SoFOG
SOCIÉTÉ FRANCOPHONE D'ONCO-GÉRIATRIE

DIALOG
Gerico · Ucog

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Comment adhérer à un programme de recherche avec consentement en cas de troubles cognitifs

O. Le Saux

Conflits d’intérêt

- Frais personnels : Novartis, Lilly, MSD et Astrazeneca
- Subventions de recherche : Novartis, Fondation Hospira-Pfizer et Astellas

Introduction

Les patients inclus ont en moyenne 6.5 ans de moins que la population générale cancérologique

	Phase I (n=27)	Phase II (n=193)	Phase III (n=40)	P-value
CGA, n (%)	0 (0)	17 (9)	3 (8)	0.31
Components of CGA, n (%)				
Nutritional assessment	2 (7)	21 (11)	8 (20)	0.21
Cognitive assessment	1 (4)	14 (7)	5 (13)	0.42
Functional assessment	1 (4)	22 (11)	5 (13)	0.50
Psychiatric assessment	0 (0)	11 (6)	2 (5)	0.56
Functional status	18 (67)	152 (79)	30 (75)	0.34
Social assessment	0 (0)	10 (5)	1 (2)	0.67
Comorbidity assessment	1 (4)	59 (31)	14 (35)	0.0036
Overmedication	0 (0)	5 (3)	1 (2)	1
Comedication	1 (4)	7 (4)	2 (5)	0.87
Geriatric syndrome	0 (0)	8 (4)	1 (3)	0.85
G8	0 (0)	9 (5)	4 (10)	0.32
Any geriatric score*	0 (0)	18 (9)	5 (13)	0.16

Abbasi J et al. JAMA 2019; Le Saux et al. Oncologist 2019

Introduction

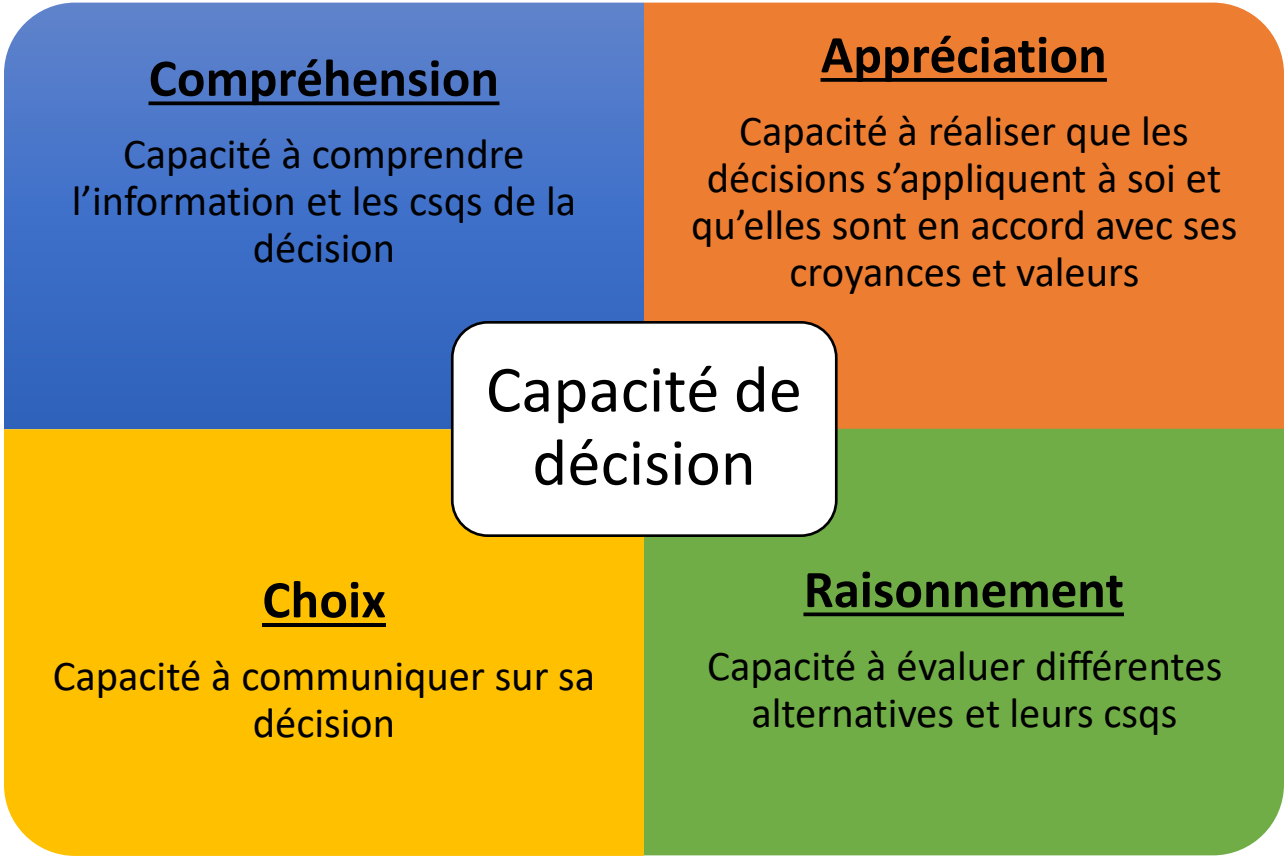
- « Capacity » : capacité de prendre une décision
- « Competency » : capacité déterminée de manière légale

- L'objectif du médecin : « Capacity »
  - À comprendre
  - Prendre une décision
  - Assumer la responsabilité des conséquences de la décision
- Nécessaire pour un consentement éclairé VALIDE

- A évaluer à un temps précis
- Attention aux causes réversibles (médicaments, syndrome confusionnel, infections, déficit sensoriel…)

Introduction

- ≠ Cognition
  - La capacité, bien que dépendante de la cognition, n’est pas la même chose que la cognition.
  - Les patients atteints de démence légère à modérée peuvent évaluer, interpréter et tirer un sens de leur vie.
- ≠ Activités fonctionnelles
  - Une personne incapable d'accomplir une tâche peut être capable de décider qui peut l'aider à l'accomplir.


Compréhension
Capacité à comprendre l'information et les csqs de la décision
Appréciation
Capacité à réaliser que les décisions s'appliquent à soi et qu'elles sont en accord avec ses croyances et valeurs
Capacité de décision
Choix
Capacité à communiquer sur sa décision
Raisonnement
Capacité à évaluer différentes alternatives et leurs csqs

Introduction

- Capacités de décision altérées dans 44 à 69% des résidents des maisons de retraite
- Marson et al. ont constaté que presque tous les patients atteints de la maladie d'Alzheimer légère à modérée présentaient des troubles quant à la prise de décision (compréhension+++), mais appréciation / raisonnement et choix préservés.
- Les patients atteints de démence frontotemporale peuvent avoir de bons résultats aux tests neuropsychologiques classiques, mais leur jugement et leur prise de décision sont altérés.

Pruchno et al. Gerontologist; Royall Exp Aging Res; Marson et al. Arch Neurol; Manes et al. Dement Geriatr Cogn Disord.

Pourquoi et comment l'évaluer ?

- Consentement à la recherche = prérequis pour garantir les intérêts des participants
- L'évaluation des risques et la balance B/R est essentielle

- Alternatives :
  - Décision par un « surrogate » mais possible manque de connaissances des envies du patient, sentiment de culpabilité ou stress à prendre la décision
  - Directives anticipées…

Le MMSE de Folstein est-il utile ?

Comparaison au MacCAT-CR (référence)

37 patients AD

Age:78.7±5.8 (moy±SD)

Score MMSE:22.9±3.8 (range:16-28)

Spécificité 85-90%

Sensibilité sup à 90%

Sensitivity and specificity of the Mini Mental State Examination in identifying, according to four standards, the capacity status of 37 persons with mild to moderate Alzheimer's disease[a]

MMSE cutoff score	Understanding (capable, N=20; incapable, N=17)[b]		Appreciation (capable, N=17; incapable, N=20)[b]		Reasoning (capable, N=24; incapable, N=13)[b]		Combined standard (capable, N=14; incapable, N=23)[b]	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
16	5.9	100	5.0	100	7.7	100	4.3	100
17	29.4	100	25.0	100	30.8	95.8	21.7	100
18	35.3	100	30.0	100	38.5	95.8	26.1	100
19	41.2	85.0	45.0	94.1	53.8	89.5	39.1	92.9
21	52.9	70.0	50.0	70.6	61.5	70.8	47.8	71.4
22	64.7	65.0	60.0	64.7	76.9	66.7	60.9	71.4
23	70.6	65.0	65.0	64.7	76.9	62.5	65.2	71.4
25	82.4	60.0	80.0	64.7	92.3	58.3	78.3	71.4
26	94.1	30.0	95.0	35.3	100	29.2	91.3	35.7
27	100	15.0	95.0	11.8	100	12.5	95.7	14.3
28	100	0	100	0	100	0	100	0

Kim et al. *Psychiatr Serv*.

Le MMSE de Folstein est-il utile ?

- Sur 51 Veterans residents
- MMSE score = 22.4 +/- 6.9
- Méthode des vignettes: 33.3% ont des CD intactes
- VS 77% par leur médecin

Fitten et al. *J Am Geriatr Soc*.[10]

Outils d’évaluation

- **MacCAT-CR** : la référence
- **Quality of Informed Consent**

MacCAT-CR

= Mac Arthur Competence Assessment Tool-Clinical Research

Questionnaire semi-structurée
Durée de passation 15-30'
21 items, échelle à 3 points de 0 à 2, (inadéquat, partiellement adéquat, ou adéquat)

Un score faible à n'importe lequel des 4 domaines suffit à mettre en doute la CD

Decision-Making Capacity Domains (Possible Score for Each Item)

UNDERSTANDING (total possible score = 26)

The subject understands that:
- —the purpose of the study is to test the effectiveness of a case-management intervention (2)
- —the study lasts 1 year (2)
- —the study requires 2 additional procedures (2 questions) (4)
- —the effectiveness of the intervention is unknown (2)
- —not all subjects will receive the intervention (2)
- —subjects who do not receive the intervention must complete surveys and undergo health evaluations (2)
- —the intervention will be assigned at random (2)
- —the study results will benefit future patients (2)
- —subjects in the study may benefit (2)
- —the study imposes 2 additional burdens (2 questions) (4)
- —subjects can refuse to participate or can withdraw from the study without penalty (2)

APPRECIATION (total possible score = 6)
The subject appreciates that he/she:
- —would not be asked to be in the study solely for his/her personal benefit (2)
- —would not be assigned to receive the intervention or not based on his/her needs (2)
- —can refuse to participate or can withdraw from the study without penalty (2)

REASONING (total possible score = 8)
The subject is able to:
- —describe 2 reasonable consequences of participating in the study (2)
- —compare the merits of participating vs. not participating (2)
- —give 2 examples of the impact of participating on his/her everyday life (2)
- —express a choice that is consistent with the consequences that he/she has described (2)

CHOICE (total possible score = 2)
The subject is able to express a choice about whether or not to enroll (2)

MAIS
pas de seuil objectif
nécessite une formation

Validé pour AD, cancéro

QIC

- 35 questions
- **Partie A = Mesure objective de leur compréhension de l'essai clinique**
- Réponses sur une échelle à 3 points « agree » / « disagree » / « unsure ».
- Pour éviter les biais : direction de la réponse varie
- Questions génériques en majorité
  - Exemple : "If I had not wanted to participate in this clinical trial, I could have declined to sign the consent form." => Réponse : Agree
- D'autres sont phase-spécifiques.
  - Exemple : "In my clinical trial, one of the researchers' major purposes is to find the highest dose of a new drug or treatment that can be given without causing severe side effects" => essais de phase I.

APPENDIX: QUALITY OF INFORMED CONSENT (QuIC), PART A

INSTRUCTIONS: Below you will find several statements about cancer clinical trials (otherwise known as cancer research studies). Thinking about your clinical trial, please read each statement carefully. Then tell us whether you agree with the statement, you disagree with the statement, or you are unsure about the statement by circling the appropriate response. Please respond to each statement as best you can. We are interested in your opinions.

A1.	When I signed the consent form for my current cancer therapy, I knew that I was agreeing to participate in a clinical trial.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A2.	The main reason cancer clinical trials are done is to improve the treatment of future cancer patients.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A3.	I have been informed how long my participation in this clinical trial is likely to last.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A4.	All the treatments and procedures in my clinical trial are standard for my type of cancer.	Disagree$_1$*	Unsure$_2$	Agree$_3$
A5.	In my clinical trial, one of the researchers' major purposes is to compare the effects (good and bad) of two or more different ways of treating patients with my type of cancer, in order to see which is better.†	Disagree$_1$	Unsure$_2$	Agree$_3$*
A6.	In my clinical trial, one of the researchers' major purposes is to test the safety of a new drug or treatment.‡	Disagree$_1$	Unsure$_2$	Agree$_3$*
A7.	In my clinical trial, one of the researchers' major purposes is to find the highest dose of a new drug or treatment that can be given without causing severe side effects.‡	Disagree$_1$	Unsure$_2$	Agree$_3$*
A8.	In my clinical trial, one of the researchers' major purposes is to find out what effects (good and bad) a new treatment has on me and my cancer.§	Disagree$_1$	Unsure$_2$	Agree$_3$*
A9.	The treatment being researched in my clinical trial has been proven to be the best treatment for my type of cancer.	Disagree$_1$*	Unsure$_2$	Agree$_3$
A10.	In my clinical trial, each group of patients receives a higher dose of the treatment than the group before, until some patients have serious side effects.	Disagree$_1$**	Unsure$_2$	Agree$_3$††
A11.	After I agreed to participate in my clinical trial, my treatment was chosen randomly (by chance) from two or more possibilities.	Disagree$_1$‡‡	Unsure$_2$	Agree$_3$§§
A12.	Compared with standard treatments for my type of cancer, my clinical trial does not carry any additional risks or discomforts.	Disagree$_1$*	Unsure$_2$	Agree$_3$
A13.	There may not be direct medical benefit to me from my participation in this clinical trial.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A14.	By participating in this clinical trial, I am helping the researchers learn information that may benefit future cancer patients.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A15.	Because I am participating in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care could review my medical records.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A16.	My doctors did not offer me any alternatives besides treatment in this clinical trial.	Disagree$_1$*	Unsure$_2$	Agree$_3$
A17.	The consent form I signed describes who will pay for treatment if I am injured or become ill as a result of participation in this clinical trial.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A18.	The consent form I signed lists the name of the person (or persons) whom I should contact if I have any questions or concerns about the clinical trial.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A19.	If I had not wanted to participate in this clinical trial, I could have declined to sign the consent form.	Disagree$_1$	Unsure$_2$	Agree$_3$*
A20.	I will have to remain in the clinical trial even if I decide someday that I want to withdraw.	Disagree$_1$*	Unsure$_2$	Agree$_3$

QIC

* Correct answer

† Scored for phase III subjects only

‡ Scored for phase I subjects only

§ Scored for phase II subjects only

** Correct answer for patients on phase II and III trials

†† Correct answer for patients on phase I trials

‡‡ Correct answer for patients on phase I and II trials

§§ Correct answer for patients on phase III trials

QIC

- **Partie B = Mesure subjective de leur compréhension de l'essai clinique**
- 15 questions pour mesurer le niveau de compréhension
- Échelle de Likert sur 5 points
  - Exemples : "When you signed the consent form to participate in your clinical trial . . . how well did you understand the treatments and procedures you will undergo"?

APPENDIX: QUALITY OF INFORMED CONSENT (QuIC), PART B

When you signed the consent form to participate in your clinical trial, how well did you understand the following aspects of your clinical trial? *If you didn't understand the item at all, please circle 1. If you understood it very well, please circle 5. If you understand it somewhat, please circle a number between 1 and 5.*

	I Didn't Understand This at All	⇒			I Understood This Very Well
B1. The fact that your treatment involves research	1	2	3	4	5
B2. What the researchers are trying to find out in the clinical trial	1	2	3	4	5
B3. How long you will be in the clinical trial	1	2	3	4	5
B4. The treatments and procedures you will undergo	1	2	3	4	5
B5. Which of these treatments and procedures are experimental	1	2	3	4	5
B6. The possible risks and discomforts of participating in the clinical trial	1	2	3	4	5
B7. The possible benefits to you of participating in the clinical trial	1	2	3	4	5
B8. How your participation in this clinical trial may benefit future patients	1	2	3	4	5
B9. The alternatives to participation in the clinical trial	1	2	3	4	5
B10. The effect of the clinical trial on the confidentiality of your medical records	1	2	3	4	5
B11. Who will pay for treatment if you are injured or become ill because of participation in this clinical trial	1	2	3	4	5
B12. Whom you should contact if you have questions or concerns about the clinical trial	1	2	3	4	5
B13. The fact that participation in the clinical trial is voluntary	1	2	3	4	5
B14. Overall, how well did you understand your clinical trial when you signed the consent form?	1	2	3	4	5

Auto-questionnaire

N'évalue que la compréhension

Pas de seuil

Validé en cancéro

En conclusion

- Zone grise pour des MMSE entre 20 et 26
- Utiliser le QIC ? Mais plutôt un outil d’audit
- Personne de confiance / directives anticipées

Merci de votre attention

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