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Original Research

Intrinsic Capacity Defined Using Four Domains and Mortality Risk: A 5-Year Follow-Up of the SarcoPhAge Cohort

M. Locquet, D. Sanchez-Rodriguez, O. Bruyère, A. Geerinck, L. Lengelé, J.-Y. Reginster, C. Beaudart

WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, CHU—Sart Tilman, Quartier Hôpital, Avenue Hippocrate 13 (Bât. B23), 4000 Liège, Belgium

Corresponding Author: Médéa Locquet, M.Sc., PhD, CHU de Liège, Avenue Hippocrate 13, 4000 Liège, Belgium, 003243662519, medea.locquet@gmail.com

Abstract

OBJECTIVES: The concept of 'intrinsic capacity' (IC) offers a new way to approach another concept, that of 'healthy aging'. The first objective of the present study was to assess the ability of the construct of 'intrinsic capacity' to predict death. The second objective was to assess whether deteriorations in intrinsic capacity, measured over 1 and 2 years, are predictive of death.

DESIGN: The present analysis was based on a prospective cohort study.

SETTING: Community-dwelling participants.

PARTICIPANTS: The study recruited older adults aged 65 years and older.

MEASUREMENTS: Intrinsic capacity (IC) encompasses five domains: sensorial (not evaluated here), cognition (Mini-Mental State Examination), nutrition (Mini-Nutritional Assessment), mobility (Short Physical Performance Battery), and psychological (Geriatric Depression Scale). Each domain was considered satisfactory when its assessment, for an individual, was above the threshold defined by the initial validation of the domain assessment tool. To explore the relationship between IC and mortality risk, a Cox model was applied. The predictive value of the dynamic aspects (i.e., changes over 1 year and 2 years) was investigated using the following categorization of IC: stable, deteriorated, improved.

RESULTS: The sample was composed of 481 volunteers aged 73.4±6.12 years (60.1% women). Two satisfactory IC domains appeared to be significantly associated with reduced mortality risk: the satisfactory mobility domain (adjusted HR=0.45 [0.26-0.79]) and the satisfactory psychological domain (adjusted HR = 0.56 [1.04-3.09]). When considering intrinsic capacity as a whole construct, using a composite Z-score, we noticed that the risk of death was decreased by 49% for an increase of 1 standard deviation in IC. Changes in intrinsic capacity in the mobility and psychological domains led to an increased risk of death (from 2.74 to 4.18-fold).

CONCLUSION: The concept of intrinsic capacity seems highly relevant in order to assess older adults' health and well-being. This concept should be considered for integration into clinical practice.

Key words: Healthy Ageing, World Health Organization, epidemiology.

Introduction

Intrinsic capacity (IC), a new concept for assessing mental and physical functioning, was recently launched by the World Health Organization (WHO) in its World Report on Aging and Health as a strategy towards healthy aging (1). IC, a multidimensional indicator, is defined as "the composite of all the physical and mental capacities of an individual". This concept searches to shift focus from the negative approach of disability to a positive approach of capacity. IC encompasses five domains of functioning: cognition, vitality (including energy/metabolism aspects), sensory, locomotion, and psychosocial (2).

The WHO encourages efforts worldwide aligned with their Healthy Ageing program, and has published guidelines on integrated care for older people (ICOPE), detailing community-level interventions to manage declines in IC (3). The WHO proposes a paradigm shift in care priorities for older people, away from episodic needs (diseases, frailty, disability...) and towards care trajectories that focus on the preservation of physical and mental capacity in the long-term (4, 5).

Evidence of the association of each individual domain of IC and health outcomes is accumulating (2, 6–8), and IC has recently been applied in a nursing home population, where a reduced IC was associated with a higher risk of mortality during its 3-year follow-up (9). Before adopting the positive approach of IC of the WHO guidelines, it seems crucial to statistically investigate the relationship between a satisfactory IC and its potential consequences on the reduction of the occurrence of health adverse outcomes and confirm that the new construct is meaningful (10), particularly in community-dwelling older people, which is the target population of the WHO guidelines.

The WHO has suggested that the concept of IC should be considered a dynamic construct, evolving over time (11). This means that the course of a patient's IC (i.e., its trajectory over time: a decline, an improvement, or a stabilization) should be monitored by clinicians and researchers, at the individual level but also for populations (12).

Based on these observations, we hypothesize that: 1) A satisfactory IC (as a whole construct) at baseline is associated with a reduced risk of mortality in community-dwelling older people over 5 years of follow-up; 2) The five domains represented in the concept of IC provide a different predictive value for the association of IC with mortality; 3) IC is a dynamic condition and a decrease in IC from baseline to the first year of follow-up, as well as from baseline to the second year of follow-up, is proportionally associated to a higher risk of mortality at the end of the 5-year follow-up period.

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Methods

Design

The present article presents the results of a post-hoc analysis of a prospective population-based cohort, part of the SarcoPhAge study, which included 534 older adults in Belgium who were seen annually from 2013 to 2019. A detailed description of the procedures and data collection in the SarcoPhAge study has been previously published (8, 13).

Population

The population consisted of community-dwelling healthy volunteers, 65 years of age or older. Participants with a body mass index (BMI) ≥50 kg/m^2 or an amputated limb were excluded.

Intrinsic capacity

Four domains of IC were evaluated in this study: cognition, nutrition, mobility, and psychosocial. We were unable to evaluate the sensory domain due to a lack of available data. The four domains were assessed using the following procedures, and thresholds were established according to previous literature:

- Cognitive domain: The Mini-Mental State Examination (MMSE) (14) has been used to assess cognitive function, and considered satisfactory when >26 points (out of a maximum of 30 points) (15).
- Nutritional domain: The Mini-Nutritional Assessment (MNA) (16) has been administered. A score higher than 17 points (maximum 30 points) indicates no risk of malnutrition, and consequently a satisfactory nutritional domain.
- Mobility domain: The Short Physical Performance Battery (SPPB) test, scored on a maximum of 12 points (17, 18) has been used. A score > 8 points indicates the absence of mobility-related disability (19), thus a satisfactory mobility domain.
- Psychological domain: The Geriatric Depression Scale (GDS), composed of 15 items, has been employed to evaluate this domain. A score of <5 points indicates the absence of depression and was thus considered satisfactory in this study (a score comprised between 12 and 15 indicates severe depression, between 9 and 11 indicates moderate depression, between 5 and 8 indicates mild depression, and between 0 and 4 indicates normal functioning) (20).

Most of the thresholds have been based on what was proposed as satisfactory cutoffs during the initial validations of the tools (for the MNA, the GDS, and the SPPB) while the MMSE satisfactory threshold has been defined according to more recent literature.

Unfortunately, the sensorial domain was not assessed in our study. Our analysis focused on the four domains separately (i.e., 4 dichotomous variables) but also on the IC as a whole, by combining the values obtained in the four domains. For this summary score, representing IC, we calculated Z-scores (which are the distance to our studied population mean expressed in standard deviations). The Z-score can be interpreted as follow: a positive z-score indicates that the raw score of the individual is higher than the mean. A negative Z-score indicates that the raw score of the individual is below the mean. The z-score indicates the number of standard deviations by which the individual's raw score deviates from the population mean. In this study, we first calculated z-scores for each of the four domains and then calculated a composite Z-score that is the sum of the four domains Z-scores divided by four. This methodology places each of the four domains on the same scale before calculating a summary measure. Cognitive, nutritional and mobility domains were identically weighted, with higher scores indicating improvement on this domain. The psychosocial domain was negatively weighted, with higher scores indicating a deterioration.

The dynamic nature of the IC concept was investigated as follows:

- Evolution of each of the four IC domains separately (stable, deteriorated, improved) between baseline (T0) and 1 year of follow-up (T1). We consider the evolution as stable when the individual presented a not satisfactory domain at T0 and at T1 or a satisfactory domain at T0 and at T1. The evolution was considered deteriorated when the individual had a satisfactory domain at T0 but had a not satisfactory domain at T1. Finally, the evolution was considered as improved when the individual presented a not satisfactory domain at T0 and a satisfactory domain at T1.
- Evolution of each of the four IC domains separately (stable, deteriorated, improved) between baseline (T0) and the 2nd year of follow-up (T2). We consider the evolution as stable when the individual presented a not satisfactory domain at T0 and at T2 or a satisfactory domain at T0 and at T2. The evolution was considered deteriorated when the individual had a satisfactory domain at T0 but had a not satisfactory domain at T2. Finally, the evolution was considered as improved when the individual presented a not satisfactory domain at T0 but no longer at T2.

Outcome measure

The main outcome measure was the mortality risk in individuals with satisfactory IC or without satisfactory IC. Regarding the dynamic evolution at baseline during the 5-year follow-up, comparison of individuals with without satisfactory IC or satisfactory IC were also performed. Mortality was collected annually by interview or phone call to the relatives of the participants of the SarcoPhAge study and confirmed by the medical record. The date of death was also recorded.

General characteristics of the population and covariates

The following demographic and clinical characteristics were used to describe the population:

- Age: employed as a covariate because known to significantly

impact mortality risk.
- Sex, employed as a covariate because known to significantly impact mortality risk.
- Body mass index (BMI); calculated as height divided by weight-squared (kg/m^2).
- Number of concomitant diseases per participant: self-reported and employed as a covariate because known to significantly impact mortality risk.
- Number of drugs per participant: self-reported.
- Quality of life: using the SF-36 (21) which was self-administered. The SF-36 is a generic questionnaire assessing the quality of life of the individual in its physical (PCS) and mental (MCS) aspects, generating scores ranging from 0 (worst quality of life) to 100 (better quality of life).

Statistical procedures

All the statistical analyses were performed using SPSS 24 software (IBM Corporation, Armonk; NY, USA) and R version 3.6.2. The distribution of numeric variables was checked using four methods: examining the histogram, examining the quantile-quantile plot, performing the Shapiro-Wilk test and comparing mean and median values. When normally distributed, data is presented as mean ± standard deviation (SD). When skewed, data are presented as median (percentile 25 – percentile 75). Binary variables are expressed in absolute (N) and relative (%) frequencies. Regarding the association between a satisfactory IC domain and mortality risk, we applied the Cox proportional hazards model to examine the effect of a satisfactory IC on time to mortality, yielding a hazard ratio (HR) and its 95% confidence interval. An HR significantly greater than 1 indicates higher risk, and an HR smaller than 1 indicates lower risk. The model was adjusted for age, sex, and number of comorbidities. Survival curves were constructed by the Kaplan-Meier method to visualize the time-to-event relationship. Log-rank tests were performed. All results were considered statistically significant at the 5% critical level.

Results

Description of the studied population

After 5 years of follow-up of the SarcoPhAge cohort, initially constituted of 534 older individuals, only 53 participants were impossible to contact and thus considered lost to follow-up, making a total sample of 481 volunteers.

In our sample of 481 community-dwelling older people, the mean age was 73.4 ± 6.12 years. Most of the participants were female (n=289; 60.1%). The individuals in our cohort had a mean body mass index of 26.6 ± 4.76 kg/m2. Individuals consumed 4 (3-6) drugs and had 5 (3-8) concomitant conditions (i.e., median scores). Quality of life in the sample, measured by the mental and the physical component scores of the SF-36, did not reach higher than 44.9 (35.4 – 53.2) points and 44.8 (37.05 – 51.9) points, respectively. Complete characteristics are described in Table 1.

Table 1. Baseline characteristics of studied 481 older participants

Characteristics	Total population (n = 481)
Age, years	73.4 ± 6.12
Sex	
Women	289 (60.1)
Body mass index, kg/m^2	26.6 ± 4.76
Number of drugs per subject	4 (3-6)
Number of concomitant diseases per subject	5 (3-8)
Quality of life	
SF-36 MCS score (/100)	44.9 (35.4-53.2)
SF-36 PCS score (/100)	44.8 (37.05-51.9)

Intrinsic capacity

The concept of IC encompasses 4 domains. Table 2 provides a detailed overview of the domains, for both participants with satisfactory or without results. The prevalence of satisfactory IC reached 84% for the cognitive domain, 86.3% for the nutritional domain, 72.8% for the mobility domain and 68% for the psychological domain.

After one year of follow-up, data was available for 366 volunteers. The 1-year follow-up showed that fewer participants presented not satisfactory domains of IC than at baseline, with the prevalence of not satisfactory domains varying, depending on the domain, from 5.7% (cognition and nutrition) to 27.2% (psychosocial) (Table 2). The same finding was established at the 2-year follow-up (n=318 individuals), with a prevalence of not satisfactory IC domains ranging from 6.0% (nutrition) to 27.4% (cognition). After 1 year of follow-up, a decrease in the prevalence of limitation was noted, the prevalence ranging from 1.9% of older individuals (cognition) to 6.8% of older individuals (psychosocial). Interestingly, an increase in the prevalence of satisfactory IC domains must also be highlighted, varying from 6.8% of the sample (psychosocial) to 9.0% (mobility). The same pattern between stabilization, deterioration and improvement was found for the evolution of IC domains after two years of follow-up (Table 2).

Association between IC and 5-year mortality risk

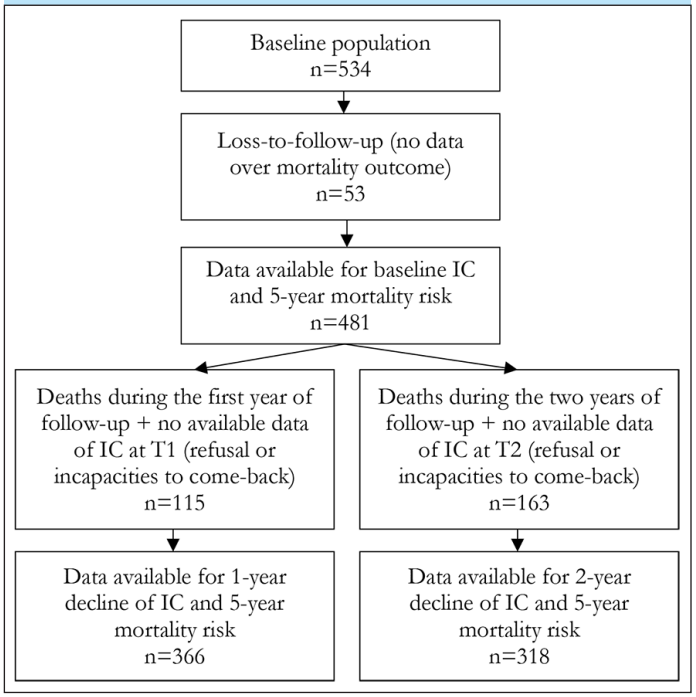
Subsequently, we observed the relationship between having a satisfactory score for each of the 4 domains of IC with mortality risk in our cohort. The first observation to be made is that two IC domains appear to have an outsized impact on mortality. Indeed, presenting with good physical abilities (i.e., satisfactory mobility) entailed a lower risk of death (which was decreased by 55%) (adjusted HR = 0.45 [0.26-0.79]). Likewise, good psychological health (i.e., satisfactory psychosocial domain) engendered a 44% lower risk of death (adjusted HR =0.56 [0.32-0.96]) (Table 3). No statistically significant association between having a satisfactory score for the other two domains

Table 2. Intrinsic capacity of the older participants

Intrinsic capacity	Cognition	Nutrition	Mobility	Psychosocial
Satisfactory IC at baseline (n=481)	404 (84.0)	415 (86.3)	350 (72.8)	323 (68.0)
Limited IC at baseline (n=481)	77 (16.0)	66 (13.7)	131 (27.2)	152 (32.0)
Limited IC at T1 (n=366)	21 (5.7)	21 (5.7)	69 (18.8)	100 (27.2)
Limited IC at T2 (n=318)	22 (6.9)	19 (6.0)	62 (19.5)	87 (27.4)
1-year evolution of IC (n=366)				
Stable	328 (89.4)	329 (89.6)	312 (85.0)	307 (83.7)
Deteriorated	7 (1.9)	10 (2.7)	21 (5.7)	25 (6.8)
Improved	31 (8.4)	27 (7.4)	33 (9.0)	25 (6.8)
2-year evolution of IC (n=318)				
Stable	280 (88.1)	283 (89.0)	271 (85.2)	262 (82.4)
Deteriorated	11 (3.5)	11 (3.5)	19 (6.0)	32 (10.1)
Improved	27 (8.5)	24 (7.5)	28 (8.8)	24 (7.5)

IC: intrinsic capacity

Figure 1. Flow chart of the study population



(cognition and nutrition) and mortality rate in our cohort was established. Figure 1 depicts the time-to-event association between these satisfactory IC domains and mortality occurring during the 5-year period of follow-up.

When looking at the association between the composite Z-score and the occurrence of deaths within the 5-year follow-up period, we observed that when the Z-score was increased (i.e., better IC), the risk of death within 5 years was reduced (-49% risk) as shown in Table 3.

Further analysis demonstrates that the observed changes for the 4 domains of IC were also of determining importance. Indeed, when we looked at the 1-year and 2-year decline of SPPB (decreased mobility), a significant increase in the risk of death was found (respectively, HR = 2.74 [95%CI: 1.09-6.9] and HR = 3.61 [95%CI: 1.23-10.6]). We also made the observation that a psychological decline (via GDS) in the 2-year period of follow-up was highly determinant of the risk of death at 5 years: the risk of death was effectively increased 4.18-fold (Table 4).

Table 3. Intrinsic capacity domains and their association with 5-year mortality risk in a sample of 481 older adults

Intrinsic capacity domains	Five-year risk of deaths HR (95%CI)*
Cognition (satisfactory MMSE at baseline)	0.94 (0.51-1.74)
Nutrition (satisfactory MNA at baseline)	0.75 (0.40-1.42)
Mobility (satisfactory SSPB at baseline)	0.45 (0.26-0.79)
Psychosocial (satisfactory GDS at baseline)	0.56 (0.32-0.96)
Composite IC score (Z-score at baseline)	0.51 (0.36-0.72)

*Age, sex and number of comorbidities as covariates; Deaths over 5 years, n=65; IC: Intrinsic capacity; MMSE: Mini-Mental State Examination; MNA: Mini-Nutritional Assessment; SPPB: Short Physical Performance Battery; GDS: Geriatric Depression Scale

Discussion

Our study sought to assess the predictive power of IC (as a single construct or as its separate domains) on mortality risk. Two main findings emerged. First, three indicators were predictive of a lower risk of death: a satisfactory mobility domain, a satisfactory psychosocial domain and the composite IC Z-score (i.e., IC as a whole construct). Second, considering IC as a dynamic entity is important given the relationship between the short-term (i.e., over 1 year or 2 years) decline in mobility and psychosocial IC domains with higher mortality risk.

Although few other studies have been carried out on this topic, they confirm our overall conclusions: the concept of IC is relevant, and has a degree of predictive power regarding mortality (2, 22, 23). A different study has focused on the topic of the individual IC domains: Charles et al. evaluated

IC domains and risk of adverse outcomes in a population of 604 subjects from nursing homes (9). They highlighted, in this specific population, that nutrition and balance predicted adverse outcomes. Therefore, our results are in accordance on the importance of the mobility domain when considering the IC of older individuals. This component should be regularly assessed during medical consultation. Our results are divergent for the other domain involved in the prediction of mortality risk: the nutrition domain was singled out as significantly associated with adverse outcomes in the population of Charles et al. as well as in other works(24, 25), while we identified the psychosocial domain as highly associated. Such discrepancies can be explained by different characteristics of the study populations (i.e., nursing home versus community-dwelling population).

Table 4. Short-term decline (i.e., over 1 or 2 years) of intrinsic capacity and association with 5-year mortality risk in older adults

Short-term decline of intrinsic capacity	Five-year risk of death HR (95%CI)*
1-year decline of cognition (deteriorated MMSE)	3.72 (0.47-29.2)
2-year decline of cognition (deteriorated MMSE)	1.13 (0.25-5.02)
1-year decline of nutrition (deteriorated MNA)	2.98 (0.38-23.15)
2-year decline of nutrition (deteriorated MNA)	Not applicable**
1-year decline of mobility (deteriorated SPPB)	2.74 (1.09-6.91)
2-year decline of mobility (deteriorated SPPB)	3.61 (1.23-10.6)
1-year decline on psychosocial domain (deteriorated GDS)	1.71 (0.63-4.61)
2-year decline on psychological domain (deteriorated GDS)	4.18 (1.43-12.2)

*Age, sex and number of comorbidities as covariates; ** Comparison of groups impossible because no death occurred in a group; Total included for 1-year decline n=366; Deaths between T1 and T5 =30; Total included for 2-year decline n=318; Deaths between T2 and T5 n=20; MMSE: Mini-Mental State Examination; MNA: Mini-Nutritional Assessment; SPPB: Short Physical Performance Battery; GDS: Geriatric Depression Scale

Another important element in this study was the analysis of IC as a whole, using the composite Z-score. When we applied this method, we noticed that the risk of death decreased by 49% for a 1 SD increase in the z-score (i.e., by improving the IC as a whole).

Considering IC as an indicator in itself seems judicious and clinically relevant. IC can therefore be considered as a whole construct and not a collection of separate entities.

We cannot conclude, on the basis of our results, that a specific determinant of IC (i.e., satisfactory mobility domain, satisfactory psychological domain or composite IC) was better adapted than the others. Indeed, even if the magnitude of the association seemed greater for the mobility domain (i.e., risk reduction of 55% compared to a risk reduced by 44% for the psychosocial domain and 49% for the IC composite score), confidence intervals overlapped. The three elements therefore appear to be of roughly equal importance in our study. Previous studies interested in each domain separately (mobility, psychosocial) have also shown the importance of these domains in predicting the all-cause mortality in older adults (26, 27).

An important aspect that our analysis highlights is the need to take a dynamic view of the notion of IC. Indeed, we have found that a short-term decline (i.e., over 1 or 2 years) in the IC mobility and psychosocial domains was associated with an increased risk of death. The finding is all the more startling when we focus on the magnitude of the association: HR ranging from 2.74 to 4.18, which reinforces the idea of a strong association. Note also that we confirmed our hypothesis that an initial decrease in IC from baseline to the first year of follow up and from baseline to the second year of follow-up was proportionally associated to a higher risk of mortality, when considering the mobility domain (over 1 year, HR = 2.74 and over 2 years, HR = 3.61).

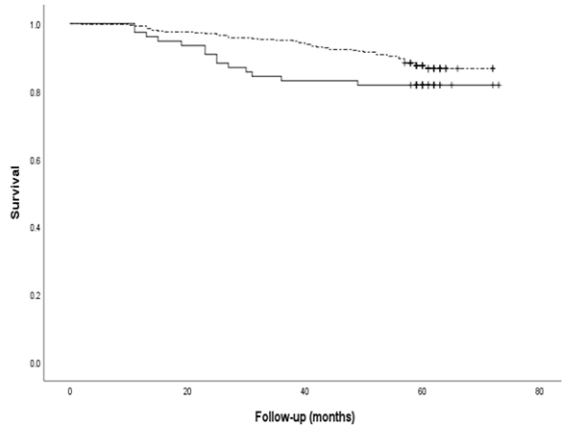
The IC model definitely seems promising, and health actors are called upon to refocus their geriatric practice on function and to move away from a strict disease-oriented approach, which would represent a paradigm-shift in the way older patients are thought of.

Our study is original, in that only one study has previously evaluated the predictive capacity of the recently introduced concept of IC on mortality. It also brings a new vision to bear on the subject, namely that a dynamic approach to the concept of IC is essential, this being key to assessing mortality risk. However, our analysis has some weaknesses. Our population consists mainly of older people who are still in good health, and is thus not representative of older people on the whole. In the same vein, a selection bias and selective survival could potentially be present: participants in better health are the ones who, presumably, come back for the in-person yearly interviews during the five years of follow-up. This is confirmed by the following observation in our results: We have observed, in our population, a higher prevalence of older adults who improved their IC, in any domain, compared to those with declining IC. These findings are probably linked to a potential selection bias. Indeed, those who were not seen again one year after baseline (n=115) were significantly older than those who participated in the follow-up interview (respectively, 72 years old versus 75 years old, p-value = 0.001), presented more often with a limited cognition domain (27% versus 12%, p-value <0.001), a limited nutrition domain (24% versus 11%, p-value <0.001), a limited mobility domain (43% versus 22%) and a limited psychosocial domain (43% versus 28%, p-value = 0.004). Therefore, a limited IC at baseline was more often encountered in individuals who were ultimately lost-to-follow up. Consequently, our analysis was carried out on a greater number of individuals in better health than those less healthy.

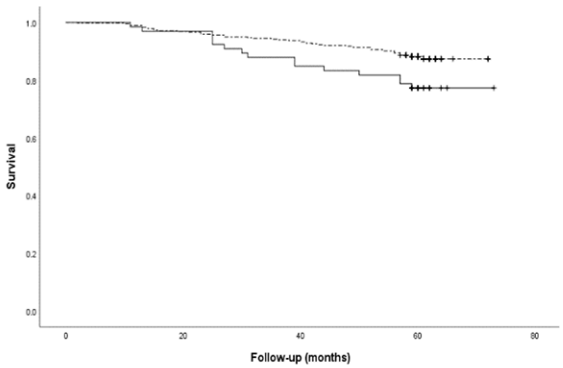
Another potential bias is linked to the choice of measurement instruments: although several are suggested by the WHO, the choice for one or another evaluation method may impact the final results. Finally, we were unfortunately not able to assess the entire concept of IC, an important area that we lack: the sensory area. Evaluating the link between this domain and the risk of death is of great importance and would allow more definitive conclusions to be drawn regarding IC.

Using fixed thresholds to define satisfactory or declining IC has also some limitations. Indeed, we can assume that the transition towards and away from the declining group could have been done even with a small change, potentially non clinically relevant. The inverse is also true.

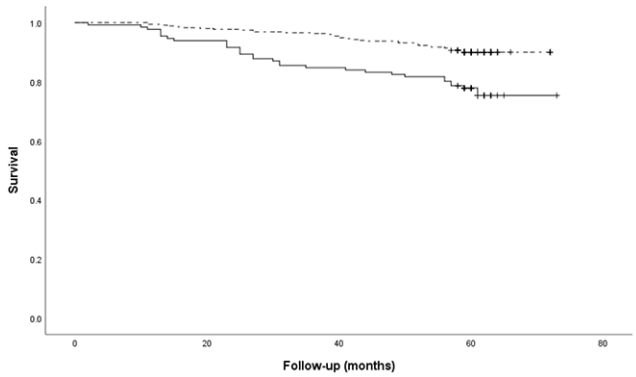
Figure 2. Kaplan-Meier curves for intrinsic capacity domains and their association with 5-year mortality risk



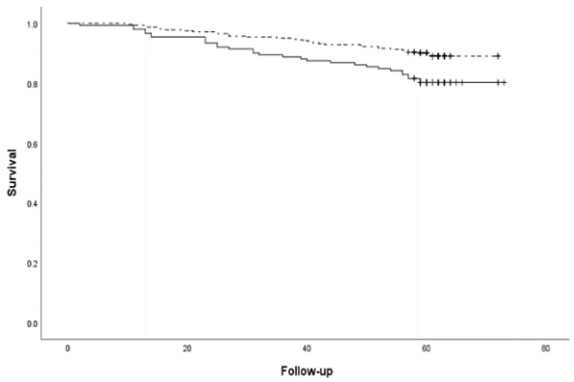
A/ IC Cognitive domain
log p=0.15
Discontinuous lines= satisfactory IC



B/ IC Nutritional domain
log **p<0.02**
Discontinuous lines= satisfactory IC



C/ IC Mobility domain
log **p<0.001**
Discontinuous lines= satisfactory IC



D/ IC Nutritional domain
log **p<0.004**
Discontinuous lines= satisfactory IC

In addition, for resource reasons, some areas of IC were not investigated in their entirety (e.g., psychological based only on depression score only, vitality based only on nutrition…). This represents a weakness in having a global understanding of the whole IC of older persons and in future comparisons of future other works on the topic. However, our results already show the importance of the 4 domains of the IC in predicting mortality, and, the sensory domain, studied separately (28), also predicted deaths. Therefore, by combining them, the predictive power of the whole IC will probably be increased. Future works will have to take this aspect into account and propose a more holistic approach of the concept.

Conclusion

The concept of IC, newly developed by the WHO, could be a valuable tool to integrate into clinical practice, in light of the relationship between limitations in IC and risk of mortality. The mobility and psychosocial domains have been shown to have a major impact on mortality risk in this study.

Conflict of interest: All the authors declare no conflict of interest.

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Ethical Standards: The present study received the approval of the Ethics Committee of the University Hospital of Liège, Belgium upon the reference 2012/277 and further amendments of the research protocol have also been approved by the institution (General Data Protection Regulation established in 2018 was strictly observed).

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