplantation-Specific Comorbidity Index: a prospective, multicenter GITMO study

Roberto Raimondi, Alberto Tosetto, Rosi Oneto, Riccardo Cavazzina, Francesco Rodeghiero, Andrea Bacigalupo, Renato Fanin, Alessandro Rambaldi, and Alberto Bosi

Prospective multicenter study. Years 2008-2011. Patients: 1937

Confirmed the predictive power of the HCT-CI

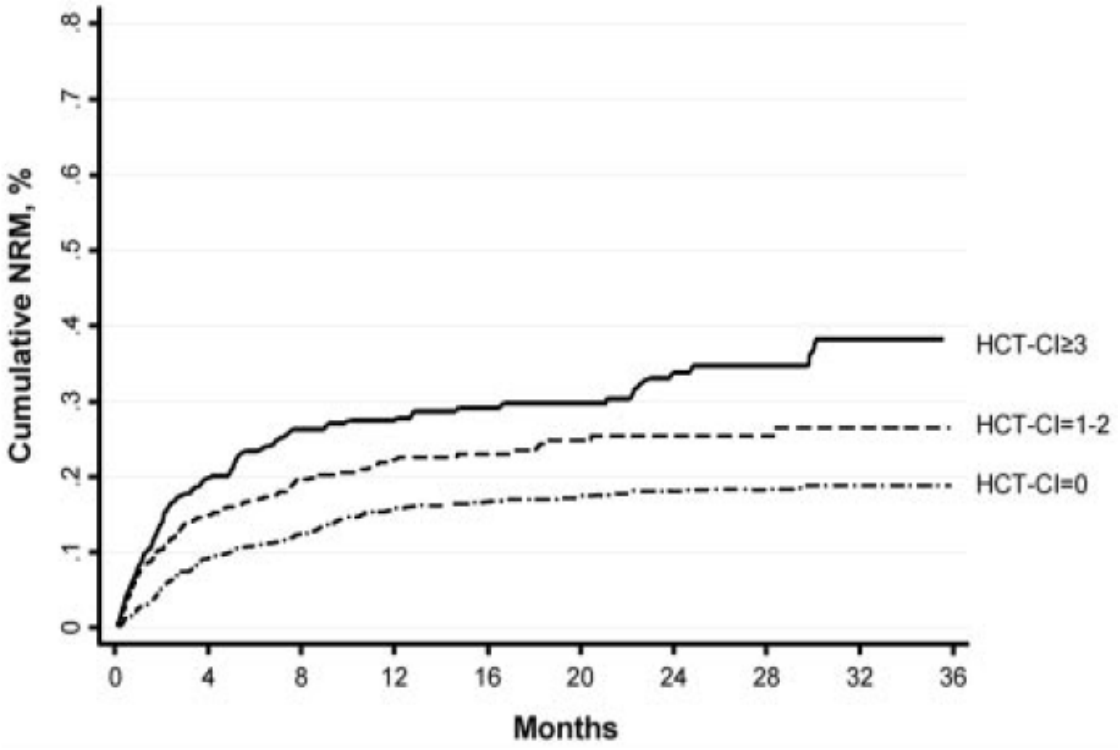


Figure 1. NRM cumulative incidence by HCT-CI score group.

Biology of Blood and Marrow Transplantation
ASBMT American Society for Blood and Marrow Transplantation
2015 Aug;21(8):1479-87

Prospective Validation of the Predictive Power of the Hematopoietic Cell Transplantation Comorbidity Index: A CIBMTR® Study

Mohamed Sorror, Brent Logan, Xiaochun Zhu, J. Douglas Rizzo, Kenneth Cooke, Philip McCarthy, Vincent Ho, Mary Horowitz, Marcelo Pasquini,

Prospective multicenter study. Years 2007-2009. Patients: 8115 Allo (and 11.652 Auto)

Allo				
Score HCT-CI	NRM %		OS %	
	1 year	3 years	1 year	3 years
0	17	24	69	54
1-2	21	28	62	47
≥ 3	26	35	56	38

The higher the score, the higher the NRM and the lower the OS

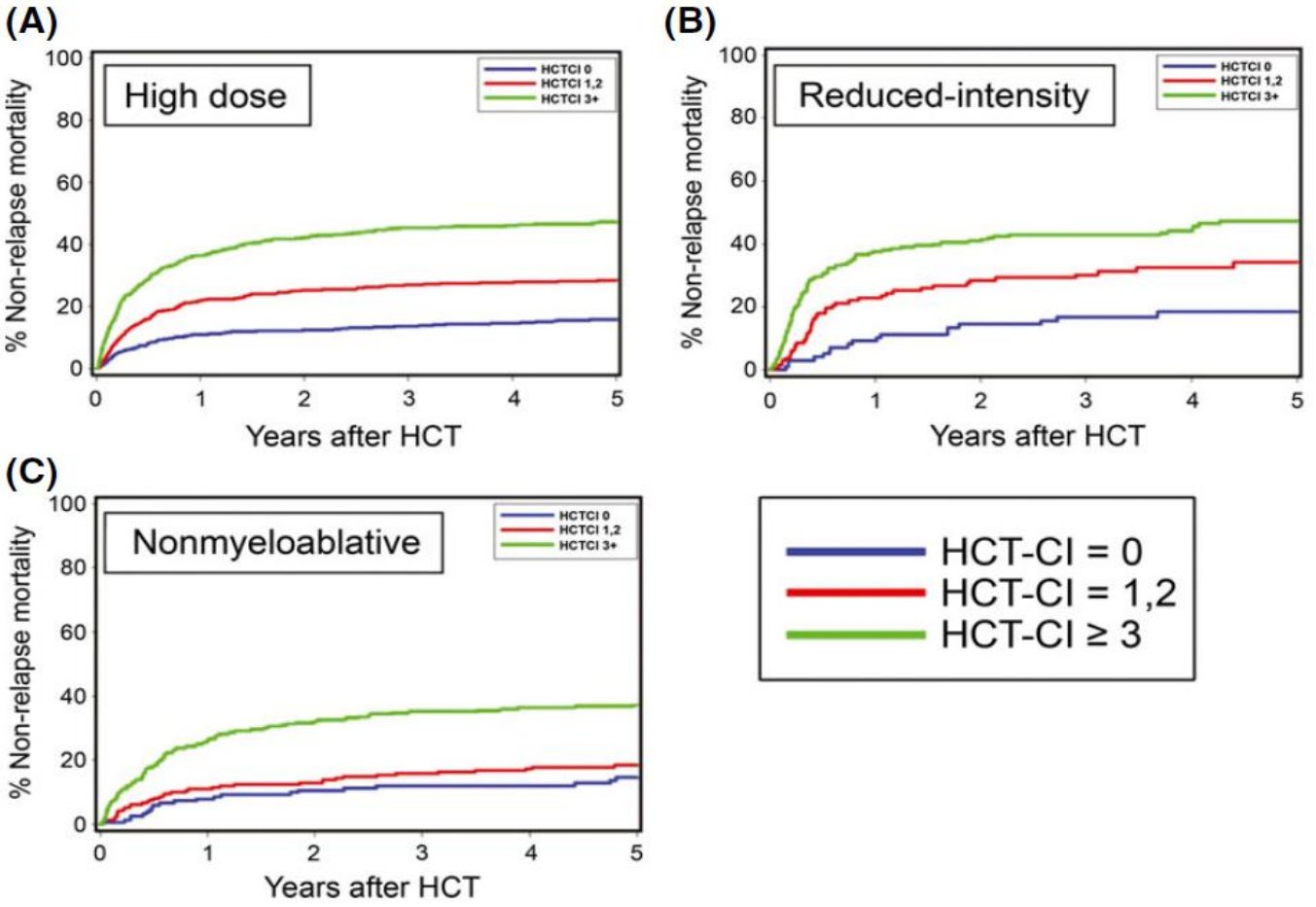
bjh BRITISH JOURNAL OF HAEMATOLOGY
2015 Aug;170(4):574-83

Multi-centre validation of the prognostic value of the haematopoietic cell transplantation - specific comorbidity index among recipient of allogeneic haematopoietic cell transplantation

Mahmoud ElSawy, Barry Storer, Michael Pulsipher, Richard Maziarz, Smita Bhatia, Michael Maris, Karen Syrjala, Paul Martin, David Maloney, Brenda Sandmaier, Rainer Storb and Mohamed Sorror

Analysis of HCT-CI within conditioning intensity groups

The stratification in risk groups is maintained also within the conditioning intensity groups, with a difference only in the NMA setting.



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Analysis of HCT-CI within age groups

	Cumulative percent incidence of NRM (2-year)				Percent overall survival (2-year)			
	HCT-CI scores				HCT-CI scores			
Age groups, years	0	1–2	≥3	*P*	0	1–2	≥3	*P*
0–19, malignant diseases	8	26	28	<0·001	73	61	41	<0·001
0–19, non-malignant diseases	NE	NE	NE		84	57	40	<0·001
20–39	11	20	39	<0·001	80	62	33	<0·001
40–49	12	26	43	<0·001	75	56	39	<0·001
50–59	21	31	39	<0·001	60	48	33	<0·001
≥60	7	27	38	<0·001	63	47	27	<0·001

The comorbidity index is also valid across the different ages

VOLUME 32 · NUMBER 29 · OCTOBER 10 2014

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Comorbidity-Age Index: A Clinical Measure of Biologic Age Before Allogeneic Hematopoietic Cell Transplantation

Mohamed L. Sorror, Rainer F. Storb, Brenda M. Sandmaier, Richard T. Maziarz, Michael A. Pulsipher, Michael B. Maris, Smita Bhatia, Fabiana Ostronoff, H. Joachim Deeg, Karen L. Syrjala, Elihu Estey, David G. Maloney, Frederick R. Appelbaum, Paul J. Martin, and Barry E. Storer

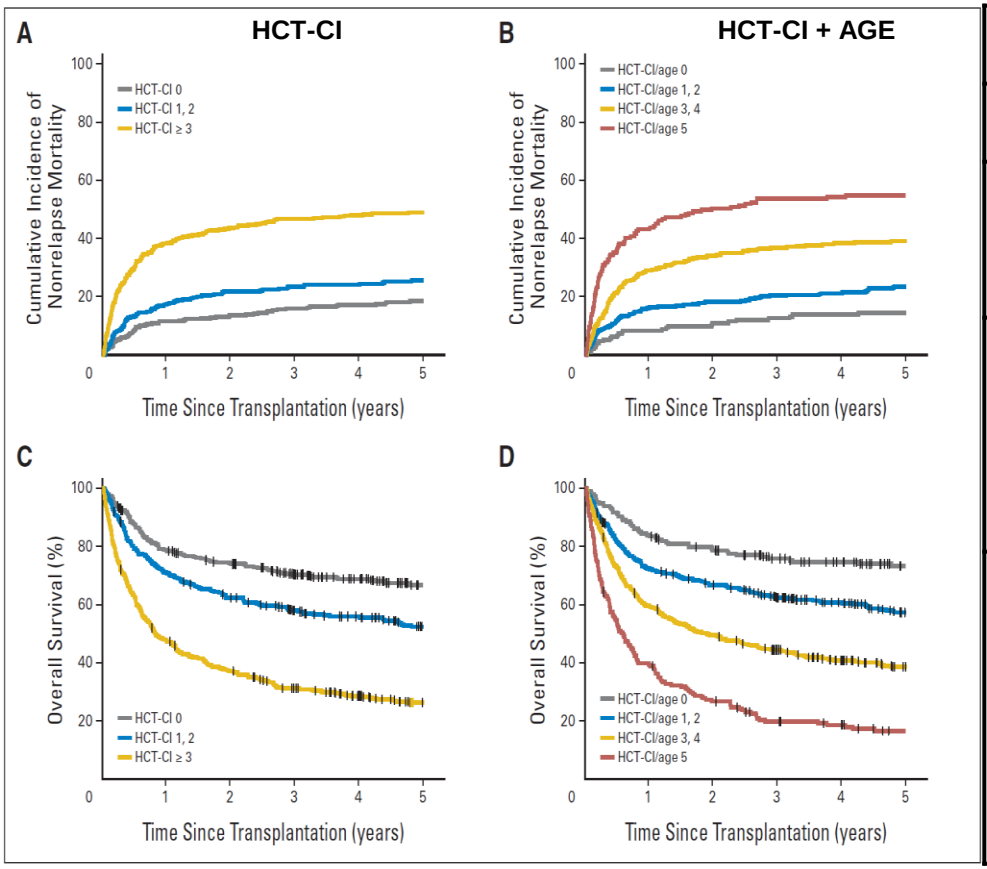
Retrospective multicenter study. Patients: 3033

The aim of this study was to incorporate the parameter "age" with the original comorbidities to obtain a more accurate index.

With the same approach used for the development of the HCT-CI, adjusted HRs for NRM were calculated for age groups.
Patients in the age ≥ 40 had HRs for NRM ranging between 1.48 and 1.84 compared with patients younger than age 20.

Age ≥ 40 was assigned a score of 1 to be added to the HCT-CI scores, to create the “composite” comorbidity/age index (HCT-CI/age).

The Composite Comorbidity/Age index:
- **has a good predictive capacity for NRM (and OS)**
- **allows integration of age among the other patient-specific conditions, without leaving it as an isolated parameter**



Validation Set			
		HR	P
Age alone	0-39	1	
	≥ 40	1.32	0.03
HCT-CI	0	1	
	1-2	1.55	0.006
	≥ 3	3.66	< 0.0001
Composite index (HCT-CI/Age)	0	1	
	1-2	1.83	0.006
	3-4	3.64	< 0.0001
	≥ 5	6.71	< 0.0001

Predictive capacity (c-statistic) for NRM
- **Age alone = 0.54**
- **HCT-CI alone = 0.64**
- **Composite index = 0.67**

Patients with a Composite index score ≥ 3 have a NRM risk 3 or even more than 6 times greater than that of patients with score 0

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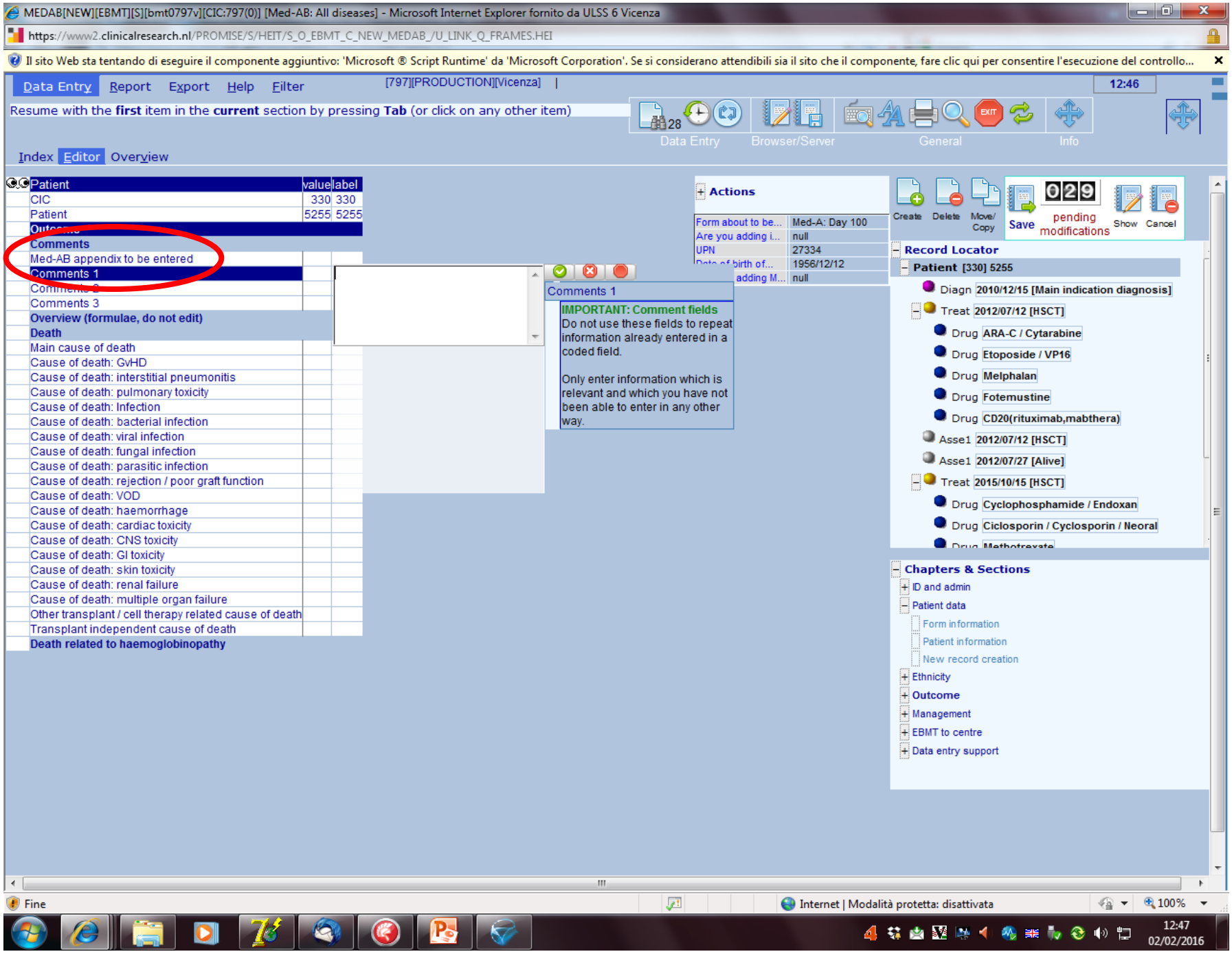
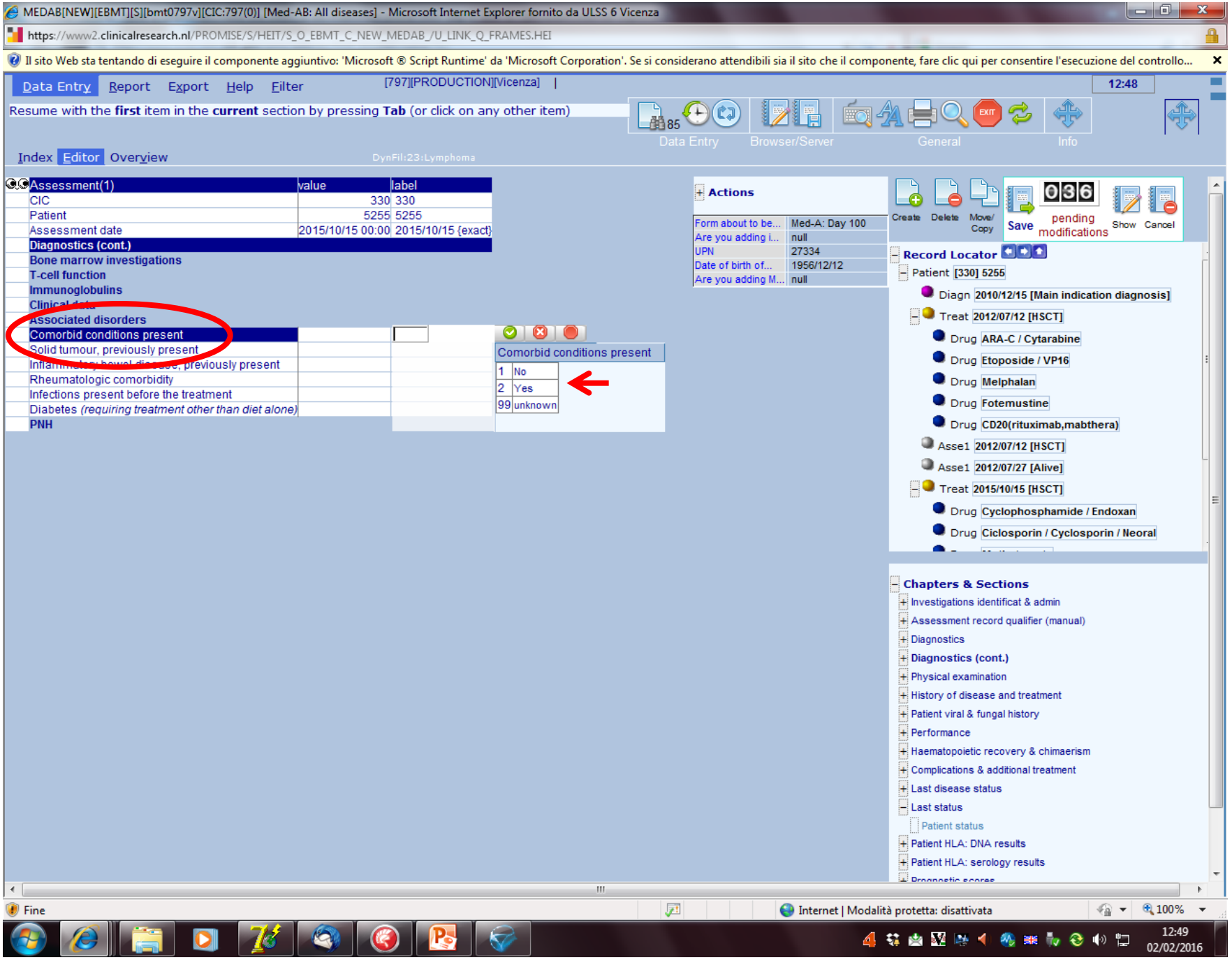
- **Where is it inserted into Promise ?**
- How can you calculate the HCT-CI ?

The HCT-CI has been integrated in Promise as an appendix of the MED-A

This is the path: Promise → MED-A → MED-A Day 0 → Appendix

The next slides demonstrate this


MEDAB[NEW][EBMT][S][bmt0797v][CIC:797(0)] [Med-AB: All diseases] - Microsoft Internet Explorer fornito da ULSS 6 Vicenza
https://www2.clinicalresearch.nl/PROMISE/S/HEIT/S_O_EBMT_C_NEW_MEDAB_/U_LINK_Q_FRAMES.HEI
Il sito Web sta tentando di eseguire il componente aggiuntivo: 'Microsoft ® Script Runtime' da 'Microsoft Corporation'. Se si considerano attendibili sia il sito che il componente, fare clic qui per consentire l'esecuzione del controllo...
Data Entry Report Export Help Filter [797][PRODUCTION][Vicenza] 12:46
Resume with the first item in the current section by pressing Tab (or click on any other item)
Data Entry Browser/Server General Info
Index Editor Overview
Patient value label
CIC 330 330
Patient 5255 5255
Comments
Med-AB appendix to be entered
Comments 1
Comments 3
Overview (formulae, do not edit)
Death
Main cause of death
Cause of death: GvHD
Cause of death: interstitial pneumonitis
Cause of death: pulmonary toxicity
Cause of death: Infection
Cause of death: bacterial infection
Cause of death: viral infection
Cause of death: fungal infection
Cause of death: parasitic infection
Cause of death: rejection / poor graft function
Cause of death: VOD
Cause of death: haemorrhage
Cause of death: cardiac toxicity
Cause of death: CNS toxicity
Cause of death: GI toxicity
Cause of death: skin toxicity
Cause of death: renal failure
Cause of death: multiple organ failure
Other transplant / cell therapy related cause of death
Transplant independent cause of death
Death related to haemoglobinopathy
Comments 1
IMPORTANT: Comment fields
Do not use these fields to repeat information already entered in a coded field.
Only enter information which is relevant and which you have not been able to enter in any other way.
Actions
Form about to be... Med-A: Day 100
Are you adding i... null
UPN 27334
1956/12/12
adding M... null
Create Delete Move/ Copy Save 029 pending modifications Show Cancel
Record Locator
Patient [330] 5255
Diagn 2010/12/15 [Main indication diagnosis]
Treat 2012/07/12 [HSCT]
Drug ARA-C / Cytarabine
Drug Etoposide / VP16
Drug Melphalan
Drug Fotemustine
Drug CD20(rituximab,mabthera)
Asse1 2012/07/12 [HSCT]
Asse1 2012/07/27 [Alive]
Treat 2015/10/15 [HSCT]
Drug Cyclophosphamide / Endoxan
Drug Ciclosporin / Cyclosporin / Neoral
Chapters & Sections
ID and admin
Patient data
Form information
Patient information
New record creation
Ethnicity
Outcome
Management
EBMT to centre
Data entry support
Fine
Internet | Modalità protetta: disattivata
100%
12:47
02/02/2016


MEDAB[NEW][EBMT][S][bmt0797v][CIC:797(0)] [Med-AB: All diseases] - Microsoft Internet Explorer fornito da ULSS 6 Vicenza
https://www2.clinicalresearch.nl/PROMISE/S/HEIT/S_O_EBMT_C_NEW_MEDAB_/U_LINK_Q_FRAMES.HEI
Il sito Web sta tentando di eseguire il componente aggiuntivo: 'Microsoft ® Script Runtime' da 'Microsoft Corporation'. Se si considerano attendibili sia il sito che il componente, fare clic qui per consentire l'esecuzione del controllo...
Data Entry Report Export Help Filter [797][PRODUCTION][Vicenza] 12:48
Resume with the first item in the current section by pressing Tab (or click on any other item)
Data Entry Browser/Server General Info
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CIC 330 330
Patient 5255 5255
Assessment date 2015/10/15 00:00 2015/10/15 {exact}
Diagnostics (cont.)
Bone marrow investigations
T-cell function
Immunoglobulins
Clinical data
Associated disorders
Comorbid conditions present
Solid tumour, previously present
Inflammatory bowel disease, previously present
Rheumatologic comorbidity
Infections present before the treatment
Diabetes (requiring treatment other than diet alone)
PNH
Comorbid conditions present
1 No
2 Yes
99 unknown
Actions
Form about to be... Med-A: Day 100
Are you adding i... null
UPN 27334
Date of birth of... 1956/12/12
Are you adding M... null
Create Delete Move/ Copy Save 036 pending modifications Show Cancel
Record Locator
Patient [330] 5255
Diagn 2010/12/15 [Main indication diagnosis]
Treat 2012/07/12 [HSCT]
Drug ARA-C / Cytarabine
Drug Etoposide / VP16
Drug Melphalan
Drug Fotemustine
Drug CD20(rituximab,mabthera)
Asse1 2012/07/12 [HSCT]
Asse1 2012/07/27 [Alive]
Treat 2015/10/15 [HSCT]
Drug Cyclophosphamide / Endoxan
Drug Ciclosporin / Cyclosporin / Neoral
Chapters & Sections
Investigations identificat & admin
Assessment record qualifier (manual)
Diagnostics
Diagnostics (cont.)
Physical examination
History of disease and treatment
Patient viral & fungal history
Performance
Haematopoietic recovery & chimaerism
Complications & additional treatment
Last disease status
Last status
Patient status
Patient HLA: DNA results
Patient HLA: serology results
Fine
Internet | Modalità protetta: disattivata
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12:49
02/02/2016

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- What is it ?
- How and why was it introduced? Why is it needed ?
- What is its clinical utility ?
- Where is it inserted into Promise ?
- **How can you calculate the HCT-CI score ?**

To calculate the final HCT-CI score is very easy, it is a simple sum and does not require a complex formula (like other risk scores).

But, to calculate exactly the HCT-CI score for that patient and to allow a correct comparision between the patients/the studies, it is essential that all the users adopt the same and the exact definitions of each comorbidity, as originally reported by Sorror.

To this end

blood **2013;121: 2854-2863**

→ **How I assess comorbidities prior to hematopoietic cell transplantation**

Mohamed L. Sorror

→ **Visit the site: http://www.hctci.org**

Some examples of definitions

Arrhythmia (score 1)

A score of 1 is assigned for any type of arrhythmia that has necessitated …… a specific antiarrhythmia treatment at any time in the patient's past medical history. ……. A score is assigned even if the patient was in normal sinus rhythm at the time of data acquisition or at the landmark date.
No score is assigned to transient arrhythmias that never required treatment.

Cerebrovascular disease (score 1)

A score of 1 is assigned for cerebrovascular disease on the basis of a prior diagnosis of transient ischemic attack, subarachnoid hemorrhage, or cerebral thrombosis, embolism, or hemorrhage at any time in the past medical history.
No details on treatment are required for assigning a score for this comorbidity.

Inflammatory bowel disease (score 1)

A score of 1 is assigned for ……a documented prior diagnosis (history of an endoscopic examination of the mucosa with or without confirmatory histology and radiologic findings) of Crohn's disease or ulcerative colitis requiring treatment at any time in the patient's past medical history. If the patient has never received a treatment of this comorbidity, no score is assigned.

Infection (score 1)

A score of 1 is assigned in the presence of 1 or more of the following:

- a documented infection

- fever of unknown origin

- pulmonary nodules suspicious for fungal pneumonia

- a positive test for tubeculosis requiring prophylaxis.

Patient must have started a specific antimicrobial treatment before the landmark date with a recommendation to continue the therapy during the days of the conditioning regimen and beyond day 0 of HCT.

Pulmonary comorbidity (2 levels of severity)

		Score 2 (moderate)	Score 3 (severe)
Pulmonary function tests	FEV1 %	66-80	≤ 65
	DLCO %	66-80	≤ 65
shortness of breath		on slight activity	at rest
the need for oxygen therapy			yes

Note: the measured DLCO value should be corrected for the concurrent hemoglobin value using the Dinakara equation.

Some questions from you

Condition	HCT-CI comorbidity ?	Answer
Pulmonary bleeding	Pulmonary	No/Yes (1)
Acute respiratory failure/intubation	Pulmonary	No/Yes (1)
Candidemia	Infection	No/Yes (2)
Clostridium difficile colitis	Infection	No/Yes (2)
Clostridium difficile colitis	Inflammatory bowel disease	No
Hydrocefalus/ Nystagmus Facial nerve palsy/Ataxia	Cerebrovascular disease	No

(1) Yes only if there are FEV1/DLCO reduction or shortness of breath or need for oxygen supplementation as assessed during a clinic visit within the immediate period of 2 - 4 weeks before the landmark date.

(2) Yes if it requires therapy (not the standard prophylaxis that almost all patients do) to continue before, during and after the conditioning regimen.

Renal comorbidity (score 2)

It is assigned in the presence of 1 or more of the following 3 clinical presentations:

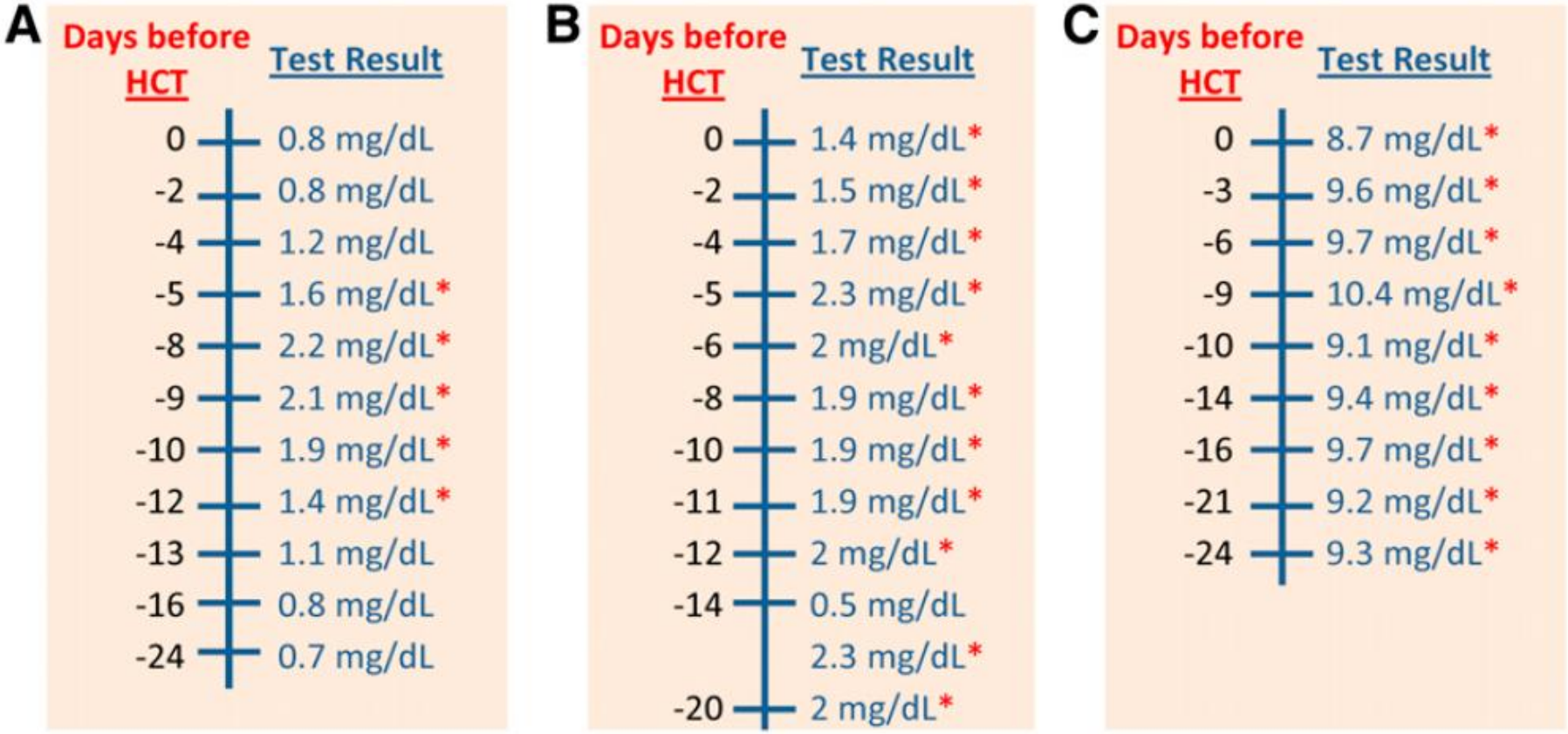
1. elevated values of serum creatinine to more than 2 mg/dL (or more than 176.8 mmol/L) as detected in at least 2 laboratory tests on 2 different days within a period extending between days – 24 and – 10 before HCT (this evaluation period could be extended to span between days – 40 and – 10 if serum creatinine was evaluated only once between days – 24 and – 10 before HCT)

2. chronic renal disease requiring weekly dialysis within the instantaneous period of 4 weeks before the landmark date

3. a documented prior history of renal transplantation at any point in the patient's past medical history.

Renal comorbidity - Creatinine

(here the only values considered are those between day – 24 and day – 10)

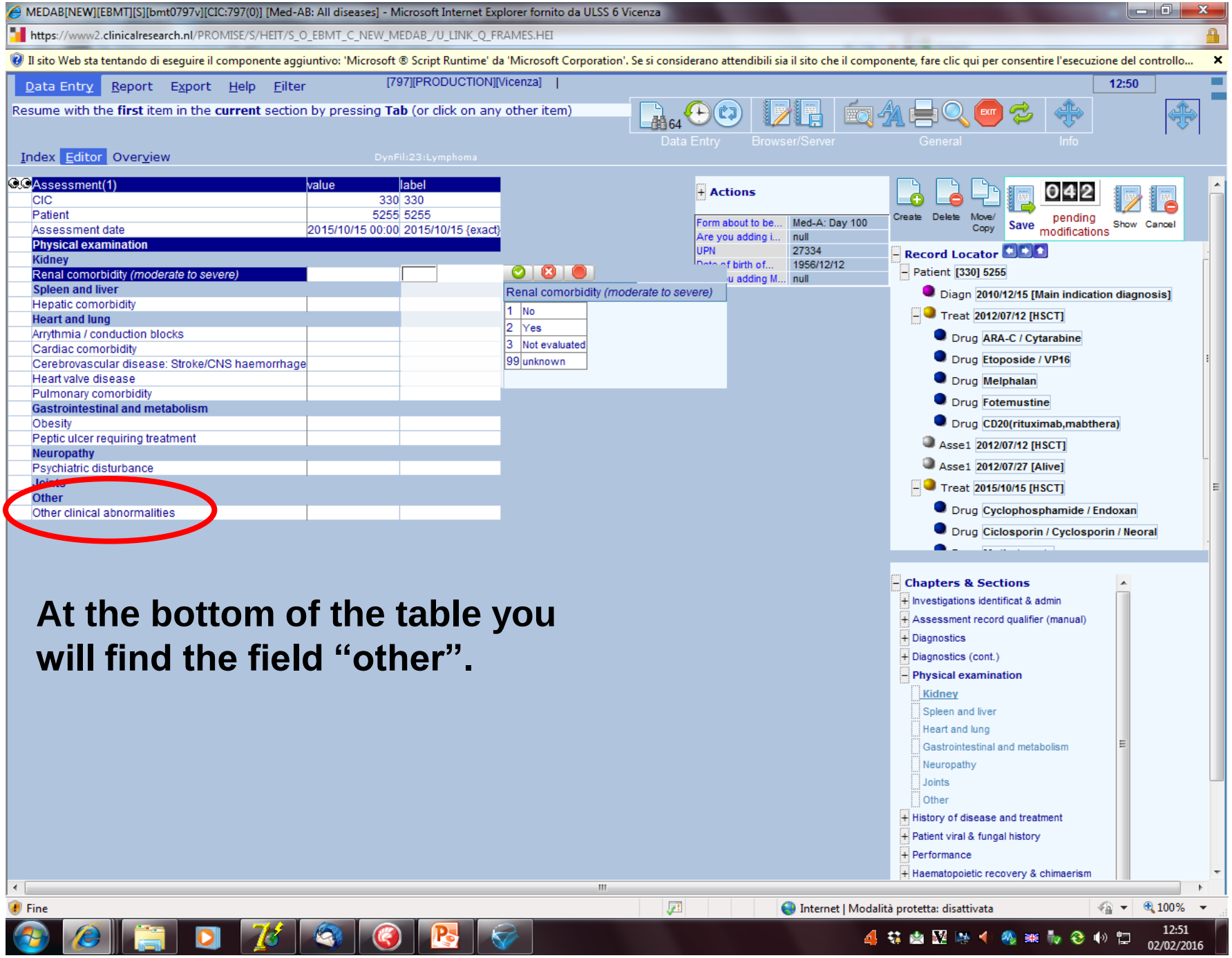


should this comorbidity be scored?

no
(no value is more than 2 mg in the time period)

no
(only 1 value is more than 2 mg in the time period)

yes



At the bottom of the table you will find the field “other”.

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Mohamed Sorror, Brent Logan, Xiaochun Zhu, J. Douglas Rizzo, Kenneth Cooke, Philip McCarthy, Vincent Ho, Mary Horowitz, Marcelo Pasquini,

In a recent paper Sorror and Colleagues have analized these "other conditions" and found that the presence of other comorbidities did not induce any significant change in the performance of the original score.

Overall, 11% of the samples within each of the 3 risk groups were reported as having other comorbidities that did not acquire a score per the HCT-CI.

Patients with an HCT-CI score of 0 but with any "other comorbidity" reported in the free text field were analyzed as a separate risk group and it was found that this group had no different outcomes compared with patients with score 0 alone.

The Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI)

Some uses

- **The HCT-CI score is often one of the inclusion/exclusion criteria for the eligibility of a patient to enter in a clinical study.**
- **It is often requested by the referee of a submitted paper.**
- **The Center for International Blood and Marrow Transplantation Research (CIBMTR) has incorporated comorbidities and other variables into Centre-Outcome Analyses designed to compare outcomes across transplant centres and to provide this information to patients, insurance companies and academic investigators.**
- **The HCT-CI has been incorporated in some decision processes to evaluate the risk/benefit ratio and the eligibility of a patient for the transplant.**

Expert Rev. Hematol. 6(5), 547–562 (2013)

EXPERT REVIEWS

Risk assessment before allogeneic hematopoietic cell transplantation for older adults with acute myeloid leukemia

Mohamed L Sorror and Frederick R Appelbaum*

Box 1. Risk-benefit ratio system for eligibility, ineligibility and risk-categorization of allogeneic hematopoietic cell transplantation as a treatment option for older patients with acute myeloid leukemia.

Category 1: Too good for early HCT
First CR; plus either:
- inv(16), t(16;16) or t(8;21) together with c-kit$^-$
- Normal cytogenetics together with NPM$^+$ Flt3$^-$ or CEBPA gene mutation

Category 2: Good-risk transplant candidates
Age <76 years
HCT-CI scores of 0
KPS scores of 90–100%
Favorable socioeconomic factors: high income and education levels and good social support
First CR; plus
- Normal cytogenetics together with NPM$^-$ Flt3$^+$ or without CEBPA gene mutation

Second CR; plus
- inv(16), t(16;16) or t(8;21)
- Normal cytogenetics together with NPM$^+$ Flt3$^-$ or CEBPA gene mutation

Reduced-intensity conditioning regimens
HLA-identical sibling donor

Category 3: Intermediate-risk transplant candidates
Age <76 years
HCT-CI scores of 1–2
KPS scores of 80–85%
Intermediate-risk socioeconomic factors: moderate income, education levels and social support
First CR; plus
- Adverse cytogenetics

Second or higher CR; plus
- Normal cytogenetics together with NPM$^-$ Flt3$^+$ or without CEBPA gene mutation

Non-myeloablative or reduced-intensity conditioning regimens
HLA-8/8 allele matched or single antigen or allele mismatched unrelated donor

Category 4: High-risk transplant candidates
Age <76 years
HCT-CI scores of 3–7
KPS scores of 60–70%
Poor-risk socioeconomic factors: low income, education levels and social support
Not in CR
Unfavorable or complex cytogenetics
Monosomal karyotype
Short duration between first CR and relapse
Reduced-intensity conditioning regimens
No available HLA-matched related or unrelated donors: UCB, single antigen HLA-mismatched, or HLA-haploidentical donor is available

Category 5: Non-transplant candidates[†]
Age >75 years
HCT-CI scores of ≥8 and/or major organ dysfunction (decompensated liver cirrhosis, decompensated heart failure with low survival probabilities, active severe infection, or pulmonary function tests <40% normal), or another malignancy or major illness with limited survival chances
- KPS scores of 50%
- Extremely poor-risk socioeconomic factors: no income or very limited education, no social support
- Behavioral issues: lack of compliance in past medical history, persistent or frequent use of drugs after diagnosis with cancer, and anger or high-risk behaviors with medical teams

Rapidly progressive or refractory disease after induction failure
Complex cytogenetics plus monosomal karyotype
Lack of a suitable donor

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The European LeukemiaNet AML Working Party consensus statement on allogeneic HSCT for patients with AML in remission: an integrated-risk adapted approach

Jan J. Cornelissen, Alois Gratwohl, Richard F. Schlenk, Jorge Sierra, Martin Bornhäuser, Gunnar Juliusson, Zdenek Råcil, Jacob M. Rowe, Nigel Russell, Mohamad Mohty, Bob Löwenberg, Gerard Socié, Dietger Niederwieser and Gert J. Ossenkoppele

Table 4 | Recommendations for allogeneic HSCT in patients with AML in their first complete remission based on integrated-risk profiles*

AML risk group‡	AML risk assessment§	Risk of relapse following consolidation approach		Prognostic scores for nonrelapse mortality that would indicate allogeneic HSCT as preferred consolidation		
		Chemotherapy or autologous HSCT (%)	Allogeneic HSCT (%)	EBMT score	HCT–CI score	Nonrelapse mortality risk (%)
Good	t(8;21) with WBC ≤20 Inv(16)/t(16;16) Mutated *CEBPA* (double allelic) Mutated NPM1 (No *FLT3*–ITD mutation) Early first complete remission and no MRD	35–40	15–20	NA (≤1)	NA (<1)	10–15
Intermediate	T(8;21) with WBC >20 Cytogenetically normal (or with loss of X and Y chromosomes), WBC count ≤100 and early first complete remission (after first cycle of chemotherapy)	50–55	20–25	≤2	≤2	<20–25
Poor	Otherwise good or intermediate, but no complete remission after first cycle of chemotherapy Cytogenetically normal and WBC >100 Cytogenetically abnormal	70–80	30–40	≤3–4	≤3–4	<30
Very poor	Monosomal karyotype Abn3q26 Enhanced Evi-1 expression	>90	40–50	≤5	≤5	<40

Conclusions (I)

The comorbidity index HCT-CI:

- **has confirmed its validity in predicting NRM and OS among recipients of allogeneic (and autologous) HSCT as an independent variable across ages, conditioning regimen intensity, and diagnosis. Increasing HCT-CI scores are associated with increased risks for NRM and reduced survival.**

- **at the moment it is the best tool we have to assess the "frailty" of a patient. The "composite score" has certainly a better predictive capacity than the chronological age alone.**

- **allows to group the patient's comorbidities and evaluate them for the benefit/risk assessment together with other characteristics of the transplant procedure.**
  The NRM risk calculated by the HCT-CI needs however to be always weighed with the relapse risk of the disease.

Conclusions (II)

The comorbidity index HCT-CI:

- **permits to discuss with the patient in a more personalized manner during the counseling process.**

- **permits to compare clinical trials at different institutions. It is necessary therefore that the original definitions of the comorbidities are respected.**

The future probably will offer wider possibilities to personalize the transplant procedure, and a tool like the HCT-CI, of course updated and supplemented with other new parameters, could help us to better evaluate the patient and to choose the best therapeutic strategy for them.

Thank you for your attention