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Impact of comprehensive geriatric assessment on treatment decisions in older prostate cancer patients

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Abstract

Background Prostate cancer is the most common cancer in men aged above 75 years old. Given their heterogeneity, the International Society of Geriatric Oncology recommends using a comprehensive geriatric assessment (CGA) to adapt anticancer treatment management according to their geriatric status. While the theoretical value of this approach is in no doubt, the impact of the CGA on the final therapeutic decision remains elusive. This study therefore investigated the impact of comprehensive geriatric assessment on treatment decisions in older patients diagnosed with prostate cancer and described the factors associated with a change in treatment plan.

Methods This single-centre retrospective study included prostate cancer patients who received a CGA prior to a therapeutic decision from January 2012 to December 2022. The CGA included medical, nutritional, cognitive, social, functional and psychological evaluation.

Results 140 patients were included, of whom 57 (40.7%) benefited from a change in their therapeutic plan after CGA, all in favour of a less aggressive treatment. There was no difference in event-free (EFS) or overall survival (OS) between patients with or without a therapeutic modification (HR for OS = 1.12 [0.68;1.84] $p = 0.048$). Factors associated with a change in treatment plan were a WHO performance status > 1, a high age-adjusted Charlson score, polymedication, an impaired functional independence with the ADL (Activities of Daily Living) scale and a 'frail' or 'vulnerable' geriatric profile according to Balducci's classification.

Conclusion A comprehensive geriatric assessment prior to prostate cancer treatment plan initiation lead to therapeutic de-escalation in 40% of cases of without affecting overall survival or event-free survival. This adaptation offering a more tailored cancer management while preventing functional impact of treatment due to toxicity and improving patient quality of life.

Trial registration The study was registered as (number's register: F20240123102237) and MR004 (CNIL number: 23RDUROL01).

Keywords Prostate cancer, Older patients, Comprehensive geriatric assessment

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Introduction

Prostate cancer is the leading cause of cancer in men with almost 60,000 new cases diagnosed each year, accounting for a quarter of all male cancers [1]. Its incidence increases with age, peaking in the 75–79 age group. Its prognosis for all stages combined is good with an overall survival rate over 90% at 5 years, and even better in patients aged over 80 years, who frequently present a more indolent form [2, 3]. However, patients aged above 75 often suffer from delay of diagnosis, fewer additional investigations, and sub-optimal treatments due to the presence of comorbidities or geriatric syndromes, which can lead to under-treatment and poorer survival [4, 5].

In localised forms of prostate cancer, treatment depends on the risk of distant progression. When the risk is low, active surveillance is recommended and surgery or external radiotherapy is proposed for those at intermediate risk [6]. In metastatic forms, as a hormone-dependent cancer, hormone therapy is the cornerstone of treatment. And finally, in patients with a life expectancy of less than 10 years, a watchful waiting approach is preferred, they are closely monitored and treated if symptoms appear [7].

In older patients, treatment decisions are often complex due to their heterogeneity in terms of comorbidities and/or geriatric syndromes. Indeed, chronological age alone is not sufficient to determine the best therapeutic strategy in this population set. To better understand this heterogeneity, the International Society of Geriatric Oncology (SIOG) recommends using a comprehensive geriatric assessment (CGA) [8]. This assessment evaluates various domains such as cognition, nutrition, autonomy, functional and social status, and has shown to predict treatment toxicity, morbidity, and mortality [9]. Hamaker et al. found that tools assessing frailty, functional status, and nutritional status predict all-cause mortality [10]. Whereas, frailty predicts chemo-induced toxicity, and cognitive impairment and loss of autonomy predict early chemotherapy discontinuation [11, 12]. Thus CGA helps oncologists tailor treatment plans according to the individuals' geriatric profile [13].

As such, older patients cannot follow the same treatments recommended by current guidelines. However, very few studies have defined treatment algorithms in this population set. To our knowledge, Droz and al. have elaborated the only validated algorithm for therapeutic decision making in prostate cancer based on geriatric assessment. They suggest adapting treatment to the patient's health status (prior to an assessment of patients' autonomy, comorbidities and nutritional status) [14]. However, the impact of a comprehensive geriatric assessment on treatment plans and overall survival remains elusive in clinical practice [15, 16].

The main objective of this study is to assess the impact of a comprehensive geriatric assessment on treatment decisions in older patients diagnosed with prostate cancer. The secondary objective is to describe the factors associated with a change in treatment and to assess the prognostic impact in terms of overall survival (OS) and event-free survival (EFS) in case of a change in treatment plan.

Method

Study design

This is a retrospective, single-centre study on older patients diagnosed with prostate cancer and assessed by the oncogeriatric team (EMOG) upon diagnosis or before a treatment change, during their care at Toulouse University Hospital or in the Toulouse University Cancer Institute (IUC-T). Prostate cancer was diagnosed histologically or when the diagnosis was strongly suspected on the basis of clinical, iconographic, and biological data, even in the absence of histological evidence. All stages of prostate cancer were included. All the patients benefitted from the establishment of a treatment plan by an oncologist before their geriatric assessment. Patients assessed by the EMOG solely for geriatric reasons or to decide whether they should undergo further investigations, or who had no established reason for consultation were not included. Patients under conservatorship were included, an informed consent letter was sought priori to data analysis to the patients' legal guardian. All potential participants received a letter of information about the research and an opt-out approach was implemented.

Objectives

The primary endpoint was the concordance between the oncologist's initial choice of treatment before the CGA, and the final treatment received by the patient.

When there was a change in the patients' initial treatment plan after the CGA, the final treatments were classified as follow:

- Final treatment corresponding to the geriatrician's proposal.
- Final treatment corresponding to a compromise between the two choices, e.g. a compromise in the dosage or timing of treatment, a geriatric intervention prior to initiation of treatment, or an alternative treatment considered as 'intermediate'.
- Final treatment corresponding to a different treatment from the initial therapeutic plans and not considered as a compromise between the two.
- The following groups were defined according to the intensity of the treatments:
- For metastatic patients, from most aggressive to least aggressive treatment: chemotherapy + dual

hormone therapy; chemotherapy + hormone therapy +/- radiotherapy; radiotherapy + dual hormone therapy or dual hormone therapy or chemotherapy alone or chemo-radiotherapy; hormone therapy +/- radiotherapy; palliative care.
- For non-metastatic patients, from most aggressive to least aggressive treatment: surgery; radiotherapy + hormone therapy; radiotherapy; hormone therapy; active surveillance; palliative care.

The secondary endpoints were as follows:

- OS, i.e. time between start of treatment and date of death, all causes combined.
- Event-free survival, i.e. time between date of treatment and date of clinical, biochemical or radiologic progression or death. Biochemical recurrence was defined as a PSA level above 0.2 ng/ml after a radical prostatectomy or a rise of PSA level of more than 2 ng/ml from the nadir after prostatic radiotherapy.

Data collection

Data were collected from computerised or archived paper patient records:

- Socio demographic data: marital status, presence of family or professional carers at home.
- Co-morbidities were assessed: presence of hypertension, diabetes, heart failure defined as an alteration of ventricular ejection < 50%, stroke, kidney failure defined as a glomerular filtration rate (GFR) under 60 milliliters per minute, hypoacusis defined as the need of an acoustic device, reduced visual acuity and osteoporosis. The age-adjusted Charlson Comorbidity index (CCI) was assessed as a proxy of comorbidity burden. Patients were considered comorbid if the score was ≥ 1 [17].
- G8 score which is a screening tool assessing frailty. The total G8 score varies from 0 to 17. A higher score indicates a better health status. A G8 score ≤ 14 indicates that the patient is at risk of frailty and a CGA must be performed for a more complete geriatric assessment by a geriatrician [18].
- Patient autonomy was measured with the Activities of Daily Living score (ADL) and Instrumental Activities of Daily Living score IADL (simplified on four items), WHO performance status and walking speed (in m/s) [19, 20].
- Cognition was assessed with the Mini-Mental State Examination (MMSE), a score of 27/30 or more is considered normal; or MiniCOG, a score of 4/5 or more is considered normal [21].
- Presence of depression or anxiety on Geriatric Depression Scale (GDS) was defined as a score of 10 or more [22].
- Number of medications: polymedication was considered as five or more medications [23, 24].
- Nutritional status: weight and height, mini-nutritional assessment (MNA) score, weight loss over 10% over the last six months or more than 5% over the last month, albumin level in g/L at the time of geriatric assessment [25].
- Biological parameters at the time of geriatric assessment: creatinine (in µmol/L) and glomerular filtration rate in ml/min (according to CKD-EPI), haemoglobin (in g/dL).
- Neoplastic characteristics at the time of geriatric assessment: date of diagnosis; metastatic status with number, location and volume of metastases according to CHAARTED for metastatic patients; d'Amico score for non-metastatic patients; cTNM stage; Gleason score and ISUP grade; PSA (in ng/mL); somatic BRCA status [26–29].
- Date of treatment initiation.
- Geriatric profile determined by CGA according to Balducci's classification: (1) Robust patients with no impairment in their autonomy and no significant comorbidity, (2) Frail patients with one or more impairment in the IADL scale and one stabilized comorbidity, and (3) Dependant patients with one or more impairment in the IADL scale and three or more stabilized comorbidity or one uncontrolled comorbidity or a geriatric syndrome [30].
- Initial therapeutic proposal: chemotherapy, radiotherapy, hormone therapy, dual hormone therapy, surgery, active surveillance, palliative care.
- EMOG treatment proposal after CGA: chemotherapy, radiotherapy, hormone therapy, dual hormone therapy, surgery, active surveillance, palliative care.
- Final treatment received by the patient: chemotherapy, radiotherapy, hormone therapy, dual hormone therapy, surgery, active surveillance, palliative care.
- Presence of biological, clinical or radiological progression, and date if available.
- Date and cause of death for deceased patients, and date and status at last news for alive patients.

Statistical analysis

Data were described by median, minimum and maximum for quantitative variables and by numbers and percentages for qualitative variables. Comparisons between groups were made using the Chi-2 test or Fisher's exact test for qualitative variables and the Kruskal Wallis test for quantitative variables.

Survival data were estimated using the Kaplan-Meier method with 95% confidence intervals. Univariate analyses were performed using the Log-rank test for qualitative variables and the Cox proportional hazards model for quantitative variables. All statistical tests were two-tailed and a $p < 0.05$ value was considered statistically significant. Statistical analyses were performed using Stata version 18 software (StataCorp LLC, College Station, TX).

Results

From January 2012 to December 2022, 270 patients with prostate cancer were assessed by the EMOG. A total of 140 patients were included in the analysis. (Fig. 1). Median age at diagnosis was 82 years in non-metastatic patients and 79 years in metastatic patients, ranging from 69 years to 102.

Of the patients included, 40 patients (28.8%) had a localised disease at initial management, 62.2% of whom were at high risk of recurrence according to the d'Amico classification. Ninety nine (71.2%) were metastatic at the start of management, with 80 (80.8%) and 41 (41.4%) having secondary bone metastasis and lymph node disease, respectively.

Patients characteristics

In our study, 77 patients (55%) had a spouse or family or a professional carer at home. One hundred and twenty-one patients (86.4%) had at least one competing comorbidity, and the age-adjusted Charlson score averaged 11. One hundred and one patients (90%) received a G8 frailty assessment, with a mean score of 10.5 and with an indication for geriatric assessment in more than 90% of cases. Seventy seven patients (63.6%) had a WHO performance status > 1, 27 (22.3%) = 1 and 17 (14.0%) < 1. Median ADL was 5.5/6 and IADL was 3/4.

Primary endpoint

After EMOG assessment, 83 patients (59.3%) received the treatment initially proposed by the specialist, and 57 (40.7%) had a therapeutic switch (Table 1). Of the latter, 42 patients (73%) received the treatment proposed by the geriatrician, 14 patients (24%) received a treatment that did not correspond to either of the therapeutic proposals, and 1 (2%) received a compromise between the choice of the geriatrician and the oncologist. All treatment changes were to treatments considered as less aggressive.

Factors associated with a change with treatment plan

For non-metastatic patients, four factors were significantly associated with a change of treatment plan after

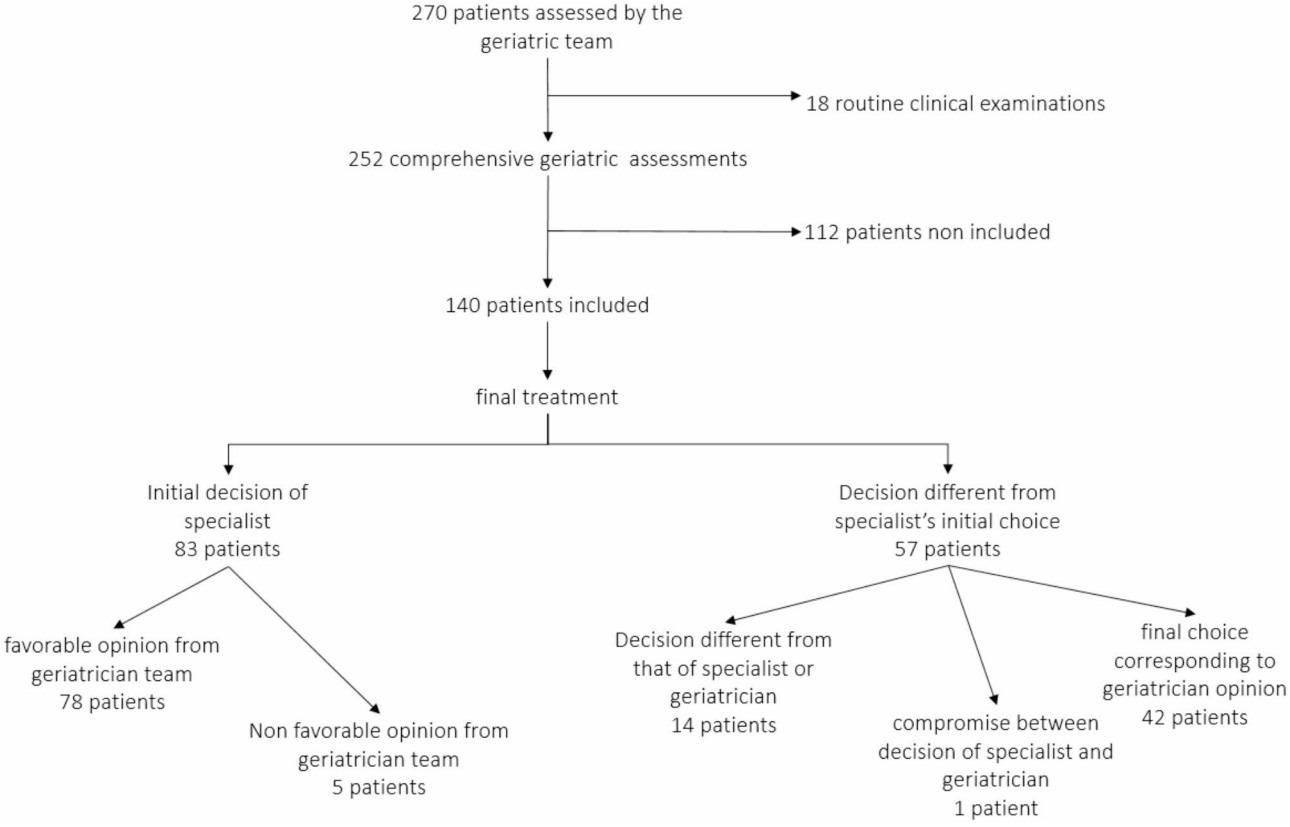

Fig. 1 Flow chart

Table 1 Final management

	Total (n=140)
Final treatment (n=140)	
Initial proposal, despite geriatrician disagreement	5 (3,60%)
Geriatrician proposal, different from initial oncologist proposal	42 (30,00%)
Concordance between initial oncologist proposal and geriatrician proposal	78 (55,70%)
Compromise between initial oncologist proposal and geriatrician proposal	1 (0,70%)
Change of treatment plan after geriatric assessment (n=140)	
No	89 (59,30%)
Yes, in favour of a less aggressive treatment	57 (40,70%)
Yes, in favour of a more aggressive treatment	0 (0%)

Table 2 Factors associated with a change in treatment plan: non- metastatic patients

		Treatment switch after geriatric assessment		
	Total (n=40)	No (n=20)	Yes (n=20)	p-value
WHO PS (n=33)				**0.049***
0-1	22 (66.67%)	14 (82.40%)	8 (50.00%)	
>1	11 (33.33%)	3 (17.60%)	8 (50.00%)	
Diabetes (n=39)				**0.044***
No	32 (82.10%)	19 (95.00%)	13 (68.40%)	
Yes	7 (17.90%)	1 (5.00%)	6 (31.60%)	
CCI score (n=40)				**0.005***
median	7.00	6.00	8.00	
(range)	(5.00;12.00)	(5.00;11.00)	(6.00;12.00)	
Number of medication (n=39)				**0.034***
median	4.00	3.00	5.50	
(range)	(1.00;22.0)	(1.00;8.00)	(1.00;22.00)	

Abbreviations : WHO : World Health Organisation, PS : performance status, CCI : Charlson Comorbidity Index

**P < 0.05*

geriatric assessment: patients with a higher performance status, a higher age-adjusted Charlson score and a higher number of medications. They also had more often diabetes, with 32 (82.1%) patients with diabetes (Table 2).

Among patients in the metastatic group, a change of cancer treatment plan was associated with a higher performance index, and better renal function. Their autonomy was significantly poorer according to ADL score and their weight lower without significant weight loss of more than 10%. They were more often polymedicated, with 66 (72.5%) patients who had polymedication. The geriatric profile according to Balducci's classification was significantly associated with a switch in management, with the majority of patients classified as dependent or frail (Table 3).

The median follow-up of patients was 44.1 months. Overall survival of the study population at one year was 66.50% (CI95% [57.96; 73.94]), 94.57% (CI95% [79.93; 98.62]) in non-metastatic patients and 56.71% (CI95% [46.22; 65.90]) in metastatic patients (Fig. 2).

Event-free survival at one year was estimated at 49.83% ([41.01; 58.03]), with 89.01% (CI95% [73.20; 95.75]) in the

Table 3 Factors associated with a change in treatment plan: metastatic patients. Survival data

	Treatment switch after geriatric assessment			
	Total (n=99)	No (n=63)	Yes (n=36)	p-value
WHO PS (n=33)				**0.036***
0-1	22 (25.30%)	18 (32.70%)	4 (12.50%)	
>1	65 (74.70%)	37 (67.30%)	28 (87.50%)	
ADL (n=98)				**0.029***
median	5.00	5.20	3.5	
(range)	(0.00;6.00)	(0.00;6.00)	(0.00;6.00)	
Number of medication (n=91)				**0.013***
≤ 4	25 (27.50%)	21 (36.20%)	4 (12.10%)	
> 4	66 (72.50%)	37 (63.80%)	29 (87.90%)	
Weight (kg) (n=95)				**0.041***
median	70.00	72.00	68.0	
(range)	(37.00;102.00)	(37.00;96.00)	(49.00;102.00)	
Creatininemia (µmol/L) (n=93)				**0.011***
median	95.00	103.00	78.00	
(range)	(39.00;610.00)	(45.00;610.00)	(39.00;448.00)	
GFR (mL/mn) (n=91)				**0.039***
median	60.00	56.00	68.00	
(range)	(7.00;151.00)	(7.00;100.00)	(10.00;151.00)	
Geriatric profile (n=88)				**0.015***
Robust	11 (12.50%)	9 (16.40%)	2 (6.10%)	
Frail	57 (64.80%)	39 (70.90%)	18 (54.50%)	
Dependant	20 (22.70%)	7 (12.70%)	13 (39.40%)	

Abbreviations : GFR : glomerular filtration rate

**P <0.05*

non-metastatic group and 35.54% (CI95% [26.06; 45.12]) in the metastatic group (Fig. 3).

In multivariate analysis, there was no significant difference in OS or event-free survival between patients who had a change in cancer treatment plan and those who continued with the initial treatment plan. For OS, hazard ratio was 1.12 (CI95% [0.68; 1.84]) with a p-value of 0.664. For EFS, hazard ratio was 1.30 (CI95% [0.80; 2.09] with a p-value of 0.288.

All patients who benefited from a change in treatment were switched to a less aggressive one (Fig. 4).

Discussion

In our study, comprehensive geriatric assessments in older patients with prostate cancer prior to cancer treatment initiation modified the final treatment plan in 40% of cases. For non-metastatic patients, four factors were significantly associated with a change of treatment: high

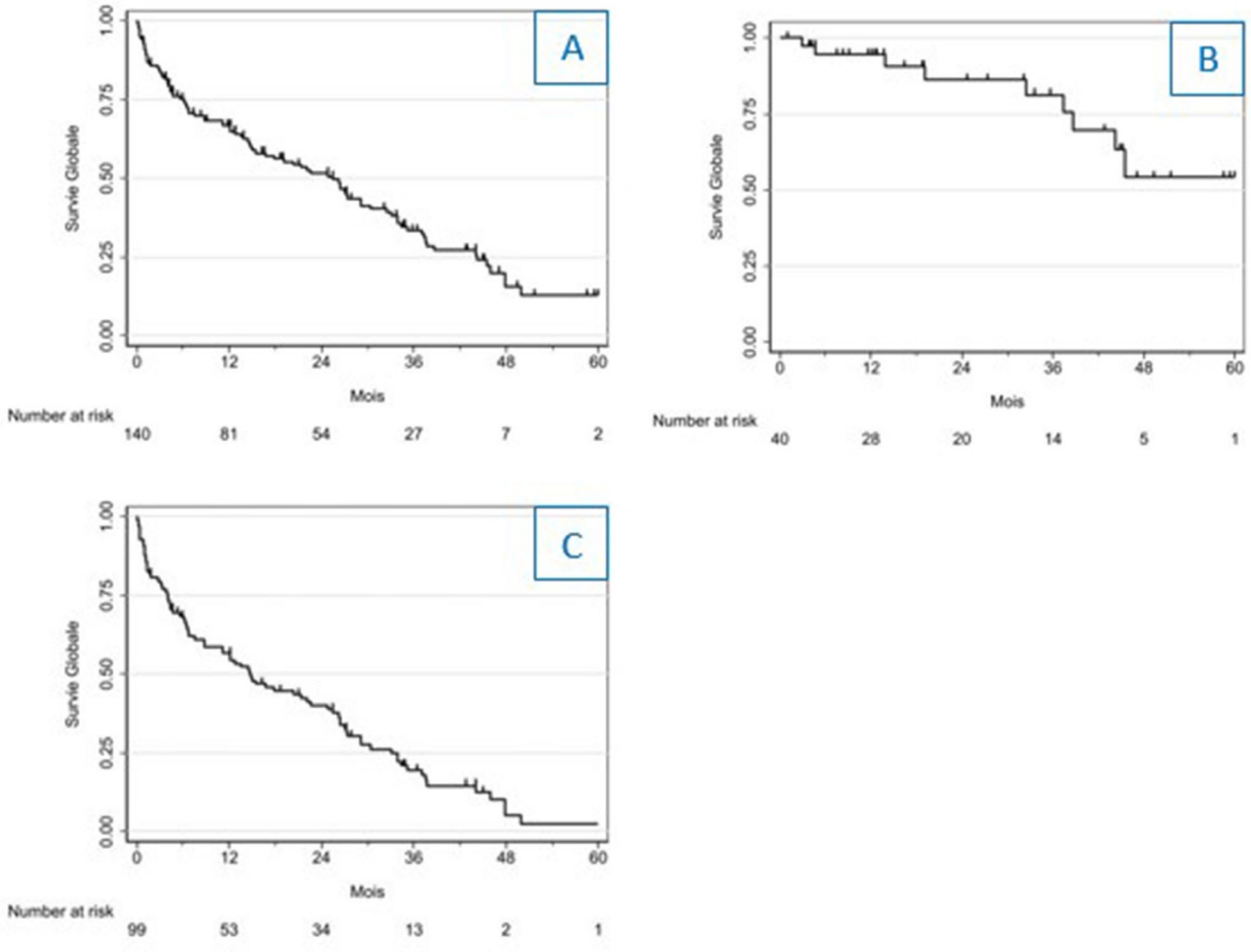

Fig. 2 Overall survival (**A**), survival in non-metastatic (**B**) and metastatic (**C**) subgroups

WHO performance status, the age-adjusted Charlson score and polymedication as well as the presence of diabetes. For metastatic patients, those factors were high PS, number of medications, better renal function, lower autonomy, lower weight and being dependant or frail with the geriatric profile according to Balducci's classification. No difference was found in overall survival nor in event-free survival in patients who underwent a change in their treatment in favour of a less aggressive treatment.

The value of performing CGA to reduce the risk of toxicity from anti-cancer treatments is well known, but to our knowledge, few studies to date have evaluated the real-life impact of CGA on therapeutic management of prostate cancer patients [31–34]. While SIOG recommends performing CGA, it is not clear what impact this has on patients' course of disease or whether the geriatricians' proposals are adopted.

In this systematic review of six studies, Hamaker and al. found that CGA resulted in a change of treatment in approximately 32% of cases [35]. Although the authors investigated different types of cancer with varying treatment modalities, the rates found are similar to ours. Of the treatment changes, approximately two thirds consisted of less intensive treatment. Handforth and al in 2019, in a study including 24 patients with 13 patients with prostate cancer, showed that CGA resulted in 20% of changes in overall management. These changes did not concern change of cancer treatment but suggested geriatric interventions or supportive care to optimize patient care [36].

In our study, when the treatment was changed, the one proposed by the geriatricians was opted in 73% of cases. These findings show that the geriatrician's assessment influences the choice of treatment for patients. Indeed, several randomized trials have demonstrated the contribution of geriatric expertise through the performance of a CGA, which reduces the toxicity of systemic treatments without altering overall survival [37–39].

That's where geriatricians have a crucial role to play within a multidisciplinary oncology team, helping to decide the most appropriate treatment. Beyond guiding therapeutic decisions, oncogeriatric assessment is key

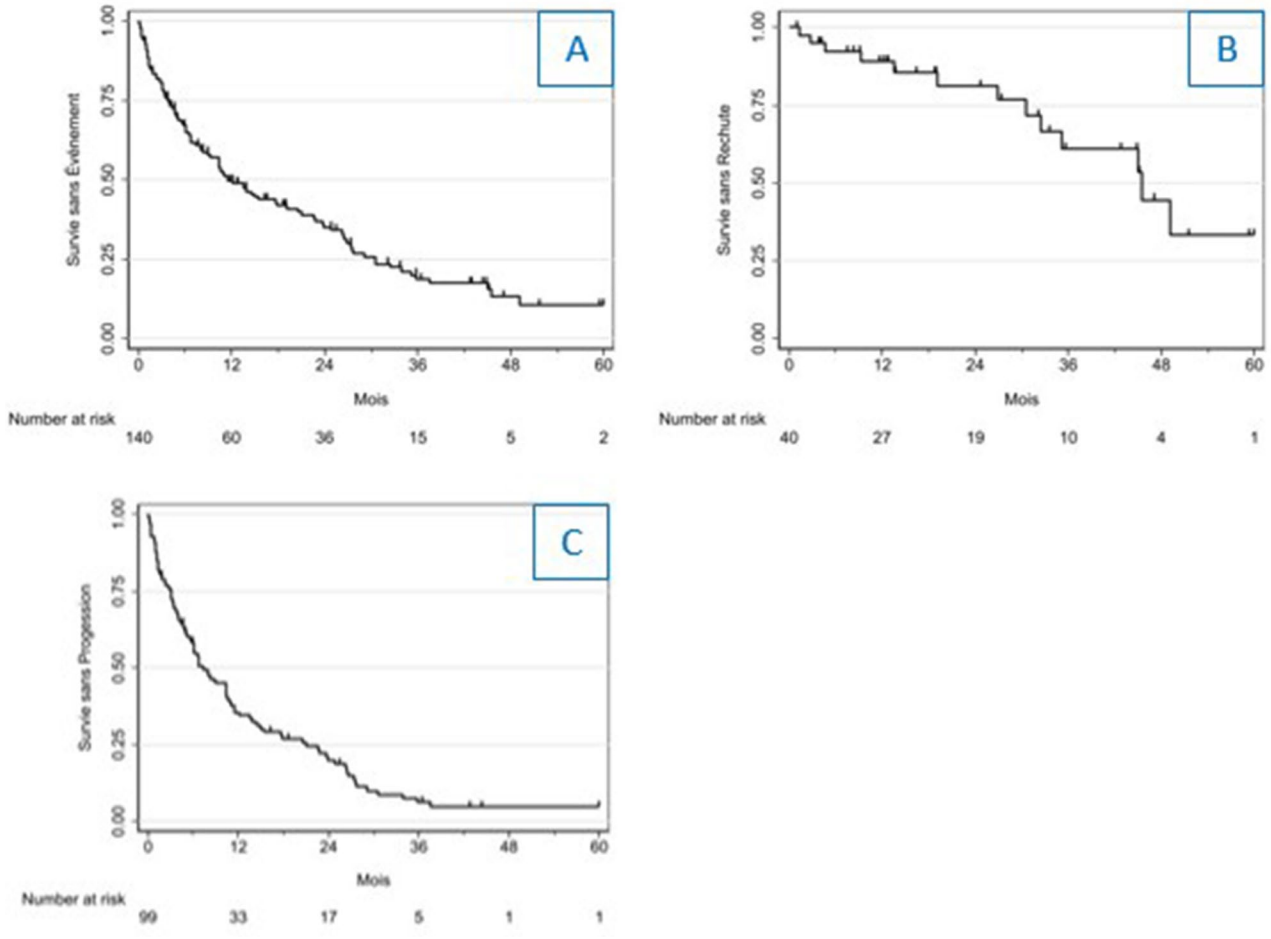

Fig. 3 Event-free survival in overall population (**A**), and in non-metastatic (**B**) and metastatic (**C**) subgroups

to identify patients' physical and mental vulnerabilities, ensuring they receive appropriate care throughout their treatment journey [40].

Our study shows a correlation between WHO performance status and a treatment switch, with more patients switching therapy as the WHO performance status increases. These results are similar to those of Italiano and al. where patients with a performance status ≥ 2 were more likely to benefit from a chemotherapy dose reduction in prostate cancer patients [41].

Our study showed that a "frail" or "dependent" geriatric profile according to Balducci's classification was associated with therapeutic de-escalation, probably because these patients have poorer tolerance of anti-cancer treatments, with more frequent grade III side effects [42]. This can lead to premature discontinuation of treatment, which is associated with a poorer prognosis. It is therefore expected that patients identified as "frail" will benefit from a modification of their cancer treatment plan, and confirmed by Aliamus and al who found up to 60% of patients identified as « dependant » who benefited from a change in their treatment plan [43, 44].

For patients with metastatic or non-metastatic prostate cancer, polymedication was associated in our study with a change in the therapeutic care plan. This is a crucial parameter to take into account when deciding on a therapeutic plan, as polymedication can lead to potential drug interactions, especially with chemotherapies or hormonal therapies, and increases the risk of severe non-hematological toxicity up to threefold [45].

All patients whose management was changed were switched to a less aggressive treatment. In our study, these patients did not present any increased risk of mortality. This result is crucial, because it demonstrates that personalised treatment plans after CGA affects overall patient survival by proposing less aggressive treatments. Decrease of treatment regimen will decrease potential side effects and improve one's quality of life [46]. If the prognostic factors of older patients undergoing anticancer treatments are well known, data of the impact of a de-escalation of treatment on overall survival is an unmet need [47, 48]. Our study is the first to our knowledge to provide data on the subject.

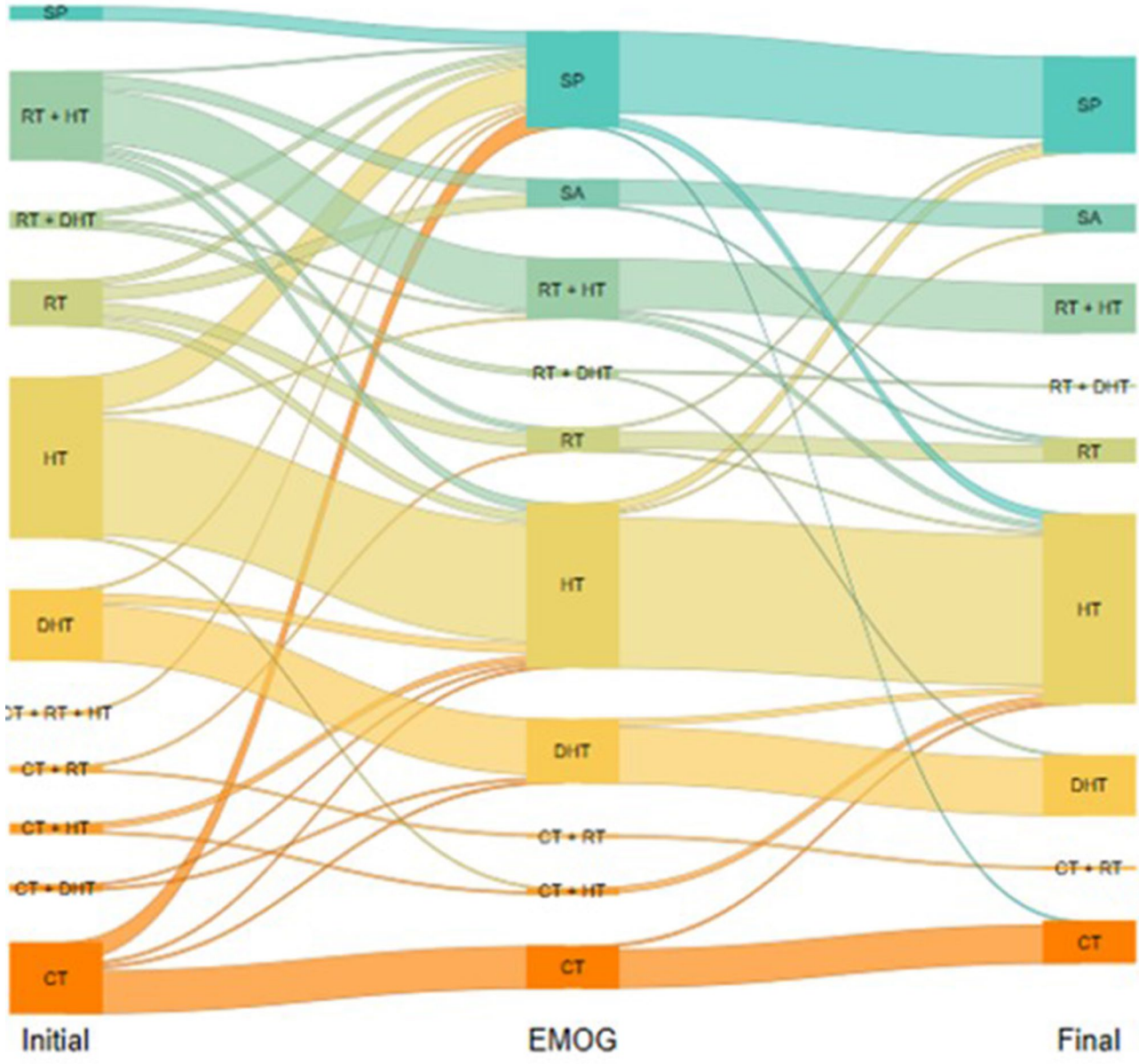

Fig. 4 Sankey plot of treatments in overall population, presented in order of increasing aggressiveness from top to bottom. Abbreviation: SP = palliative care, RT = radiotherapy, HT = hormone therapy, DHT = dual hormone therapy, CT = chemotherapy

These findings are consistent with the results of the randomised phase III ESOGIA trial, which found no difference in survival for patients whose lung cancer management included CGA versus those with standard management [49].

This study has some limitations linked to its retrospective nature and small sample size. Some data was also missing, particularly for cognitive tests such as the GDS, mini-COG, and MMSE as well as sensory function assessments, where data was collected subjectively. Another limitation of our study, was the method chosen to classifying the aggressiveness of the treatments.

Conclusion

Comprehensive geriatric assessment (CGA) prior to treatment plan initiation lead to therapeutic de-escalation in 40% of cases of without affecting overall survival or event-free survival. These findings highlight that CGA helps adapt intensity of cancer treatments and decreases patient exposure to overtreatment while ensuring their survival and maintaining their quality of life.

Abbreviations

ADL	Activities of Daily Living
CCI	Charlson Comorbidity index
CGA	Comprehensive Geriatric Assessment
CNIL	Commission Nationale de l'Informatique et des Libertés

ECOG	Eastern Cooperative Oncology Group
EFS	Event-free survival
EMOG	Equipe mobile d'oncogériatrie
GDS	Geriatric Depression Scale
GFR	Glomerular filtration rate
IADL	Instrumental Activities of Daily Living
ISUP	International Society of Urological Pathology
IUCT	Institut Universitaire du Cancer de Toulouse
MMSE	Mini-Mental State Examination
MNA	Mini-nutritional assessment
OS	Overall survival
PFS	progression free survival
PSA	Prostate specific antigen
PS	Performance status
SIOG	International Society of Geriatric Oncology
WHO	World health Organisation

Author contributions
Designed research: MB, LM, LB; Performed research: MB, LM, LB; Contributed analytical tools: MB, LM, LB, MM; Collected data: MB, PB, CC, SL, DB; analyzed and interpreted data: MB, MM, LB; Performed statistical analysis: MB, MM; Writing - review & editing: MB, ZS, LM, LB.

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Data availability
Data sharing upon request to corresponding author by email.

Declarations

Ethics approval and consent to participate
The database containing health data was approved by the French National Commission for Computing and Liberties in 2024. This study was approved by the Toulouse University Hospital, in compliance with the declaration of Helsinki declaration. It was registered as (F20240123102237) in the HealthDataHub and approved by the French national commission for computing and liberties methodology MR_004 (registration number: 23RDUROL01). All potential participants received a letter of information about the research and an opt-out approach was implemented.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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